STATE REPRESENTATIVE
JON RICHARDS
REPRESENTING MILWAUKEE'S
EAST SIDE, DOWNTOWN AND
BAY VIEW NEIGHBORHOODS

TESTIMONY OF REP. JON RICHARDS IN SUPPORT OF SB 182

Before the Senate Committee on Human Services and Aging
October 7, 1999

In doing my research in support of this bill, I have learned some surprising and disturbing things about the cost of women's health care. I have learned that although birth control pills are one of the most commonly used drugs on the market, they are often not covered by insurance. They are one of the few FDA-approved drugs that aren't routinely covered even though they are routinely used. Contraceptives are basic health care. When you consider that a one year prescription of oral contraceptives, the most commonly used contraceptive, costs about $422 it is clear that Wisconsin women are paying a large out of pocket cost each year for a basic health care need. That is unfair. When you consider that most insurance companies rushed to cover Viagra but few routinely cover the pill, this situation looks grossly unfair.

Wisconsin has a long and proud tradition of providing equality for women. In line with that tradition, we need justice and fairness in health care insurance coverage in Wisconsin.

I urge you to vote in favor of SB 182.

CAPITOL
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AWHONN
Association of Women's Health, Obstetric and Neonatal Nurses

Promoting the health of women and newborns.

POLICY POSITION STATEMENT

Insurance Coverage for Contraceptives

AWHONN supports legislation and policies that mandate insurance coverage of contraceptives.

A woman should have the right to choose a particular contraceptive based on whether it is the most appropriate one for her – not whether the method happens to be covered by her plan. AWHONN supports legislation that includes contraceptive services as part of the basic health care plan in order to allow women and families the option to space pregnancies.

- One common inequity in many health plans is the coverage of continuation of pregnancy (prenatal care and delivery and termination of pregnancy) but no coverage of an untimely pregnancy.

- Mandated coverage for contraceptives will inevitably result in cost savings to the health care system by decreasing unwanted pregnancies and providing women the health benefit from oral contraceptives e.g. protection from benign breast changes, cancer of the uterus, cancer of the ovary, pelvic infection and anemia.

Background
Most employment related insurance policies in the United States provide some level of prescription drug coverage. The vast majority of these plans while covering other prescription drugs do not include coverage for prescription contraceptive drugs and devices.

Coverage of contraceptive drugs and devices by health insurance plans varies greatly, depending on the type of plan. Coverage is best (though not comprehensive) in health maintenance organizations (HMOs) and worse in traditional indemnity plans. Coverage by other types of managed care plans like point-of-service plans (POS) and preferred provider organizations (PPOs) falls somewhere between.

Approved by the AWHONN Board, June 1999

2000 L Street, NW ■ Suite 740 ■ Washington, DC 20036 ■ 202/261-2400 ■ Fax 202/728-0575 ■ www.awhonn.org

TESTIMONY OF JEANNE M. WILTON, RN, MS, IBCLC
FOR
SENATE BILL 182
OCTOBER 7, 1999

My name is Jeanne M. Wilton, RN, MS, IBCLC and I am a Women's Health Nurse Practitioner at All Saints OB/GYN in Racine, Wisconsin. I am also Chair of the Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN) for the State of Wisconsin.

Thank you for the opportunity to submit my position on Senate Bill 182, the Contraceptive Coverage Equity Act. This bill would require insurance companies to cover contraception if they provide coverage for other prescriptions. As a working nurse practitioner and consumer I support this legislation.

I have been working as a nurse practitioner since 1981 in a number of states and have seen women struggle to pay out of pocket for contraception. Even more recently, in my practice in Racine, I have seen women become pregnant because they could not afford to buy their next packet of birth control pills: Over 50% of pregnancies in the United States are unplanned when we have so many options for women to prevent pregnancy. Cost is an issue for many women, including those on Medicaid who may have an HMO that does not cover contraception. Twenty-five dollars a month for a packet of birth control pills is certainly cheaper for that company to cover than a nine month pregnancy that has the risk of complications such as preterm birth, diabetes, or pregnancy-induced hypertension. If an insurance company covers all other medications fully or with a co-pay it is only equitable for them to cover contraception as well.

AWHONN is the premier nursing organization in the United States representing women's health, obstetric and neonatal nurses. We have over 350 members in Wisconsin and over 17,000 in North America. I have included a copy of AWHONN's position statement on this issue for your reference.

I encourage the committee to pass this bill to help prevent more unintended pregnancies. Thank you for the opportunity to submit my testimony to you.

Milwaukee National Organization for Women
611 North Broadway, Suite 505 • Milwaukee, WI 53202 • 414/276-3112 (phone and fax) • now@milwaukeenow.org • http://www.milwaukeenow.org

Statement of Milwaukee NOW in support of the Contraceptive Coverage Equity Act AB362/SB182

October 7, 1999

Contraceptive services are part of women's basic health care and allow families to both adequately space desired pregnancies and avoid unintended pregnancies. Women spend 68% more for basic health care than men because they disproportionately bear the brunt of the cost of contraceptives.

Women do not have real choices over their reproductive lives unless they have access to affordable, reliable birth control. A primary barrier to that access is the lack of insurance coverage for prescription contraceptives. Although most health insurers cover prescription drugs, many routinely exclude contraceptives. For instance, while 97% of large group health insurance plans cover prescriptions, half of those plans do not cover **any** contraceptive method and only 33% cover birth control pills.

Three in four women say cost is an important factor when choosing between a contraceptive method that is covered by their insurance and one that is not. Without coverage, women choose the method they can afford, which is not always the method that is best for them. SB 182 would help eliminate this grave inequality in women's health care by requiring private insurers to cover contraceptive drugs and services to the same extent that other prescriptions are covered.

The lack of contraceptive coverage in health insurance places the most effective forms of contraception beyond the financial reach of many women, leading to unintended pregnancies. Over three million unintended pregnancies occur each year, half of which end in abortion. It is vital that women and their families have the means to responsibly manage their reproductive lives. Women and their families must have access to affordable contraception in order to prevent unintended pregnancies and thus reduce the need for abortion.

Ninety percent of Americans support access to family planning because they know it is essential to maintaining the health of women and families, and nearly two-thirds support requiring insurance policies to cover the most effective methods of contraception. Women on Medicaid have contraceptive coverage--it is time that private insurance measured up to the public insurance program.

Birth control is basic health care and is a medically necessary immunization for unwanted pregnancies. Most sexually active women spend four-fifths of their reproductive years trying to avoid pregnancy. There is a tremendous need for this bill and for contraceptive services. If women desire small families, which is the universal

preference in industrialized societies, then the need to practice contraception is great. For example, a woman who is sexually active throughout her reproductive years and wants only two children will need contraceptive protection for more than **20 years** of her life.

Because birth control is classified as "optional" health care, insurers are allowed to skimp on equitable coverage. And because contraception is so essential, women will pay out-of-pocket to have it. Women need and deserve the best available contraceptive method for them to be covered by insurance so it is accessible and affordable. It is time to close the gender gap in health care by passing the Contraceptive Coverage Equity Act.

Statement on Contraceptive Methods

Debate on several pieces of legislation has recently raised questions regarding how different methods of contraceptives work. This document summarizes what is known about each method.

Essential steps necessary for pregnancy include:

1. normal maturation of sperm and egg,
2. release of sperm,
3. release of egg (ovulation),
4. transport of sperm through the woman's vagina, cervix, uterus and Fallopian tube,
5. final maturation of sperm in preparation for fusion and fertilization
6. transport of egg from the ovary into the Fallopian tube,
7. fusion of sperm and egg and normal steps in fertilization
8. transport of the fertilized egg from the Fallopian tube to the uterus
9. maturation and cell division leading to the blastocyst stage,
10. readiness of the uterine lining for implantation, and
11. implantation of the blastocyst into the lining of the uterus at the conclusion of which pregnancy is established.

Barrier methods such as the male and female condoms and the diaphragm and cervical cap, along with female and male sterilization, impose a physical barrier between sperm and egg and thereby prevent fertilization. The contraceptive effectiveness of abstinence, periodic abstinence, and withdrawal also depends on their role in preventing contract between sperm and egg.

The mechanism of action of hormonal contraceptives such as oral contraceptive pills, emergency contraceptive pills, injectable and implant hormone products, and of IUDs (intrauterine devices), cannot be described quite so simply. Each of these methods involves multiple biologic effects that potentially could alter several of the steps involved in becoming pregnant. Oral contraceptives (the "Pill") containing estrogen and progestin are highly effective in preventing ovulation, which is considered their primary mechanism of action. In addition, Pill hormones also result in thick cervical mucus that interferes with sperm transport and may have an effect on fluids in the uterus and Fallopian tubes and on transport for sperm and egg in the Fallopian tube. These hormones may also affect sperm final maturation and

readiness of the uterine lining for implantation.

Hormonal contraceptives that contain only progestin, such as mini-pills, implants, and injectables, as well as emergency contraceptive treatment using hormone pills, also act by blocking ovulation. For these methods, however, the other mechanisms described for Pills also pertain and are believed to play a more important role than is the case for Pills. Women using mini-pills and implants, especially, are somewhat more likely to ovulate than are Pill users or injectable users, and emergency contraceptive hormone treatment is in some cases provided after ovulation has already occurred. Thus, the contraceptive efficacy of these methods may involve inhibition of fertilization or steps subsequent to fertilization. Once implantation has occurred and pregnancy is established, none of these methods is effective in interrupting pregnancy or causing abortion.

Two IUDs are currently available in the United States; one releases the hormone progesterone and the other releases copper. Progesterone release causes thickened cervical mucus that blocks sperm transport; the release of copper alters fluids in the Fallopian tubes and uterus in a way that interferes with sperm and egg transport and function. Both can act by inhibiting fertilization, which is considered their primary mechanism of action. In addition, both also alter the lining of the uterus in a way that may be unfavorable for implantation; this effect is probably responsible for the high level of efficacy when copper IUD insertion is used for emergency contraception. Insertion of an IUD in early pregnancy is contraindicated because it may lead to spontaneous abortion and may also result in uterine infection associated with incomplete spontaneous abortion.

In summary, the primary contraceptive effect of all the non-barrier methods, including emergency use of contraceptive pills, is to prevent ovulation and/or fertilization. Additional contraceptive actions for all of these also may affect the process beyond fertilization but prior to pregnancy. For some methods these actions may be significant in contributing to their overall contraceptive efficacy.

breathed into Adam the breath of "lives," not "life," before the first conception. Eph 1:4 says people were chosen before the creation of the world -- they existed in the mind of God before conception. Heb 7:9 says that Levi paid tithes through Abraham and was in the body of Abraham -- two generations before conception. In fact, I have yet to find any Scripture stating that life begins at conception. The Bible teaches that life begins before that point.

13. Eph 5:22-25, 5:32 tell us of the symbolism of marriage. The relationship between husband and wife is a picture of the relationship between Christ and His Church. Although sin often separates us from full, close communion with Christ, can you imagine a congregation purposely coming before the Lord in a service and telling Him that they want to feel good, but don't want any fruit of the Spirit (love, joy, peace, patience...), and they certainly don't want any new converts because the new converts are a nuisance to care for and train? If the original example of marital relations (Christ and the Church) is to be open and eager for fruitfulness, are we Christian couples not "profaning His name among the Gentiles" when we project a different picture of that relationship to society? We were given a holy trust when Christ conferred marriage on us. If we want to be consistent in our Christian witness, we need our marital relations submitted to His eternal example.

From the various passages in Scripture relating to the Lord seeking children, forming children, having plans for children, and granting or withholding children and from our knowledge of the Lordship of Christ over all creation, it should be obvious that children are not caused by chance or probability. If couples decide to let the Lord, rather than birth control measures, control their marital relations, they can be assured that any additional children they may have are not merely the "natural" products of probability.

Since I surrendered to the Potter, I have experienced deep contentment, fulfillment, and joy and an eagerness for the future unlike anything I had before. Before I thought I had a close relationship with the Lord; now He not only possesses my heart, but my body and thus my whole life. Before I had three children; now I have five and am jubilant and content that the Lord is in control of the granting or withholding of any more according to His schedule. His Lordship is freeing and invigorating.

Our society has been so permeated by the Planned Parenthood mentality that we Christians live by it as a matter of course. The Word of our God, however, stands diametrically opposed to that mentality and so should we.

Sometimes I still think of colleagues and friends who are active in their careers, oblivious to family life, and my mind wanders off. Each time the Holy Spirit gently pulls in the reins and I review these Scriptures again. The Lord renews my mind in His Word that I might not conform to the world around me, but instead worship Him with my body and life (Rom 12:1-2), letting Him be Lord of it all.

-- Cynthia Raatz

What the Bible Says about Birth Control

During 1991, I was earnestly seeking the Lord's will for my life regarding birth control. I found quite a few Scriptures concerning birth control, none of them in support. I got advice from many people and was appalled to learn that most Christians prevent children for the same selfish reasons pro-death people kill them -- the sin is merely a matter of degree. We all have wicked hearts. These are some of the Scriptures I found:

1. Surgical or chemical means of birth control are disallowed in I Cor 6:19-20, I Cor 3:16-17. Sterilization is a means of destroying part of God's temple. The pill and spermicides are known to cause an increased incidence of infections and irritations. All three are means of tampering with the function of and access to the Temple of the Holy Spirit. What right do we have to permanently (or temporarily) forbid Him to use a room of His Temple?

2. Barrier means of birth control are disallowed in Gen 2:24, Mal 2:14, Matt 19:5-6, Mk 10:7-9. Barrier means of birth control are the erection of man-made walls, however thin, of separation between husband and wife.

3. Interruption of relations is disallowed in Gen 38:8-10, in which Onan avoided having a child for financial reasons and was killed by God for it.

4. Natural family planning is disallowed in I Cor 7:5. The current Evangelical/Catholic paraphrase of this seems to be "Do not refuse each other except by mutual consent, and for a time, so that you may devote yourselves to natural family planning." God does not give us license for any time of contrived separation except for prayer and fasting. Ex 19:15-19 is similar to this but was not done on a regular basis.

5. Psalm 127:5 says "Blessed is the man whose quiver is full of arrows." Deut. 28, I Chron 25:5, and I Chron 26:5 support this. In every other area of our lives, we Christians pray for the blessing of God. Why do we insist on hoping for His curse (limited physical fruitfulness) regarding children?

6. Psalm 127:5 also talks about a man's full quiver contending victoriously with enemies in the gate. The gate throughout scripture is known as the seat of civil government. Do we believers want to have civil victories God's way, or will we insist on beating our heads against the wall and grumbling when we can't have substantial or lasting victory our way? Two ways we can have victory God's way are to outnumber the opposition in the polls, because they have limited or killed their children, and by the favor of God resting on our side because we have been obedient and let Him be Lord.

7. Mal 2:15 tells us that the reason the Lord God Almighty made husband and wife to be one flesh is that He was seeking godly offspring.

8. Job 31:14, Ps 139:13-16, Is 44:2, Is 44:24 tell us that the Lord forms babies in the womb. Rom 9:20-21, Is 64:8 tell us Who the Potter is. Think for a minute what His pottery shop is. Feminists keep screaming, "I'm not a baby factory." However, by a simple look at creation, we see the Potter has obviously made women to be His shop. According to Rom 9:20, we women have no right to talk back to God and wonder why we were made this way. Have you ever heard of a pot closing a pottery shop, or the shop opening and closing itself? Who do we think we are? Our rightful (and truly blessed) position is to allow our Lord continual welcomed access to His shop so that He can freely fashion vessels for His service according to His timing.

9. Some women shy away from childbearing due to histories of miscarriages or birth defects. Ex 4:11-12, Jn 9:3 tell Who creates children in differing ways and one reason He may do so. Jer 18:1-6 tells us that He has the right to do with His pots what He will. Perhaps an encouragement is the example of Susanna Wesley. Susanna (herself the last of 25 children and educated in Greek, Latin, French, and theology) had 19 children in 21 years. Eight (or ten) of them died in birth, infancy, or childhood. But, numbers 15 and 18 were John and Charles -- mightily anointed revivalists and hymn writers. What are we willing to sacrifice to give birth to a revival? By the way, the Wesleys lived in abject poverty.

10. Even in the case of a woman's life being in jeopardy should she conceive again, that does not mean she should necessarily contracept. I Cor 6:19-20 and I Cor 3:16-17 say her body is the temple of the Holy Spirit and not her own. The couple should ask the Holy Spirit what He wants done with His temple. He may answer "I want you to protect My temple," or "I will protect you through a pregnancy," or even possibly "I want to use this next child and you are to offer yourself as a martyr for the cause of Christ." In any event, this issue is not up to the discretion of the couple. They are not their own.

11. To some people, God will give only 1 or 2 children. Examples of this are Abraham, Isaac, Ruth, and Elizabeth. There are people whom God will call to other service -- perhaps by directing them toward a single lifestyle (Paul); perhaps by Himself limiting family size; perhaps by giving an extra measure of energy and organizational skills to carry on other service in the midst of children. It is, however, an act of presumption for us to arrange our lives as though we are "called" to another service merely because we enjoy it or it pays. Who are we, Christian parents, to assume we are all exceptions to God's command to be fruitful and multiply? If God doesn't want someone to have children, we have assurance in Scripture that they won't have them (e.g. II Sam 6:23, Gen 20:18). We don't need to orchestrate His will!

12. Gen 2:7 says in the Hebrew that God

...be important in minimizing ...this drug for you and you alone. ...supplements as part of the ...osteoporosis, check with your ...of the reach of children. In case of ...hospital or poison control center ...of the most important infor- ...you want more information, ask ...you the professional label- ...is also published in a book ...reference," which is available ...Generic drugs carry virtu- ...as their brand name

...Cream, USP, 0.01%). ...containing 42.5 g with a cali- ...for delivery of 1, 2, 3, or 4 g. ...Protect from temperatures in

J4-503

...Section, page 318

OTC

...supplement with

	4,000
	400
	15
	70
	0.5
	1.5
	1.6
	17
	2.6
	2.5
	200
	30
	100
	1.5
	15

...hydroxide, ferrous fuma- ...microcrystalline cellulose, ...acacia, zinc oxide, polacrilin ...beta-carotene, hydroxypropyl ...cellulose, polyethylene glycol, ...pyridoxine hydrochloride, ...oxide, riboflavin (color), thia- ...hloride, folic acid, vitamin B_{12}.

...RATION

...of counsel and guidance in

P2834-01

...fication Section, page 318

℞

...supplement with ...acid and 60 mg Iron ...or flower from

...ble vitamins and five miner- ...during pregnancy or lactation.

	4,000
	400
	15
	80
Folic acid (Folacin), mg	1
Thiamin (Vitamin B_1), mg	1.5
Riboflavin (Vitamin B_2), mg	1.6
Niacin, mg	17
Vitamin B_6, mg	4
Vitamin B_{12}, μg	2.5
Biotin, mg	0.03
Pantothenic acid, mg	7
Minerals	
Calcium, mg	200
Iron, mg	60
Magnesium, mg	100
Copper, mg	3
Zinc, mg	25

Active Ingredient

Each tablet contains 1 mg folic acid.

Other Ingredients

Acacia, biotin, calcium carbonate, calcium pantothenate, beta-carotene, cholecalciferol, colloidal silicon dioxide, cupric oxide, cyanocobalamin, ferrous fumarate, hydroxypropyl cellulose, hydroxypropyl methylcellulose, magnesium hydroxide, magnesium stearate, niacinamide, polacrilin potassium, polyethylene glycol, povidone, pyridoxine hydrochloride, riboflavin, sodium ascorbate, thiamine mononitrate, titanium dioxide, dl-alpha-tocopheryl acetate, vitamin A acetate, zinc oxide.

INDICATIONS AND USAGE

Natalins Rx tablets help assure an adequate intake of the vitamins and minerals listed above. Folic acid helps prevent the development of megaloblastic anemia during pregnancy.

CONTRAINDICATIONS

Supplemental vitamins and minerals should not be prescribed for patients with hemochromatosis or Wilson's disease.

WARNING

Keep Natalins Rx tablets out of the reach of children.

PRECAUTIONS

General

Pernicious anemia should be excluded before using this product since folic acid may mask the symptoms of pernicious anemia. The calcium content should be considered before prescribing for patients with kidney stones. Do not exceed the recommended dose.

ADVERSE REACTIONS

No adverse reactions or undesirable side effects have been attributed to the use of Natalins Rx tablets.

DOSAGE AND ADMINISTRATION

One tablet daily, or as prescribed.

HOW SUPPLIED

NDC 0087-0702-01 Bottles of 100
NDC 0087-0702-02 Bottles of 1000

P4757-05/P9735-00

Shown in Product Identification Section, page 318

OVCON® 35 ℞
OVCON® 50

[ŏv'kŏn]

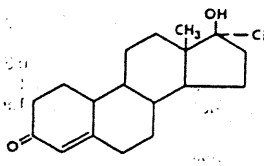
(Norethindrone and Ethinyl Estradiol Tablets, USP)

Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

DESCRIPTION

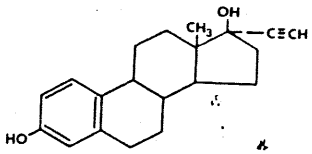
21-Day OVCON 35 and OVCON 50 tablets (norethindrone and ethinyl estradiol tablets, USP) provide a regimen for oral contraception derived from 21 tablets composed of norethindrone and ethinyl estradiol. The chemical name for norethindrone is 17-hydroxy-19-nor-17α-pregn-4-en-20-yn-3-one and for ethinyl estradiol the chemical name is 19-nor-17α-pregna-1,3,5 (10)-trien-20-yne-3,17-diol.

28-Day OVCON® 35 and OVCON® 50 tablets provide a continuous regimen for oral contraception derived from 21 tablets composed of norethindrone and ethinyl estradiol to be followed by 7 green tablets of inert ingredients. The structural formulas are:



NORETHINDRONE

[See chemical structure at top of next column.]



ETHINYL ESTRADIOL

The active OVCON 35 tablets contain 0.4 mg norethindrone and 0.035 mg ethinyl estradiol. The active OVCON 50 tablets contain 1 mg norethindrone and 0.05 mg ethinyl estradiol. The green tablets contain inert ingredients.

OVCON 35, 21-Day contains the following inactive ingredients: dibasic calcium phosphate, FD&C Yellow No. 6 (aluminum lake), lactose, magnesium stearate, povidone, and sodium starch glycolate.

OVCON 35, 28-Day contains the following inactive ingredients: acacia, dibasic calcium phosphate, D&C Yellow No. 10 (aluminum lake), FD&C Blue No. 1 (aluminum lake), FD&C Yellow No. 6 (aluminum lake), lactose, magnesium stearate, povidone, sodium starch glycolate, starch (corn), and talc.

OVCON 50, 21-Day contains the following inactive ingredients: dibasic calcium phosphate, D&C Yellow No. 10 (aluminum lake), FD&C Yellow No. 6 (aluminum lake), lactose, magnesium stearate, povidone, and sodium starch glycolate.

OVCON 50, 28-Day contains the following inactive ingredients: acacia, dibasic calcium phosphate, D&C Yellow No. 10 (aluminum lake), FD&C Blue No. 1 (aluminum lake), FD&C Yellow No. 6 (aluminum lake), lactose, magnesium stearate, povidone, sodium starch glycolate, starch (corn), and talc.

CLINICAL PHARMACOLOGY

Combination oral contraceptives act by suppression of gonadotropins. Although the primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus (which increase the difficulty of sperm entry into the uterus) and the endometrium (which reduce the likelihood of implantation).

INDICATIONS AND USAGE

Oral contraceptives are indicated for the prevention of pregnancy in women who elect to use this product as a method of contraception.

Oral contraceptives are highly effective. Table 1 lists the typical accidental pregnancy rates for users of combination oral contraceptives and other methods of contraception. The efficacy of these contraceptive methods, except sterilization, depends upon the reliability with which they are used. Correct and consistent use of methods can result in lower failure rates.

[See table 1 next page.]

CONTRAINDICATIONS

Oral contraceptives should not be used in women who currently have the following conditions:

- Thrombophlebitis or thromboembolic disorders
- A past history of deep vein thrombophlebitis or thromboembolic disorders
- Cerebrovascular or coronary artery disease
- Known or suspected carcinoma of the breast
- Carcinoma of the endometrium or other known or suspected estrogen-dependent neoplasia
- Undiagnosed abnormal genital bleeding
- Cholestatic jaundice of pregnancy or jaundice with prior pill use
- Hepatic adenomas or carcinomas
- Known or suspected pregnancy

WARNINGS

Cigarette smoking increases the risk of serious cardiovascular side effects from oral contraceptive use. This risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives should be strongly advised not to smoke.

The use of oral contraceptives is associated with increased risk of several serious conditions including myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gallbladder disease, although the risk of serious morbidity or mortality is very small in healthy women without underlying risk factors. The risk of morbidity and mortality increases significantly in the presence of other underlying risk factors such as hypertension, hyperlipidemias, obesity, and diabetes.

Practitioners prescribing oral contraceptives should be familiar with the following information relating to these risks. The information contained in this package insert is principally based on studies carried out in patients who used oral

Continued on next page

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for Estrogens

SHOULD KNOW ABOUT ESTROGENS

female hormones produced by the ovaries. The several different kinds of estrogens. In addi- have been able to make a variety of synthetic far as we know, all these estrogens have simi- and, therefore, much the same usefulness, side This leaflet is intended to help you under- estrogens are used for, the risks involved in their to use them as safely as possible.
includes the most important information about all the information. If you want to know ask your doctor or pharmacist to let you read insert prepared for the doctor.

ESTROGEN

prescribed by doctors for a number of pur- the following:
estrogen during a period of adjustment when ovaries no longer produce estrogen, in order to uncomfortable symptoms of estrogen defi- women normally stop producing estrogens, gen- the ages of 45 and 55; this is called the meno-

symptoms of estrogen deficiency when a uterus have been removed surgically before the

pregnancy. (Estrogens are given along with a another female hormone; these combinations contraceptives or birth control pills. Patient available to women taking oral contraceptives will not be discussed in this leaflet.)
certain cancers in women and men.
painful swelling of the breasts after preg- women who choose not to nurse their babies.
PROPER USE OF ESTROGENS IN A PREG-

IN THE MENOPAUSE

course of their lives, all women eventually decrease in estrogen production. This usually ages 45 and 55 but may occur earlier or later. ovaries may need to be removed before natu- by an operation, producing a "surgical meno-

amount of estrogen in the blood begins to decrease, may develop typical symptoms: feelings of the face, neck, and chest; or sudden intense epi- and sweating throughout the body (called "hot flashes"). These symptoms are sometimes uncomfortable. A few women eventually develop in the vagina (called "atrophic vaginitis") which discomfort, especially during and after intercourse. may be prescribed to treat these symptoms of the It is estimated that considerably more than half undergoing the menopause have only mild no symptoms at all and, therefore, do not need Other women may need estrogens for a few their bodies adjust to lower estrogen levels. need will be for periods longer than six attempt to avoid overstimulation of the uterus are usually given cyclically during each that is, three weeks of pills followed by one pills. However, Estrovis (quinestrol tablets, USP) is given once daily for seven days, followed by once weekly use beginning two weeks after the start of treatment.
Sometimes, women experience nervous symptoms or depression during menopause. There is no evidence that estrogens are effective for such symptoms and they should not be used to treat them, although other treatment may be needed.
You may have heard that taking estrogens for long periods (years) after the menopause will keep your skin soft and supple and keep you feeling young. There is no evidence that this is so, however, and such long-term treatment carries important risks.

THE DANGERS OF ESTROGEN

1. *Cancer of the uterus.* If estrogens are used in the postmenopausal period for more than a year, there is an increased risk of *endometrial cancer* (cancer of the uterus). Women taking estrogens have roughly 5 to 10 times as great a chance of getting this cancer as women who take no estrogens. To put this another way, while a postmenopausal woman not taking estrogens has 1 chance in 1,000 each year of getting cancer of the uterus, a woman taking estrogens has 5 to 10 chances in 1,000 each year. For this reason *it is important to take estrogens only when you really need them.*
The risk of this cancer is greater the longer estrogens are used and also seems to be greater when larger doses are taken. For this reason *it is important to take the lowest dosage of estrogens that will control symptoms and to take it only as long as it is needed.* If estrogens are needed for longer periods of time, your doctor will want to reevaluate your need for estrogens at least every six months.
Women using estrogens should report any irregular vaginal bleeding to their doctors; although such bleeding may be of no importance, it can be an early warning of cancer of the uterus. If you have undiagnosed vaginal bleeding, you should not use estrogens until a diagnosis is made and you are certain there is no cancer of the uterus.
If you have had your uterus completely removed (total hysterectomy), there is no danger of developing cancer of the uterus.
2. *Other possible cancers.* Estrogens can cause development of other tumors in animals, such as tumors of the breast, cervix, vagina, or liver, when given for a long time. At present, there is no good evidence that women using estrogen in the menopause have an increased risk of such tumors, but there is no way yet to be sure they do not. One study raises the possibility that use of estrogen in the menopause may increase the risk of breast cancer many years later. This is a further reason to use estrogens only when clearly needed. While you are taking estrogens, it is important that you go to your doctor at least once a year for a physical examination. Also, if members of your family have had breast cancer or if you have breast nodules or abnormal mammograms (breast x-rays), your doctor may wish to carry out more frequent examinations of your breasts.
3. *Gallbladder disease.* Women who use estrogens after menopause are more likely to develop gallbladder disease requiring surgery than women who do not use estrogens. Birth control pills have a similar effect.
4. *Abnormal blood clotting.* Oral contraceptives increase the risk of blood clotting in various parts of the body. This can result in a stroke (if the clot is in the brain), a heart attack (a clot in a blood vessel of the heart), or a pulmonary embolus (a clot which forms in the legs or pelvis, then breaks off and travels to the lungs.) Any of these can be fatal.
At this time use of estrogens in the menopause is not known to cause such blood clotting, but this has not been fully studied and there could still prove to be such a risk. It is recommended that if you have had clotting in the legs or lungs or a heart attack or stroke while you were using estrogens or birth control pills, you should not use estrogens (unless they are being used to treat cancer of the breast or prostate.) If you have had a stroke or heart attack or if you have angina pectoris, estrogens should be used with great caution and only if clearly needed (for example, if you have severe symptoms of the menopause).
The larger dosages of estrogen used to prevent swelling of the breasts after pregnancy have been reported to cause clotting in the legs and lungs.

SPECIAL WARNING ABOUT PREGNANCY

You should not receive estrogen if you are pregnant. If this should occur, there is a greater than usual chance that the developing child will be born with a birth defect, although the possibility remains fairly small. A female child may have an increased risk of developing cancer of the vagina or cervix later in life (in the teens or twenties). Every possible effort should be made to avoid exposure to estrogens during pregnancy. If exposure occurs, see your doctor.

OTHER EFFECTS OF ESTROGENS

In addition to the serious known risks of estrogens previously described, estrogens have the following side effects and potential risks:
1. *Nausea and vomiting.* The most common side effect of estrogen therapy is nausea. Vomiting is less common.
2. *Effects on the breasts.* Estrogens may cause breast tenderness or enlargement and may cause the breasts to secrete a liquid. These effects are not dangerous.
3. *Effects on the uterus.* Estrogens may cause benign fibroid tumors of the uterus to enlarge.
Some women will have menstrual bleeding when estrogens are stopped. However, if the bleeding occurs on days you are still taking estrogens, you should report this to your doctor.
4. *Effects on the liver.* On rare occasions, women taking oral contraceptives develop a tumor of the liver which can rupture and bleed into the abdomen. So far, these tumors have not been reported in women using estrogens in the menopause, but you should report to your doctor immediately any swelling or unusual pain or tenderness in the abdomen.
Women with a past history of jaundice (yellowing of the skin and white parts of the eyes) may get jaundice again during estrogen use. If this occurs, stop taking estrogens and see your doctor.
5. *Other effects.* Estrogens may cause excess fluid to be retained in the body. This may make some conditions worse, such as epilepsy, migraine, heart disease, or kidney disease.

SUMMARY

Estrogens have important uses, but they have serious risks as well. You must decide, with your doctor, whether the risks are acceptable to you in view of the benefits of treatment. Except where your doctor has prescribed estrogens for use in special cases of cancer of the breast or prostate, you should not use estrogens if you have cancer of the breast or uterus, are pregnant, have undiagnosed abnormal vaginal bleeding, clotting in the legs or lungs, or have had a stroke, heart attack or angina, or clotting in the legs or lungs in the past while you were taking estrogens.
You can use estrogens as safely as possible by understanding that your doctor will require regular physical examinations while you are taking them and will try to use the smallest dosage possible and discontinue the drug as soon as possible.
Be alert for signs of trouble including:
1. Abnormal bleeding from the vagina
2. Pains in the calves or chest or sudden shortness of breath, or coughing blood (indicating possible clots in the legs, heart, or lungs)
3. Severe headache, dizziness, faintness, or changes in vision (indicating possible developing clots in the brain or eye)
4. Breast lumps (you should ask you doctor how to examine your own breasts)
5. Jaundice (yellowing of the skin)
6. Mental depression
Based on his or her assessment of your medical needs, your doctor has prescribed this drug for you. Do not give this drug to anyone else.
Storage—Store between 15°–30°C (59°–86°F).
Caution—Federal law prohibits dispensing without prescription

0437G027

Shown in Product Identification Section, page 322

LOESTRIN® 21 ℞
(Norethindrone Acetate and Ethinyl Estradiol Tablets, USP)

LOESTRIN® 21 1/20 ℞
(Each white tablet contains 1 mg norethindrone acetate and 20 mcg ethinyl estradiol.)

LOESTRIN® 21 1.5/30 ℞
(Each green tablet contains 1.5 mg norethindrone acetate and 30 mcg ethinyl estradiol.)

LOESTRIN® Fe ℞
(Norethindrone Acetate and Ethinyl Estradiol Tablets, USP and Ferrous Fumarate Tablets, USP)

LOESTRIN® Fe 1/20 ℞
(Each white tablet contains 1 mg norethindrone acetate and 20 mcg ethinyl estradiol. Each brown tablet contains 75 mg ferrous fumarate, USP)

LOESTRIN® Fe 1.5/30 ℞
(Each green tablet contains 1.5 mg norethindrone acetate and 30 mcg ethinyl estradiol. Each brown tablet contains 75 mg ferrous fumarate)

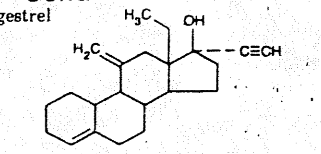
Each white tablet contains norethindrone acetate (17 alpha-ethinyl-19-nortestosterone acetate), 1 mg; ethinyl estradiol

Continued on next page

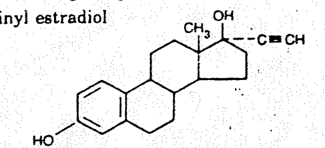
This product information was prepared in August 1993. On these and other Parke-Davis Products, information may be obtained by addressing PARKE-DAVIS, Division of Warner-Lambert Company, Morris Plains, New Jersey 07950.

Ortho—Cont.

desogestrel



ethinyl estradiol



in the cervical mucus, which increase the difficulty of sperm entry into the uterus, and changes in the endometrium which reduce the likelihood of implantation.

Receptor binding studies, as well as studies in animals and humans, have shown that 3-keto-desogestrel, the biologically active metabolite of desogestrel, combines high progestational activity with minimal intrinsic androgenicity[91,92]. Desogestrel, in combination with ethinyl estradiol, does not counteract the estrogen-induced increases in SHBG, resulting in lower serum levels of free testosterone[96–99].

Pharmacokinetics

Desogestrel is rapidly and almost completely absorbed and converted into 3-keto-desogestrel, its biologically active metabolite. Following oral administration, the relative bioavailability of desogestrel, as measured by serum levels of 3-keto-desogestrel, is approximately 84%.

In the third cycle of use after a single dose of ORTHO-CEPT, maximum concentrations of 3-keto-desogestrel of 2,805±1,203 pg/mL (mean±SD) are reached at 1.4±0.8 hours. The area under the curve ($AUC_{0-\infty}$) is 33,858±11,043 pg/mL·hr after a single dose. At steady state, attained from at least day 19 onwards, maximum concentrations of 5,840±1,667 pg/mL are reached at 1.4±0.9 hours. The minimum plasma levels of 3-keto-desogestrel at steady state are 1,400±560 pg/mL. The AUC_{0-24} at steady state is 52,299±17,878 pg/mL·hr. The mean $AUC_{0-\infty}$ for 3-keto-desogestrel at single dose is significantly lower than the mean AUC_{0-24} at steady state. This indicates that the kinetics of 3-keto-desogestrel are non-linear due to an increase in binding of 3-keto-desogestrel to sex hormone-binding globulin in the cycle, attributed to increased sex hormone-binding globulin levels which are induced by the daily administration of ethinyl estradiol. Sex hormone-binding globulin levels increased significantly in the third treatment cycle from day 1 (150±64 nmol/L) to day 21 (230±59 nmol/L).

The elimination half-life for 3-keto-desogestrel is approximately 38±20 hours at steady state. In addition to 3-keto-desogestrel, other phase I metabolites are 3α-OH-desogestrel, 3β-OH-desogestrel, and 3α-OH-5α-H-desogestrel. These other metabolites are not known to have any pharmacologic effects, and are further converted in part by conjugation (phase II metabolism) into polar metabolites, mainly sulfates and glucuronides.

Ethinyl estradiol is rapidly and almost completely absorbed. In the third cycle of use after a single dose of ORTHO-CEPT, the relative bioavailability is approximately 83%.

In the third cycle of use after a single dose of ORTHO-CEPT, maximum concentrations of ethinyl estradiol of 95±34 pg/mL are reached at 1.5±0.8 hours. The $AUC_{0-\infty}$ is 1,471±268 pg/mL·hr after a single dose. At steady state, attained from at least day 19 onwards, maximum ethinyl estradiol concentrations of 141±48 pg/mL are reached at about 1.4±0.7 hours. The minimum serum levels of ethinyl estradiol at steady state are 24±8.3 pg/mL. The AUC_{0-24}, at steady state is 1,117±302 pg/mL·hr. The mean $AUC_{0-\infty}$ for ethinyl estradiol following a single dose during treatment cycle 3 does not significantly differ from the mean AUC_{0-24} at steady state. This finding indicates linear kinetics for ethinyl estradiol.

The elimination half-life is 26±6.8 hours at steady state. Ethinyl estradiol is subject to a significant degree of presystemic conjugation (phase II metabolism). Ethinyl estradiol escaping gut wall conjugation undergoes phase I metabolism and hepatic conjugation (phase II metabolism). Major phase I metabolites are 2-OH-ethinyl estradiol and 2-methoxy-ethinyl estradiol. Sulfate and glucuronide conjugates of both ethinyl estradiol and phase I metabolites, which are excreted in bile, can undergo enterohepatic circulation.

INDICATIONS AND USAGE

ORTHO-CEPT Tablets are indicated for the prevention of pregnancy in women who elect to use oral contraceptives as a method of contraception.

Oral contraceptives are highly effective. Table I lists the typical accidental pregnancy rates for users of combination oral contraceptives and other methods of contraception. The efficacy of these contraceptive methods, except sterilization, depends upon the reliability with which they are used. Correct and consistent use of these methods can result in lower failure rates.

[See table below.]

In a clinical trial with ORTHO-CEPT, 1,195 subjects completed 11,656 cycles and a total of 10 pregnancies were reported. This represents an overall user-efficacy (typical user-efficacy) pregnancy rate of 1.12 per 100 women-years. This rate includes patients who did not take the drug correctly.

CONTRAINDICATIONS

Oral contraceptives should not be used in women who currently have the following conditions:

- Thrombophlebitis or thromboembolic disorders
- A past history of deep vein thrombophlebitis or thromboembolic disorders
- Cerebral vascular or coronary artery disease
- Known or suspected carcinoma of the breast
- Carcinoma of the endometrium or other known or suspected estrogen-dependent neoplasia
- Undiagnosed abnormal
- Cholestatic jaundice of pill use
- Hepatic adenomas or
- Known or suspected

WARNINGS

Cigarette smoking increases vascular side effects from risk increases with age more cigarettes per day over 35 years of age. tives should be strongly

The use of oral contra risks of several serious farction, thromboembol gallbladder disease, alth mortality is very small ing risk factors. The ris creases significantly in t factors such as hypert diabetes.

Practitioners prescribing miliar with the following The information contained pally based on studies c contraceptives with for gens and progestogens effect of long term use of lations of lower doses of remains to be determined. Throughout this labeling, are of two types: retro prospective or cohort st measure of the relative r the incidence of a disea that among nonusers. Th formation on the actual hort studies provide a the *difference* in the inc ceptive users and nonu vide information about th the population (Adapted permission). For further to a text on epidemiolo

1. THROMBOEMBOLIC D CULAR PROBLEMS

a. Myocardial infarctio

An increased risk of uted to oral contraceptive ers or women with other artery disease such as morbid obesity, and di tack for current oral co to be two to six[4–10]. Th age of 30.

Smoking in combinati been shown to contrib myocardial infarctions older with smoking cases[11]. Mortality rate have been shown to inc cially in those 35 years use oral contraceptives.

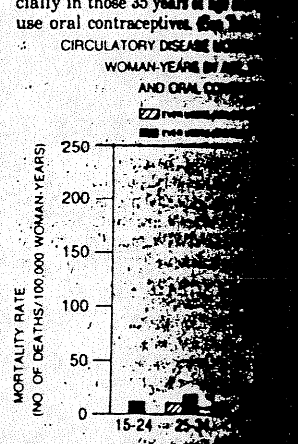


TABLE II. (Adapted ref. #12.)

Oral contraceptives may risk factors, such as hyp age and obesity.[13] In known to decrease HDL erance, while estrogens ism[14–18]. Oral contrac blood pressure among

TABLE I: LOWEST EXPECTED AND TYPICAL FAILURE RATES (%) DURING THE FIRST YEAR OF USE OF A CONTRACEPTIVE METHOD

Method	Lowest Expected*	Typical**
Oral Contraceptives		3
combined	0.1	N/A
progestin only	0.5	N/A
Diaphragm with spermicidal cream or jelly	6	18
Spermicides alone (foam, creams, jellies and vaginal suppositories)	3	21
Vaginal Sponge		
nulliparous	6	18
parous	9	28
IUD (medicated)	2	3
Implant		
capsules	0.04	0.04
rods	0.03	0.03
Condom without spermicide	2	12
Cervical Cap	6	18
Periodic abstinence (all methods)	1-9	20
Female sterilization	0.2	0.4
Male sterilization	0.1	0.15
No contraception (planned pregnancy)	85	85

Adapted from J. Trussell, et al. Table 1, ref. #1.

N/A—Data not available.

* The author's best estimate of the percentage of women expected to experience an accidental pregnancy among couples who initiate a method (not necessarily for the first time) and who use it consistently and correctly during the first year, if they do not stop for any other reason.

** This term represents "typical" couples who initiate use of a method (not necessarily for the first time), who experience an accidental pregnancy during the first year, if they do not stop use for any other reason.

OL® Contraceptive Jelly OTC

prescription Drugs.)

UM® Tablets ℞
stranol) or
inyl estradiol)

Tablets ℞
inyl estradiol)

Tablets ℞

ORAL CONTRACEPTIVES

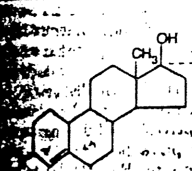
products is a combination oral contra- the progestational compound norethin- strogenic compound ethinyl estradiol:
7/7/7 ☐ 21 Tablets and ORTHO-NOVUM Each white tablet contains 0.5 mg of and 0.035 mg of ethinyl estradiol. Inactive lactose, magnesium stearate and starch. Each light peach tablet contains 0.75 and 0.035 mg of ethinyl estradiol. Inac include FD&C Yellow No. 6, lactose, magne and pregelatinized starch. Each peach tablet norethindrone and 0.035 mg of ethinyl es- ingredients include FD&C Yellow No. 6, stearate and pregelatinized starch. Each the ORTHO-NOVUM 7/7/7 ☐ 28 package ingredients, as follows: D&C Yellow No. Lake, FD&C Blue No. 2 Aluminum Lake, lac- stearate, microcrystalline cellulose and starch.
10/11 ☐ 21 Tablets and ORTHO-NOVUM Each white tablet contains 0.5 mg of and 0.035 mg of ethinyl estradiol. Inactive lactose, magnesium stearate and starch. Each peach tablet contains 1 mg nor- 0.035 mg of ethinyl estradiol. Inactive ingre- FD&C Yellow No. 6, lactose, magnesium stea- latinized starch. Each green tablet in the 10/11 ☐ 28 package contains only inert listed under green tablets in ORTHO- ☐ 28.
1/35 ☐ 21 Tablets and ORTHO-NOVUM Each peach tablet contains 1 mg of nor- 0.035 mg of ethinyl estradiol. Inactive ingre- FD&C Yellow No. 6, lactose, magnesium stea- latinized starch. Each green tablet in the 1/35 ☐ 28 package contains only inert listed under green tablets in ORTHO- ☐ 28.
Tablets and MODICON 28 Tablets: Each 0.5 mg of norethindrone and 0.035 mg Inactive ingredients include lactose, and pregelatinized starch. Each green MODICON 28 package contains only inert in- under green tablets in ORTHO-NOVUM

products is a combination oral contra- the progestational compound norethin- estrogenic compound mestranol:
1/50 ☐ 21 Tablets and ORTHO-NOVUM Each yellow tablet contains 1 mg of nor- mg of mestranol. Inactive ingredients No. 10, lactose, magnesium stearate and starch. Each green tablet in the ORTHO- 28 package contains only inert ingredients, tablets in ORTHO-NOVUM 7/7/7 ☐

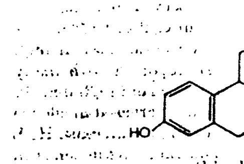
ONLY ORAL CONTRACEPTIVE

product is a progestogen-only oral contracep- the progestational compound norethindrone: Each tablet contains 0.35 mg of nor- ingredients include D&C Green No. 5, lactose, magnesium stearate, povidone

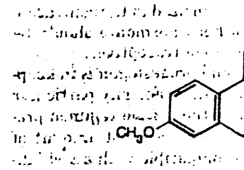
for norethindrone is 17-hydroxy-19-nor- yn-3-one, for ethinyl estradiol is 19-nor- (10)-trien-20-yne-3,17-diol, and for mestra- 19-nor-17α-pregna-1,3,5(10)-trien-20-yn-17- formulas are as follows:



norethindrone



ethinyl estradiol



mestranol

CLINICAL PHARMACOLOGY
COMBINATION ORAL CONTRACEPTIVES

Combination oral contraceptives act by suppression of gonadotropins. Although the primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus (which increase the difficulty of sperm entry into the uterus) and the endometrium (which reduce the likelihood of implantation).

CLINICAL PHARMACOLOGY
PROGESTOGEN-ONLY ORAL CONTRACEPTIVES

The primary mechanism through which MICRONOR prevents conception is not known, but progestogen-only contraceptives are known to alter the cervical mucus, exert a progestational effect on the endometrium, interfering with implantation, and, in some patients, suppress ovulation.

INDICATIONS AND USAGE

ORTHO-NOVUM 7/7/7 ☐ 21, ORTHO-NOVUM 7/7/7 ☐ 28, ORTHO-NOVUM 10/11 ☐ 21, ORTHO-NOVUM 10/11 ☐ 28, ORTHO-NOVUM 1/35 ☐ 21, ORTHO-NOVUM 1/35 ☐ 28, MODICON 21, MODICON 28, ORTHO-NOVUM 1/50 ☐ 21, ORTHO-NOVUM 1/50 ☐ 28, and MICRONOR are indicated for the prevention of pregnancy in women who elect to use this product as a method of contraception.
Oral contraceptives are highly effective. Table I lists the typical accidental pregnancy rates for users of combination oral contraceptives and other methods of contraception. The efficacy of these contraceptive methods, except sterilization, depends upon the reliability with which they are used. Correct and consistent use of methods can result in lower failure rates.

TABLE I: LOWEST EXPECTED AND TYPICAL FAILURE RATES DURING THE FIRST YEAR OF CONTINUOUS USE OF A METHOD
% of Women Experiencing an Accidental Pregnancy in the First Year of Continuous Use

Method	Lowest Expected*	Typical**
(No contraception)	(89)	(89)
Oral contraceptives		3
combined	0.1	N/A***
progestin only	0.5	N/A***
Diaphragm with spermicidal cream or jelly	3	18
Spermicides alone (foam, creams, jellies and vaginal suppositories)	3	21
Vaginal sponge		
nulliparous	5	18
multiparous	>8	>28
IUD (medicated)	1	6#
Condom without spermicides	2	12
Periodic abstinence (all methods)	2–10	20
Female sterilization	0.2	0.4
Male sterilization	0.1	0.15

Adapted from J. Trussell and K. Kost, Table II, ref. #1.
* The authors' best guess of the percentage of women expected to experience an accidental pregnancy among couples who initiate a method (not necessarily for the first time) and who use it consistently and correctly during the first year if they do not stop for any other reason.
** This term represents "typical" couples who initiate use of a method (not necessarily for the first time), who experience an accidental pregnancy during the first year if they do not stop for any other reason.
*** N/A—Data not available
# Combined typical rate for both medicated and non-medicated IUD. The rate for medicated IUD alone is not available.

CONTRAINDICATIONS

Oral contraceptives should not be used in women who currently have the following conditions:
- Thrombophlebitis or thromboembolic disorders
- A past history of deep vein thrombophlebitis or thromboembolic disorders
- Cerebral vascular or coronary artery disease
- Known or suspected carcinoma of the breast
- Carcinoma of the endometrium or other known or suspected estrogen-dependent neoplasia
- Undiagnosed abnormal genital bleeding
- Cholestatic jaundice of pregnancy or jaundice with prior pill use
- Hepatic adenomas or carcinomas
- Known or suspected pregnancy

WARNINGS

Cigarette smoking increases the risk of serious cardiovascular side effects from oral contraceptive use. This risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives should be strongly advised not to smoke.

The use of oral contraceptives is associated with increased risks of several serious conditions including myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gallbladder disease, although the risk of serious morbidity or mortality is very small in healthy women without underlying factors. The risk of morbidity and mortality increases significantly in the presence of other underlying risk factors such as hypertension, hyperlipidemias, obesity and diabetes.
Practitioners prescribing oral contraceptives should be familiar with the following information relating to these risks.
The information contained in this package insert is principally based on studies carried out in patients who used oral contraceptives with higher formulations of estrogens and progestogens than those in common use today. The effect of long term use of the oral contraceptives with lower formulations of both estrogens and progestogens remains to be determined.
Throughout this labeling, epidemiological studies reported are of two types: retrospective or case control studies and prospective or cohort studies. Case control studies provide a measure of the relative risk of a disease, namely, a *ratio* of the incidence of a disease among oral contraceptive users to that among nonusers. The relative risk does not provide information on the actual clinical occurrence of a disease. Cohort studies provide a measure of attributable risk, which is the *difference* in the incidence of disease between oral contraceptive users and nonusers. The attributable risk does provide information about the actual occurrence of a disease in the population (adapted from refs. 2 and 3 with the author's permission). For further information, the reader is referred to a text on epidemiological methods.

1. THROMBOEMBOLIC DISORDERS AND OTHER VASCULAR PROBLEMS

a. Myocardial Infarction

An increased risk of myocardial infarction has been associated with oral contraceptive use. This risk is primarily in smokers or women with other underlying risk factors for coronary artery disease such as hypertension, hypercholesterolemia, morbid obesity, and diabetes. The relative risk of heart attack for current oral contraceptive users has been estimated to be two to six[4–10]. The risk is very low under the age of 30.
Smoking in combination with oral contraceptive use has been shown to contribute substantially to the incidence of myocardial infarctions in women in their mid-thirties or older with smoking accounting for the majority of excess cases[11]. Mortality rates associated with circulatory disease have been shown to increase substantially in smokers, especially in those 35 years of age and older among women who use oral contraceptives.

[See illustration next page.]

Oral contraceptives may compound the effects of well-known risk factors, such as hypertension, diabetes, hyperlipidemias, age and obesity[13]. In particular, some progestogens are known to decrease HDL cholesterol and cause glucose intolerance, while estrogens may create a state of hyperinsulinism[14–18]. Oral contraceptives have been shown to increase blood pressure among users (see section 9 in WARNINGS). Similar effects on risk factors have been associated with an increased risk of heart disease. Oral contraceptives must be used with caution in women with cardiovascular disease risk factors.

b. Thromboembolism

An increased risk of thromboembolic and thrombotic disease associated with the use of oral contraceptives is well estab-

Continued on next page

weeks after the overdose ingestion. Methemoglobinuria can be acutely reversed with intravenous 1% methylene blue. Sulfamethizole is only minimally dialyzable by hemodialysis and is not dialyzable by peritoneal dialysis. Other supportive measures should be instituted appropriate to signs and symptoms.

ɔOSAGE AND ADMINISTRATION

JSUAL DOSAGE

ɩdults: 500 mg to 1 g, three or four times daily.
:hildren and infants (over 2 months of age): 30 to .5 mg/kg/24 hours, divided into 4 doses.

ɪOW SUPPLIED

'hiosulfil Forte—Each white, biconvex, scored, oval tablet ontains sulfamethizole 500 mg (scored), in bottles of 100 NDC 0046-0786-81).

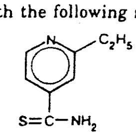
tore at room temperature (approximately 25° C)

Shown in Product Identification Section, page 337

'RECATOR®-SC ℞
rek "ă 'tōre]
:thionamide)
ugar-Coated Tablets

'ESCRIPTION

recator-SC (ethionamide) is used in the treatment of tuber-ılosis. The chemical name for ethionamide is 2-ethyl-thi-sonicotinamide with the following structural formula:



.hionamide is a yellow, crystalline, nonhygroscopic com-·und with a faint-to-moderate sulfide odor. It is practically soluble in water and ether but soluble in methanol and hanol. It melts at about 162°C and is stable at ordinary mperatures and humidities.
ecator-SC tablets contain 250 mg of ethionamide. The in-tive ingredients present are acacia, calcium carbonate, rnauba wax, confectioners sugar, FD&C Yellow 6, gelatin, :tose, magnesium stearate, methylcellulose, pharmaceuti-: glaze, polacrilin potassium, povidone, sodium benzoate, :crose, talc, titanium dioxide, and white wax.

:TION

cteriostatic against *Mycobacterium tuberculosis*.

DICATIONS

ılure after adequate treatment with primary drugs (i.e., niazid, streptomycin, aminosalicylic acid) in any form of ive tuberculosis. Ethionamide should only be given with er effective antituberculous agents.

NTRAINDICATIONS

'ere hypersensitivity.
'ere hepatic damage.

ıRNING

E IN PREGNANCY

atogenic effects have been demonstrated in animals (rab-, rats) receiving doses in excess of those recommended in nans. Use of the drug should be avoided during preg-:cy or in women of childbearing potential unless the bene-outweigh its possible hazard.

Ɛ IN CHILDREN

imum dosage for children has not been established. This, 'ever, does not preclude use of the drug when its use is :ial to therapy.

ECAUTIONS

:reatment examinations should include *in vitro* suscepti-y tests of recent cultures of *M. tuberculosis* from the pa-t as measured against ethionamide and the usual pri-y antituberculous drugs.
:rminations of serum transaminase (SGOT, SGPT) ıld be made prior to and every 2 to 4 weeks during apy.
ıatients with diabetes mellitus, management may be ɘ difficult and hepatitis occurs more frequently.
onamide may intensify the adverse effects of the other :uberculous drugs administered concomitantly. Convul-ɜ have been reported, and special care should be taken, icularly when ethionamide is administered with cyclo-ıe.

'ERSE REACTIONS

most common side effect is gastrointestinal intolerance. r adverse effects similar to those seen with isoniazid been reported: peripheral neuritis, optic neuritis, psy-disturbances (including mental depression), postural tension, skin rashes, thrombocytopenia, pellagralike ·ome, jaundice and/or hepatitis, increased difficulty in ıgement of diabetes mellitus, stomatitis, gynecomastia, mpotence.

DOSAGE AND ADMINISTRATION

Ethionamide should be administered with at least one other effective antituberculous drug.
Average Adult Dose: 0.5 gram to 1.0 gram/day in divided doses.
Concomitant administration of pyridoxine is recommended.

HOW SUPPLIED

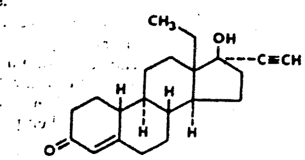
Trecator®-SC (ethionamide) Tablets are supplied in bottles of 100 tablets as follows:
250 mg, NDC 0008-4130, orange, sugar-coated tablet marked "WYETH" and "4130".
Store at room temperature, approximately 25°C (77°F)
Keep tightly closed
Dispense in tight container

TRIPHASIL®-21 ℞
[tri-fa 'sil]
Tablets
(levonorgestrel and ethinyl estradiol tablets—triphasic regimen)

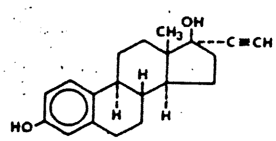
Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

DESCRIPTION

Each Triphasil cycle of 21 tablets consists of three different drug phases as follows: Phase 1 comprised of 6 brown tablets, each containing 0.050 mg of levonorgestrel (d(-)-13 beta-ethyl-17-alpha-ethinyl-17-beta-hydroxygon-4-en-3-one), a totally synthetic progestogen, and 0.030 mg of ethinyl estradiol (19-nor-17α-pregna-1,3,5(10)-trien-20-yne-3,17-diol); phase 2 comprised of 5 white tablets, each containing 0.075 mg levonorgestrel and 0.040 mg ethinyl estradiol; and phase 3 comprised of 10 light-yellow tablets, each containing 0.125 mg levonorgestrel and 0.030 mg ethinyl estradiol. The inactive ingredients present are cellulose, iron oxides, lactose, magnesium stearate, polacrilin potassium, polyethylene glycol, titanium dioxide, and hydroxypropyl methylcellulose.



Levonorgestrel



Ethinyl Estradiol

CLINICAL PHARMACOLOGY

Combination oral contraceptives act by suppression of gonadotropins. Although the primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus (which increase the difficulty of sperm entry into the uterus) and the endometrium (which reduce the likelihood of implantation).

INDICATIONS AND USAGE

Oral contraceptives are indicated for the prevention of pregnancy in women who elect to use this product as a method of contraception.
Oral contraceptives are highly effective. Table I lists the typical accidental pregnancy rates for users of combination oral contraceptives and other methods of contraception. The efficacy of these contraceptive methods, except sterilization and the IUD, depends upon the reliability with which they are used. Correct and consistent use of methods can result in lower failure rates.
[See table at top of next column.]

CONTRAINDICATIONS

Oral contraceptives should not be used in women with any of the following conditions:
Thrombophlebitis or thromboembolic disorders
A past history of deep-vein thrombophlebitis or thromboembolic disorders
Cerebral-vascular or coronary-artery disease
Known or suspected carcinoma of the breast
Carcinoma of the endometrium or other known or suspected estrogen-dependent neoplasia
Undiagnosed abnormal genital bleeding
Cholestatic jaundice of pregnancy or jaundice with prior pill use
Hepatic adenomas or carcinomas
Known or suspected pregnancy

TABLE I: LOWEST EXPECTED AND TYPICAL FAILURE RATES DURING THE FIRST YEAR OF CONTINUOUS USE OF A METHOD

% of Women Experiencing an Accidental Pregnancy in the First Year of Continuous Use

Method	Lowest Expected*	Typical**
(No Contraception)	(89)	(89)
Oral contraceptives		3
combined	0.1	N/A***
progestin only	0.5	N/A***
Diaphragm with spermicidal cream or jelly	3	18
Spermicides alone (foam, creams, jellies and vaginal suppositories)	3	21
Vaginal Sponge		
nulliparous	5	18
multiparous	>8	>28
IUD (medicated)	1	6#
Condom without spermicides	2	12
Periodic abstinence (all methods)	2–10	20
Female sterilization	0.2	0.4
Male sterilization	0.1	0.15

Adapted from J. Trussell and K. Kost, Table 11, Studies in Family Planning, 18(5), Sept.–Oct. 1987.

* The authors' best guess of the percentage of women expected to experience an accidental pregnancy among couples who initiate a method (not necessarily for the first time) and who use it consistently and correctly during the first year if they do not stop for any other reason.
** This term represents "typical" couples who initiate use of a method (not necessarily for the first time), who experience an accidental pregnancy during the first year if they do not stop use for any other reason.
*** N/A—Data not available.
\# Combined typical rate for both medicated and non-medicated IUD. The rate for medicated IUD alone is not available.

WARNINGS

Cigarette smoking increases the risk of serious cardiovascular side effects from oral-contraceptive use. This risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives should be strongly advised not to smoke.

The use of oral contraceptives is associated with increased risks of several serious conditions including myocardial infarction, thromboembolism, stroke, hepatic neoplasia, gallbladder disease, and hypertension, although the risk of serious morbidity or mortality is very small in healthy women without underlying factors. The risk of morbidity and mortality increases significantly in the presence of other underlying risk factors such as hypertension, hyperlipidemias, obesity, and diabetes.
Practitioners prescribing oral contraceptives should be familiar with the following information relating to these risks.
The information contained in this package insert is based principally on studies carried out in patients who used oral contraceptives with higher formulations of estrogens and progestogens than those in common use today. The effect of long-term use of the oral contraceptives with lower formulations of both estrogens and progestogens remains to be determined.
Throughout this labeling, epidemiological studies reported are of two types: retrospective or case control studies and prospective or cohort studies. Case control studies provide a measure of the relative risk of disease, namely, a ratio of the incidence of a disease among oral-contraceptive users to that among nonusers. The relative risk does not provide information on the actual clinical occurrence of a disease. Cohort studies provide a measure of attributable risk, which is the difference in the incidence of disease between oral-contraceptive users and nonusers. The attributable risk does provide information about the actual occurrence of a disease in the population. For further information, the reader is referred to a text on epidemiological methods.

1. THROMBOEMBOLIC DISORDERS AND OTHER VASCULAR PROBLEMS

a. *Myocardial Infarction*

An increased risk of myocardial infarction has been attributed to oral-contraceptive use. This risk is primarily in smok-

Continued on next page

Wyeth-Ayerst Laboratories—Cont.

Triphasil-28 Tablets contain 21 active pills divided among 6 brown pills, 5 white pills, and 10 light-yellow pills plus 7 light-green inactive pills per package.

The dosage of Triphasil-28 Tablets is one active pill daily for 21 days in a row beginning with the 6 brown pills, followed by the 5 white pills, followed by the 10 light-yellow pills, and then one of the 7 light-green inactive pills daily for the next 7 days, in that order, for a total of 28 days or 4 weeks. The basic schedule is 21 days on active pills (brown, white, and light-yellow)—7 days on light-green inactive pills. Always take all of the 21 active pills (brown, white, and light-yellow) in each package before taking the light-green pills.

When you start your first cycle of Triphasil-28 Tablets, you should begin taking your pills on the first day of your next menstrual period, regardless of the day of the week or the amount of the bleeding or spotting. NOTE: During the first month on Triphasil-28 Tablets, if you start taking pills later than day 1 of your menstrual cycle, you should protect yourself by also using another method of birth control until you have taken a pill daily for seven days in a row (6 brown pills followed by 1 white pill). Thereafter, if you follow directions carefully you should obtain the full contraceptive benefit. If you begin taking pills later than the proper day, the possibility of ovulation and pregnancy occurring before or during the taking of the brown pills should be considered. Take one pill every day until you finish all 6 brown, 5 white, and 10 light-yellow pills in a package followed by all 7 light-green pills. Your period will usually begin about three days after you take the last light-yellow pill, which will be during the time you are taking the light-green pills. Don't be alarmed if the amount of bleeding is not the same as before.

The day after you have taken your last light-green pill, begin a new package of pills (first taking the 6 brown, then the 5 white, and then the 10 light-yellow pills, one a day just as you did before) so that you will take a pill every day without interruption. **If you have taken the pills as directed,** the starting day for each new package will always be the same day as in the previous cycle. When switching from another oral contraceptive, Triphasil-28 Tablets should be started on the first day of bleeding following the last active pill taken of the previous oral contraceptive.

SPOTTING OR BREAKTHROUGH BLEEDING:

Spotting is slight staining between menstrual periods which may not even require a pad. Breakthrough bleeding is a flow much like a regular period, requiring sanitary protection. Spotting is more common than breakthrough bleeding, and both occur more often in the first few cycles than in later cycles. These types of bleeding are usually temporary and without significance. It is important to continue taking your pills on schedule. If the bleeding persists for more than a few days, consult your doctor.

2. If You Forget to Take Your Pill

If you miss only one pill in a cycle, the chance of becoming pregnant is small. Take the missed pill as soon as you realize that you have forgotten it. Since the risk of pregnancy increases with each additional pill you skip, it is very important that you take one pill a day.

There is a chance of becoming pregnant if you miss one brown, white, or light-yellow pill, and that chance increases with each additional brown, white, or light-yellow pill missed. If you miss any one of these pills, it is important that it be taken as soon as remembered, and also take your next pill at the regular time, which means that you will be taking two pills on that day. If you miss any two of these pills consecutively, it is important that you take the second missed pill as soon as you remember, discard the first missed pill, and take your regular pill that day at the proper time (which means you will be taking two pills on that day). Furthermore, you should use an additional method of birth control for the remainder of the cycle in addition to taking your pills as directed above. If breakthrough occurs following missed pills, it will usually be temporary and of no consequence. If you miss three or more of any of the brown, white, or light-yellow pills in succession, discontinue the medication and discard the pill card. Then start a new refill card beginning with the first brown pill on the first day of bleeding of your next period. During the days without pills and until you have taken a pill daily for seven consecutive days (six brown and one white), you should also use another means of birth control. If you miss one or more light-green inactive pills (Triphasil-28 Tablets only), you are still protected against pregnancy provided you begin taking your next brown pill on the proper day.

At times there may be no menstrual period after a cycle of pills. Therefore, if you miss one menstrual period but have taken the pills **exactly as you were supposed to,** continue as usual into the next cycle. If you have not taken the pills correctly and miss a menstrual period, you may be pregnant and should stop taking oral contraceptives until your doctor determines whether or not you are pregnant. Until you can get to your doctor, use another form of nonhormonal contraception. If two consecutive menstrual periods are missed, you should stop taking pills until it is determined by a physician whether you are pregnant.

If you do become pregnant while using oral contraceptives, the risk to the fetus is small, on the order of no more than one per thousand. You should, however, discuss the risks to the developing child with your doctor.

3. Pregnancy Due to Pill Failure

The incidence of pill failure resulting in pregnancy is approximately less than 1.0% if taken every day as directed, but more typical failure rates are less than 3.0%. If failure does occur, the risk to the fetus is minimal.

4. Pregnancy After Stopping the Pill

There may be some delay in becoming pregnant after you stop using oral contraceptives, especially if you had irregular menstrual cycles before you used oral contraceptives. It may be advisable to postpone conception until you begin menstruating regularly once you have stopped taking the pill and desire pregnancy.

There does not appear to be any increase in birth defects in newborn babies when pregnancy occurs soon after stopping the pill.

5. Overdosage

Serious ill effects have not been reported following ingestion of large doses of oral contraceptives by young children. Overdosage may cause nausea and withdrawal bleeding in females. In case of overdosage, contact your health-care provider or pharmacist.

6. Other Information

Your health-care provider will take a medical and family history before prescribing oral contraceptives and will examine you. You should be reexamined at least once a year. Be sure to inform your health-care provider if there is a family history of any of the conditions listed previously in this leaflet. Be sure to keep all appointments with your health care provider, because this is a time to determine if there are early signs of side effects of oral-contraceptive use.

Do not use the drug for any condition other than the one for which it was prescribed. This drug has been prescribed specifically for you; do not give it to others who may want birth control pills.

HEALTH BENEFITS FROM ORAL CONTRACEPTIVES

In addition to preventing pregnancy, use of oral contraceptives may provide certain benefits. They are:

- Menstrual cycles may become more regular
- Blood flow during menstruation may be lighter and less iron may be lost. Therefore, anemia due to iron deficiency is less likely to occur.
- Pain or other symptoms during menstruation may be encountered less frequently
- Ovarian cysts may occur less frequently
- Ectopic (tubal) pregnancy may occur less frequently
- Noncancerous cysts or lumps in the breast may occur less frequently
- Acute pelvic inflammatory disease may occur less frequently
- Oral contraceptive use may provide some protection against developing two forms of cancer: cancer of the ovaries and cancer of the lining of the uterus.

If you want more information about birth-control pills, ask your doctor or pharmacist. They have a more technical leaflet called the Professional Labeling which you may wish to read.

Shown in Product Identification Section, page 336

TRIPHASIL®-28 ℞

[tri-fa 'sil]

Tablets

(levonorgestrel and ethinyl estradiol tablets—triphasic regimen)

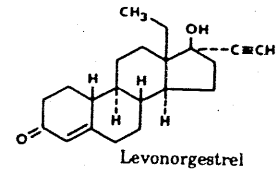
Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

DESCRIPTION

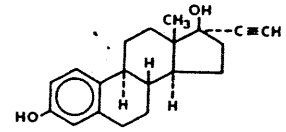
Each Triphasil cycle of 28 tablets consists of three different drug phases as follows: Phase 1 comprised of 6 brown tablets, each containing 0.050 mg of levonorgestrel (d(-)-13-beta-ethyl-17-alpha-ethinyl-17-beta-hydroxygon-4-en-3-one), a totally synthetic progestogen, and 0.030 mg of ethinyl estradiol (19-nor-17α-pregna-1,3,5(10)-trien-20-yne-3,17-diol); phase 2 comprised of 5 white tablets, each containing 0.075 mg levonorgestrel and 0.040 mg ethinyl estradiol; and phase 3 comprised of 10 light-yellow tablets, each containing 0.125 mg levonorgestrel and 0.030 mg ethinyl estradiol; then followed by 7 light-green inert tablets. The inactive ingredients present are cellulose, FD&C Blue 1, iron oxides, lactose, magnesium stearate, polacrilin potassium, polyethylene glycol, titanium dioxide, and hydroxypropyl methylcellulose.

[See chemical structure at top of next column.]

[See second chemical structure at top of next column.]



Levonorgestrel



Ethinyl Estradiol

CLINICAL PHARMACOLOGY

See Triphasil®-21.

INDICATIONS AND USAGE

See Triphasil-21.

CONTRAINDICATIONS

See Triphasil-21.

WARNINGS

See Triphasil-21.

PRECAUTIONS

See Triphasil-21.

DRUG INTERACTIONS

See Triphasil-21.

CARCINOGENESIS

See Triphasil-21.

PREGNANCY

See Triphasil-21.

NURSING MOTHERS

See Triphasil-21.

INFORMATION FOR THE PATIENT

See Triphasil-21.

ADVERSE REACTIONS

See Triphasil-21.

OVERDOSAGE

See Triphasil-21.

NONCONTRACEPTIVE HEALTH BENEFITS

See Triphasil-21.

DOSAGE AND ADMINISTRATION

To achieve maximum contraceptive effectiveness, Triphasil-28 Tablets (Levonorgestrel and Ethinyl Estradiol Tablets—Triphasic Regimen) must be taken exactly as directed and at intervals not exceeding 24 hours.

Triphasil-28 Tablets are a three-phase preparation plus 7 inert tablets. The dosage of Triphasil-28 Tablets is **one tablet daily** for 28 consecutive days per menstrual cycle in the following order: 6 brown tablets (phase 1), followed by 5 white tablets (phase 2), followed by 10 light-yellow tablets (phase 3), plus 7 light-green inert tablets, according to the prescribed schedule.

It is recommended that Triphasil-28 Tablets be taken at the same time each day, preferably after the evening meal or at bedtime. During the first cycle of medication, the patient should be instructed to take one Triphasil-28 Tablet daily in the order of 6 brown, 5 white, 10 light-yellow tablets, and then 7 light-green inert tablets for twenty-eight (28) consecutive days, beginning on day one (1) of her menstrual cycle. (The first day of menstruation is day one.) Withdrawal bleeding usually occurs within 3 days following the last light-yellow tablet. (If Triphasil-28 Tablets are first taken later than the first day of the first menstrual cycle of medication or postpartum, contraceptive reliance should not be placed on Triphasil-28 Tablets until after the first 7 consecutive days of administration. The possibility of ovulation and conception prior to initiation of medication should be considered.)

When switching from another oral contraceptive, Triphasil-28 Tablets should be started on the first day of bleeding following the last active tablet taken of the previous oral contraceptive.

The patient begins her next and all subsequent 28-day courses of Triphasil-28 Tablets on the same day of the week that she began her first course, following the same schedule. She begins taking her brown tablets on the next day after ingestion of the last light-green tablet, regardless of whether or not a menstrual period has occurred or is still in progress. Any time a subsequent cycle of Triphasil-28 Tablets is started later than the next day, the patient should be protected by another means of contraception until she has taken a tablet daily for seven consecutive days.

If spotting or breakthrough bleeding occurs, the patient is instructed to continue on the same regimen. This type of bleeding is usually transient and without significance; how-

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...AGE

...of overdosage with Orudis are rare. Of the 20 ...reported in Great Britain (5 children, 14 adolescents ...adults, and 1 man 80-years-old), only 4 had mild ...vomiting in 3, drowsiness in 1 child). The highest ...was 5,000 mg in the elderly man who displayed ...

...and metabolic acidosis were reported in ...female who attempted suicide by ingestion of ...quantity of ketoprofen, hydrocodone, and ... The patient recovered within 18 hours of ...

...ingest a large number of capsules, the stomach ...emptied by gastric lavage or induction of vomiting ...supportive measures employed. The drug is ...therefore, hemodialysis may be useful to remove ...drug and to assist in case of renal failure.

...AND ADMINISTRATION

...ARTHRITIS AND OSTEOARTHRITIS

...recommended daily dose of Orudis is 150 to 300 mg, divided ...or four doses. The recommended starting dose ...times or 50 mg four times a day. If minor side ...they may disappear at a lower dose which ...an adequate therapeutic effect. If well tolerated ...optimally effective, the dosage may be increased ...individual patients may show a better response to ...as compared to 200 mg, although in well-controlled ...trials patients on 300 mg did not show greater ... They did, however, show an increased ...upper- and lower-GI distress and headaches. It ...that women also had an increased frequency of ...effects compared to men. When treating patients ...300 mg a day, the physician should observe sufficient ...clinical benefit to offset potential increased ...higher than 300 mg per day are not recommended ...they have not been adequately studied. Relatively ...people may need smaller doses.

...eliminated primarily by renal excretion; therefore, ...should be reduced by ½ to ⅓ in patients with ...renal function, including the elderly who normally ...renal function even with normal serum creatinine ...BUN, because the lean body weight of older ...results in less creatinine formation.

...albuminemia and reduced renal function both ...fraction of free drug (biologically active form), ...have both conditions may be at greater risk of ... Therefore, it is recommended that such patients ...be started on lower doses and closely monitored.

...other nonsteroidal antiinflammatory drugs, the ...adverse effects of ketoprofen are gastrointestinal ...attempt to minimize these effects, physicians may ...prescribe that Orudis be taken with antacids, food, or ...food affects the bioavailability of Orudis (see ..."Pharmacology"), in most of the clinical trials ...taken with food or milk.

...MODERATE PAIN AND DYSMENORRHEA

...dose of Orudis recommended for mild-to-moderate ...dysmenorrhea is 25 to 50 mg every 6 to 8 hours as ... A smaller dose should be utilized initially in small ..., in debilitated or elderly patients, or in patients ...or liver disease (see "Precautions"). A larger dose ...if the patient's response to a previous dose was ...satisfactory, but doses above 75 mg have not been ...added analgesia. Daily doses above 300 mg are ...recommended because they have not been adequately ...because of its typical nonsteroidal antiinflammatory ...side-effect profile, including as its principal adverse ...GI side effects (see "Warnings" and "Adverse ..."), higher doses of Orudis should be used with caution ...patients receiving them observed carefully.

...SUPPLIED

...(ketoprofen) Capsules, Wyeth®, are available as

...NDC 0008-4186, dark-green and red capsule marked ...4186" on one side and "ORUDIS 25" on the reverse ..., in bottles of 100 capsules.

...NDC 0008-4181, dark-green and light-green capsule ..."WYETH 4181" on one side and "ORUDIS 50" on ...side, in bottles of 100 capsules.

...NDC 0008-4187, dark-green and white capsule ..."WYETH 4187" on one side and "ORUDIS 75" on ...side, in bottles of 100 and 500 capsules, and in ...cartons each containing 10 blister strips of 10 ...

...tightly closed.
...in tight container.
...temperature, approx. 25° C (77° F).
...of these capsules is a trademark of Wyeth-Laboratories.

...in Product Identification Section, page 336

OVRAL® ℞

[oh'vral]

TABLETS

(norgestrel and ethinyl estradiol tablets)

Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

DESCRIPTION

Each Ovral tablet contains 0.5 mg of norgestrel (*dl*-13-beta-ethyl-17-alpha-ethinyl -17- beta-hydroxygon -4- en -3- one), a totally synthetic progestogen, and 0.05 mg of ethinyl estradiol (19-nor-17α-pregna-1,3,5 (10)-trien-20-yne-3,17-diol). The inactive ingredients present are cellulose, lactose, magnesium stearate, and polacrilin potassium.

CLINICAL PHARMACOLOGY

See LO/OVRAL®.

INDICATIONS AND USAGE

Oral contraceptives are indicated for the prevention of pregnancy in women who elect to use this product as a method of contraception.

Oral contraceptives are highly effective. Table I lists the typical accidental pregnancy rates for users of combination oral contraceptives and other methods of contraception. The efficacy of these contraceptive methods, except sterilization and the IUD, depends upon the reliability with which they are used. Correct and consistent use of methods can result in lower failure rates.

TABLE I: LOWEST EXPECTED AND TYPICAL FAILURE RATES DURING THE FIRST YEAR OF CONTINUOUS USE OF A METHOD

% of Women Experiencing an Accidental Pregnancy in the First Year of Continuous Use

Method	Lowest Expected*	Typical**
(No Contraception)	(89)	(89)
Oral contraceptives		3
combined	0.1	N/A***
progestin only	0.5	N/A***
Diaphragm with spermicidal cream or jelly	3	18
Spermicides alone (foam, creams, jellies and vaginal suppositories)	3	21
Vaginal Sponge		
nulliparous	5	18
multiparous	>8	>28
IUD (medicated)	1	6#
Condom without spermicides	2	12
Periodic abstinence (all methods)	2–10	20
Female sterilization	0.2	0.4
Male sterilization	0.1	0.15

Adapted from J. Trussell and K. Kost, Table 11, Studies in Family Planning, 18(5), Sept.–Oct. 1987.

* The authors' best guess of the percentage of women expected to experience an accidental pregnancy among couples who initiate a method (not necessarily for the first time) and who use it consistently and correctly during the first year if they do not stop for any other reason.

** This term represents "typical" couples who initiate use of a method (not necessarily for the first time), who experience an accidental pregnancy during the first year if they do not stop use for any other reason.

*** N/A—Data not available

\# Combined typical rate for both medicated and non-medicated IUD. The rate for medicated IUD alone is not available.

CONTRAINDICATIONS

See LO/OVRAL.

WARNINGS

See LO/OVRAL.

PRECAUTIONS

See LO/OVRAL.

Drug Interactions: See LO/OVRAL

Carcinogenesis: See LO/OVRAL

Pregnancy: See LO/OVRAL

Nursing Mothers: See LO/OVRAL

Information For The Patient: See LO/OVRAL.

ADVERSE REACTIONS

See LO/OVRAL.

OVERDOSAGE

See LO/OVRAL.

NONCONTRACEPTIVE HEALTH BENEFITS

See LO/OVRAL.

DOSAGE AND ADMINISTRATION

To achieve maximum contraceptive effectiveness, ... must be taken exactly as directed and at intervals ... ceeding 24 hours.

The dosage of Ovral is one tablet daily for 21 cons... days per menstrual cycle according to prescribed sc... Tablets are then discontinued for 7 days (three weeks ... week off).

It is recommended that Ovral tablets be taken at th... time each day, preferably after the evening meal or ... time.

During the first cycle of medication, the patient is inst... to take one Ovral tablet daily for twenty-one conse... days beginning on day five of her menstrual cycle. (Th... day of menstruation is day one.) The tablets are then ... tinued for one week (7 days). Withdrawal bleeding ... usually occur within three days following discontinua... Ovral. (If Ovral is first taken later than the fifth day ... first menstrual cycle of medication or postpartum, c... ceptive reliance should not be placed on Ovral until aft... first seven consecutive days of administration. The po... ity of ovulation and conception prior to initiation of m... tion should be considered.) The patient begins her nex... all subsequent 21-day courses of Ovral tablets on the ... day of the week that she began her first course, followi... same schedule: 21 days on—7 days off. She begins takin... tablets on the 8th day after discontinuance regardl... whether or not a menstrual period has occurred or is s... progress. Any time a new cycle of Ovral is started later ... the 8th day, the patient should be protected by an... means of contraception until she has taken a tablet dai... seven consecutive days.

If spotting or breakthrough bleeding occurs, the patie... instructed to continue on the same regimen. This ty... bleeding is usually transient and without significance; ... ever, if the bleeding is persistent or prolonged, the patie... advised to consult her physician. Although the occurren... pregnancy is highly unlikely if Ovral is taken accordi... directions, if withdrawal bleeding does not occur, the p... bility of pregnancy must be considered. If the patient ha... adhered to the prescribed schedule (missed one or more ... lets or started taking them on a day later than she sh... have), the probability of pregnancy should be considere... the time of the first missed period and appropriate diagn... measures taken before the medication is resumed. If the ... tient has adhered to the prescribed regimen and misses ... consecutive periods, pregnancy should be ruled out be... continuing the contraceptive regimen.

The patient should be instructed to take a missed table... soon as it is remembered. If two consecutive tablets ... missed, they should both be taken as soon as remembe... The next tablet should be taken at the usual time.

Any time the patient misses one or two tablets, she sh... also use another method of contraception until she has ta... a tablet daily for seven consecutive days. If breakthro... bleeding occurs following missed tablets, it will usuall... transient and of no consequence. While there is little lik... hood of ovulation occurring if only one or two tablets ... missed, the possibility of ovulation increases with each ... cessive day that scheduled tablets are missed. If three con... utive tablets are missed, all medication should be disco... ued and the remainder of the package discarded. A new ... let cycle should be started on the 8th day after the last ta... was taken, and an alternate means of contraception sho... be prescribed during the seven days without tablets and ... til the patient has taken a tablet daily for seven consecut... days.

In the nonlactating mother, Ovral may be initiated postp... tum, for contraception. When the tablets are administere... the postpartum period, the increased risk of thromboemb... disease associated with the postpartum period must be c... sidered (see Contraindications, Warnings, and Precauti... concerning thromboembolic disease). It is to be noted th... early resumption of ovulation may occur if Parlodel ... (bromocriptine mesylate) has been used for the prevention ... lactation.

HOW SUPPLIED

Ovral® Tablets (0.5 mg norgestrel and 0.05 mg ethinyl e... tradiol), Wyeth®, are available in packages of 6 PILPAK... dispensers with 21 tablets each as follows: NDC 0008-005... white, round tablet marked "WYETH" and "56".

References available upon request.

Brief Summary Patient Package Insert: See LO/OVRAL

DETAILED PATIENT LABELING: See LO/OVRAL.

Shown in Product Identification Section, page 336

Continued on next page

Wyeth-Ayerst Laboratories—Cont.

OVRAL®-28 ℞

[oh 'vral-28]
Tablets
(norgestrel and ethinyl estradiol tablets)

Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

DESCRIPTION

21 white Ovral tablets, each containing 0.5 mg of norgestrel (*dl*-13-beta-ethyl-17-alpha-ethinyl-17-beta-hydroxygon-4-en-3-one), a totally synthetic progestogen, and 0.05 mg of ethinyl estradiol (19-nor-17α-pregna-1,3,5 (10)-trien-20-yne-3,17-diol), and 7 pink inert tablets. The inactive ingredients present are cellulose, D&C Red 30, lactose, magnesium stearate, and polacrilin potassium.

CLINICAL PHARMACOLOGY

See LO/OVRAL®.

INDICATIONS AND USAGE

See OVRAL®.

CONTRAINDICATIONS

See LO/OVRAL.

WARNINGS

See LO/OVRAL.

PRECAUTIONS

See LO/OVRAL.
Drug Interactions: See LO/OVRAL.
Carcinogenesis: See LO/OVRAL.
Pregnancy: See LO/OVRAL.
Nursing Mothers: See LO/OVRAL.
Information for the Patient: See LO/OVRAL.

ADVERSE REACTIONS

See LO/OVRAL.

OVERDOSAGE

See LO/OVRAL.

NONCONTRACEPTIVE HEALTH BENEFITS

See LO/OVRAL

DOSAGE AND ADMINISTRATION

To achieve maximum contraceptive effectiveness, Ovral-28 must be taken exactly as directed and at intervals not exceeding 24 hours.

The dosage of Ovral-28 is one white tablet daily for 21 consecutive days followed by one pink inert tablet daily for 7 consecutive days according to prescribed schedule. It is recommended that OVRAL-28 tablets be taken at the same time each day, preferably after the evening meal or at bedtime. During the first cycle of medication, the patient is instructed to begin taking Ovral-28 on the first Sunday after the onset of menstruation. If menstruation begins on a Sunday, the first tablet (white) is taken that day. One white tablet should be taken daily for 21 consecutive days followed by one pink inert tablet daily for 7 consecutive days. Withdrawal bleeding should usually occur within three days following discontinuation of white tablets. During the first cycle, contraceptive reliance should not be placed on Ovral-28 until a white tablet has been taken daily for 7 consecutive days. The possibility of ovulation and conception prior to initiation of medication should be considered.

The patient begins her next and all subsequent 28-day courses of tablets on the same day of the week (Sunday) on which she began her first course, following the same schedule: 21 days on white tablets—7 days on pink inert tablets. If in any cycle the patient starts tablets later than the proper day, she should protect herself by using another method of birth control until she has taken a white tablet daily for 7 consecutive days.

If spotting or breakthrough bleeding occurs, the patient is instructed to continue on the same regimen. This type of bleeding is usually transient and without significance; however, if the bleeding is persistent or prolonged, the patient is advised to consult her physician. Although the occurrence of pregnancy is highly unlikely if Ovral-28 is taken according to directions, if withdrawal bleeding does not occur, the possibility of pregnancy must be considered. If the patient has not adhered to the prescribed schedule (missed one or more tablets or started taking them on a day later than she should have), the probability of pregnancy should be considered at the time of the first missed period and appropriate diagnostic measures taken before the medication is resumed. If the patient has adhered to the prescribed regimen and misses two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen.

The patient should be instructed to take a missed white tablet as soon as it is remembered. If two consecutive white tablets are missed they should both be taken as soon as remembered. The next tablet should be taken at the usual time. Any time the patient misses one or two white tablets she should also use another method of contraception until she has taken a white tablet daily for seven consecutive days. If the patient misses one or more pink tablets she is still protected against pregnancy provided she begins taking white tablets again on the proper day.

If breakthrough bleeding occurs following missed white tablets, it will usually be transient and of no consequence. While there is little likelihood of ovulation occurring if only one or two white tablets are missed, the possibility of ovulation increases with each successive day that scheduled white tablets are missed. If three consecutive white Ovral tablets are missed, all medication should be discontinued and the remainder of the 28-day package discarded. A new tablet cycle should be started on the first Sunday following the last missed tablet, and an alternate means of contraception should be prescribed during the days without tablets and until the patient has taken a white tablet daily for 7 consecutive days.

In the nonlactating mother, Ovral-28 may be initiated postpartum, for contraception. When the tablets are administered in the postpartum period, the increased risk of thromboembolic disease associated with the postpartum period must be considered (see Contraindications, Warnings, and Precautions concerning thromboembolic disease). It is to be noted that early resumption of ovulation may occur if Parlodel® (bromocriptine mesylate) has been used for the prevention of lactation.

HOW SUPPLIED

Ovral®-28 Tablets (0.5 mg norgestrel and 0.05 mg ethinyl estradiol), Wyeth®, are available in packages of 6 PIL-PAK® dispensers, each containing 28 tablets as follows:
21 active tablets, NDC 0008-0056, white, round tablet marked "WYETH" and "56".
7 inert tablets, NDC 0008-0445, pink, round tablet marked "WYETH" and "445".

References available upon request.
Brief Summary Patient Package Insert: See LO/OVRAL.
DETAILED PATIENT LABELING: See LO/OVRAL.
Shown in Product Identification Section, page 336

OVRETTE® ℞

[oh-vret']
Tablets
(norgestrel tablets)

Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

Each OVRETTE® tablet contains 0.075 mg of norgestrel (*dl*-13-beta-ethyl-17-alpha-ethinyl-17-beta-hydroxygon-4-en-3-one). The inactive ingredients present are cellulose, FD&C Yellow 5, lactose, magnesium stearate, and polacrilin potassium.

DESCRIPTION

Each OVRETTE tablet contains 0.075 mg of a single active steroid ingredient, norgestrel, a totally synthetic progestogen. The available data suggest that the *d* (-)enantiomeric form of norgestrel is the biologically active portion. This form amounts to 0.0375 mg per OVRETTE tablet.

CLINICAL PHARMACOLOGY

The primary mechanism through which OVRETTE prevents conception is not known, but progestogen-only contraceptives are known to alter the cervical mucus, exert a progestational effect on the endometrium, interfering with implantation, and, in some patients, suppress ovulation.

INDICATIONS AND USAGE

See LO/OVRAL®.

CONTRAINDICATIONS

See LO/OVRAL.

WARNINGS

See LO/OVRAL.

PRECAUTIONS

See LO/OVRAL.

INFORMATION FOR THE PATIENT

See LO/OVRAL.

DRUG INTERACTIONS

See LO/OVRAL.

CARCINOGENESIS

See LO/OVRAL.

PREGNANCY

See LO/OVRAL.

NURSING MOTHERS

See LO/OVRAL.

ADVERSE REACTIONS

See LO/OVRAL.

OVERDOSAGE

See LO/OVRAL.

DOSAGE AND ADMINISTRATION

To achieve maximum contraceptive effecti
OVRETTE (norgestrel) must be taken exactly as d
and at intervals not exceeding 24 hours. OVRETTE is
istered on a continuous daily dosage regimen starting
first day of menstruation, i.e., one tablet each day, eve
of the year.

Tablets should be taken at the same time each day ar
tinued daily, without interruption, whether bleeding
or not. The patient should be advised that, if prolonged
ing occurs, she should consult her physician. In the n
tating mother, OVRETTE may be initiated postpartu
contraception. When the tablets are administered
postpartum period, the increased risk of thromboe
disease associated with the postpartum period must b
sidered (see "Contraindications," "Warnings," and "P
tions" concerning thromboembolic disease). It is to be
that early resumption of ovulation may occur if Parl
(bromocriptine mesylate) has been used for the prevent
lactation.

The risk of pregnancy increases with each tablet miss
the patient misses one tablet, she should be instruct
take it as soon as she remembers and to also take her
tablet at the regular time. If she misses two tablets
should take one of the missed tablets as soon as she re
bers, as well as taking her regular tablet for that day
proper time. Furthermore, she should use a meth
nonhormonal contraception in addition to t
OVRETTE until fourteen tablets have been taken. If
than 2 tablets have been missed, OVRETTE should b
continued immediately and a method of nonhormonal
traception should be used until menses has appeared or
nancy has been excluded. If menses does not appear w
45 days from the last period, a method of nonhormonal
traception should be substituted until the start of the
menstrual period or an appropriate diagnostic procedu
performed to rule out pregnancy.

HOW SUPPLIED

OVRETTE® tablets (0.075 mg norgestrel), Wyeth®,
available in packages of 6 PILPAK® dispensers wit
tablets each as follows: NDC 0008-0062, yellow, round t
marked "WYETH" and "62".

REFERENCES

Available upon request.
Brief Summary Patient Package Insert: See LO/OVRA
DETAILED PATIENT LABELING: See LO/OVRAL.

OXYTOCIN

[ok "se-to 'sin]
Injection, USP
(synthetic)

DESCRIPTION

Each mL of TUBEX® Oxytocin Injection sterile solut
contains an oxytocic activity equivalent to 10 USP Poster
Pituitary Units, chlorobutanol (a chloroform derivati
0.5%, as a preservative, and acetic acid to adjust pH (2.5
4.5). Oxytocin is intended for IM or IV use. Oxytocin is a s
thetic polypeptide; it occurs as a white powder and is solu
in water.

CLINICAL PHARMACOLOGY

The pharmacologic and clinical properties of oxytocin a
identical with those of the naturally occurring oxytocin pri
ciple of the posterior lobe of the pituitary. Oxytocin exerts
selective action on the smooth musculature of the uter
particularly toward the end of pregnancy, during labor, a
immediately following delivery. Oxytocin stimulates rhyt
mic contractions of the uterus, increases the frequency
existing contractions, and raises the tone of the uterine mu
culature.

When given in appropriate doses during pregnancy, oxytoc
is capable of eliciting graded increases in uterine motili
from a moderate increase in the rate and force of spontan
ous motor activity to sustained tetanic contraction. The se
sitivity of the uterus to oxytocic activity increases progre
sively throughout pregnancy until term when it is maximal
Oxytocin is distributed throughout the extracellular fluid
Small amounts of this drug probably reach the fetal circula
tion. Oxytocin has a plasma half-life of about 3 to 5 minutes
Following parenteral administration, uterine response oc
curs within 3 to 5 minutes and persists for 2 to 3 hours. Its
rapid removal from plasma is accomplished largely by the
kidney and the liver. Only small amounts of oxytocin are
excreted in the urine unchanged.

INDICATIONS

Mysoline, used alone or concomitantly with other anticonvulsants, is indicated in the control of grand mal, psychomotor, and focal epileptic seizures. It may control grand mal seizures refractory to other anticonvulsant therapy.

CONTRAINDICATIONS

Primidone is contraindicated in: 1) patients with porphyria and 2) patients who are hypersensitive to phenobarbital (see ACTIONS).

WARNINGS

The abrupt withdrawal of antiepileptic medication may precipitate status epilepticus.

The therapeutic efficacy of a dosage regimen takes several weeks before it can be assessed.

USAGE IN PREGNANCY

The effects of Mysoline in human pregnancy and nursing infants are unknown.

Recent reports suggest an association between the use of anticonvulsant drugs by women with epilepsy and an elevated incidence of birth defects in children born to these women. Data are more extensive with respect to diphenylhydantoin and phenobarbital, but these are also the most commonly prescribed anticonvulsants; less systematic or anecdotal reports suggest a possible similar association with the use of all known anticonvulsant drugs.

The reports suggesting an elevated incidence of birth defects in children of drug-treated epileptic women cannot be regarded as adequate to prove a definite cause and effect relationship. There are intrinsic methodologic problems in obtaining adequate data on drug teratogenicity in humans; the possibility also exists that other factors leading to birth defects, *e.g.*, genetic factors or the epileptic condition itself, may be more important than drug therapy. The majority of mothers on anticonvulsant medication deliver normal infants. It is important to note that anticonvulsant drugs should not be discontinued in patients in whom the drug is administered to prevent major seizures because of the strong possibility of precipitating status epilepticus with attendant hypoxia and threat to life. In individual cases where the severity and frequency of the seizure disorders are such that the removal of medication does not pose a serious threat to the patient, discontinuation of the drug may be considered prior to and during pregnancy, although it cannot be said with any confidence that even minor seizures do not pose some hazard to the developing embryo or fetus.

The prescribing physician will wish to weigh these considerations in treating or counseling epileptic women of childbearing potential.

Neonatal hemorrhage, with a coagulation defect resembling vitamin K deficiency, has been described in newborns whose mothers were taking primidone and other anticonvulsants. Pregnant women under anticonvulsant therapy should receive prophylactic vitamin K_1 therapy for one month prior to, and during, delivery.

PRECAUTIONS

The total daily dosage should not exceed 2 g. Since Mysoline therapy generally extends over prolonged periods, a complete blood count and a sequential multiple analysis-12 (SMA-12) test should be made every six months.

IN NURSING MOTHERS

There is evidence that in mothers treated with primidone, the drug appears in the milk in substantial quantities. Since tests for the presence of primidone in biological fluids are too complex to be carried out in the average clinical laboratory, it is suggested that the presence of undue somnolence and drowsiness in nursing newborns of Mysoline-treated mothers be taken as an indication that nursing should be discontinued.

ADVERSE REACTIONS

The most frequently occurring early side effects are ataxia and vertigo. These tend to disappear with continued therapy, or with reduction of initial dosage. Occasionally, the following have been reported: nausea, anorexia, vomiting, fatigue, hyperirritability, emotional disturbances, sexual impotency, diplopia, nystagmus, drowsiness, and morbilliform skin eruptions. Granulocytopenia, and red-cell hypoplasia and aplasia, have been reported rarely. These and, occasionally, other persistent or severe side effects may necessitate withdrawal of the drug. Megaloblastic anemia may occur as a rare idiosyncrasy to Mysoline and to other anticonvulsants. The anemia responds to folic acid without necessity of discontinuing medication.

DOSAGE AND ADMINISTRATION

ADULT DOSAGE

Patients 8 years of age and older who have received no previous treatment may be started on Mysoline according to the following regimen using either 50 mg or scored 250 mg Mysoline tablets.

Days 1 to 3: 100 to 125 mg at bedtime
Days 4 to 6: 100 to 125 mg b.i.d.
Days 7 to 9: 100 to 125 mg t.i.d.
Day 10 to maintenance: 250 mg t.i.d.

For most adults and children 8 years of age and over, the usual maintenance dosage is three to four 250 mg Mysoline tablets daily in divided doses (250 mg t.i.d. or q.i.d.). If required, an increase to five or six 250 mg tablets daily may be made but daily doses should not exceed 500 mg q.i.d.

INITIAL: ADULTS AND CHILDREN OVER 8

KEY: ·=50 mg tablet •=250 mg tablet

DAY	1	2	3	4	5	6
AM	·			· ·	· ·	· ·
NOON			·			
PM	· ·	· ·	· ·	· ·	· ·	· ·

DAY	7	8	9	10	11	12
AM	· ·	· ·	· ·	•		
NOON	· ·	· ·	· ·	•	Adjust to	
PM	· ·	· ·	· ·	•	Maintenance	

Dosage should be individualized to provide maximum benefit. In some cases, serum blood level determinations of primidone may be necessary for optimal dosage adjustment. The clinically effective serum level for primidone is between 5 to 12 µg/mL.

IN PATIENTS ALREADY RECEIVING OTHER ANTICONVULSANTS

Mysoline should be started at 100 to 125 mg at bedtime and gradually increased to maintenance level as the other drug is gradually decreased. This regimen should be continued until satisfactory dosage level is achieved for the combination, or the other medication is completely withdrawn. When therapy with Mysoline alone is the objective, the transition from concomitant therapy should not be completed in less than two weeks.

PEDIATRIC DOSAGE

For children under 8 years of age, the following regimen may be used:

Days 1 to 3: 50 mg at bedtime
Days 4 to 6: 50 mg b.i.d.
Days 7 to 9: 100 mg b.i.d.
Day 10 to maintenance: 125 mg t.i.d. to 250 mg t.i.d.

For children under 8 years of age, the usual maintenance dosage is 125 to 250 mg three times daily or, 10 to 25 mg/kg/day in divided doses.

HOW SUPPLIED

MYSOLINE TABLETS

Each square-shaped, scored, yellow tablet, identified by "MYSOLINE 250" and an embossed *M*, contains 250 mg of primidone, in bottles of 100 (NDC 0046-0430-81) and 1,000 (NDC 0046-0430-91).

Also available in a unit-dose package of 100 (NDC 0046-0430-99).

Each square-shaped, scored, white tablet, identified by "MYSOLINE 50 " and an embossed *M*, contains 50 mg of primidone, in bottles of 100 (NDC 0046-0431-81) and 500 (NDC 0046-0431-85).

The appearance of these tablets is a trademark of Wyeth-Ayerst Laboratories.

MYSOLINE SUSPENSION

Each 5 mL (teaspoonful) contains 250 mg of primidone, in bottles of 8 fluid ounces (NDC 0046-3850-08).

Store at room temperature, approximately 25° C (77° F). Dispense in a tight, light-resistant container as defined in the U.S.P.

Shown in Product Identification Section, page 336

NORDETTE®-21 ℞

[nor-det'-21]

TABLETS

(levonorgestrel and ethinyl estradiol tablets)

Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

DESCRIPTION

ORAL CONTRACEPTIVE

Each Nordette tablet contains 0.15 mg of levonorgestrel (d-(-)-13 beta-ethyl-17-alpha-ethinyl-17-beta-hydroxygon-4-en-3-one), a totally synthetic progestogen, and 0.03 mg of ethinyl estradiol (19-nor-17α-pregna-1,3,5 (10)-trien-20-yne-3,17-diol). The inactive ingredients present are cellulose, FD&C Yellow 6, lactose, magnesium stearate, and polacrilin potassium.

CLINICAL PHARMACOLOGY

Combination oral contraceptives act by suppression nadotropins. Although the primary mechanism of this is inhibition of ovulation, other alterations include ch in the cervical mucus (which increase the difficulty of entry into the uterus) and the endometrium (which the likelihood of implantation).

INDICATIONS AND USAGE

Oral contraceptives are indicated for the prevention o nancy in women who elect to use this product as a met contraception.

Oral contraceptives are highly effective. Table I lis typical accidental pregnancy rates for users of combi oral contraceptives and other methods of contraceptio efficacy of these contraceptive methods, except sterili and the IUD, depends upon the reliability with which are used. Correct and consistent use of methods can re lower failure rates.

TABLE I: LOWEST EXPECTED AND TYPICAL FAI RATES DURING THE FIRST YEAR OF CONTINU USE OF A METHOD

% of Women Experiencing an Accidental Pregnancy First Year of Continuous Use

Method	Lowest Expected*	Typi
(No Contraception)	(89)	(8
Oral contraceptives		
combined	0.1	N/A
progestin only	0.5	N/A
Diaphragm with spermicidal cream or jelly	3	18
Spermicides alone (foam, creams, jellies and vaginal suppositories)	3	21
Vaginal Sponge		
nulliparous	5	18
multiparous	> 8	> 28
IUD (medicated)	1	6
Condom without spermicides	2	12
Periodic abstinence (all methods)	2–10	20
Female sterilization	0.2	0.
Male sterilization	0.1	0.

Adapted from J. Trussell and K. Kost, Table 11, Studi Family Planning, 18(5), Sept.–Oct. 1987.

* The authors' best guess of the percentage of wome pected to experience an accidental pregnancy an couples who initiate a method (not necessarily for first time) and who use it consistently and correctly ing the first year if they do not stop for any other rea

** This term represents "typical" couples who initiate of a method (not necessarily for the first time), who e rience an accidental pregnancy during the first ye they do not stop use for any other reason.

*** N/A—Data not available

\# Combined typical rate for both medicated and medicated IUD. The rate for medicated IUD alone is available.

CONTRAINDICATIONS

Oral contraceptives should not be used in women with ar the following conditions:

Thrombophlebitis or thromboembolic disorders
A past history of deep-vein thrombophlebitis or thror embolic disorders
Cerebral-vascular or coronary-artery disease
Known or suspected carcinoma of the breast
Carcinoma of the endometrium or other known or pected estrogen-dependent neoplasia
Undiagnosed abnormal genital bleeding
Cholestatic jaundice of pregnancy or jaundice with p pill use
Hepatic adenomas or carcinomas
Known or suspected pregnancy

WARNINGS

Cigarette smoking increases the risk of serious cardiovascular side effects from oral-contraceptive use. This risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives should be strongly advised not to smoke.

The use of oral contraceptives is associated with increase risks of several serious conditions including myocardial i

Continued on next page

Wyeth-Ayerst Laboratories—Cont.

Decreased incidence of acute pelvic inflammatory disease
Decreased incidence of endometrial cancer
Decreased incidence of ovarian cancer

DOSAGE AND ADMINISTRATION

To achieve maximum contraceptive effectiveness, Nordette-21 must be taken exactly as directed and at intervals not exceeding 24 hours. The dosage of Nordette-21 is one tablet daily for 21 consecutive days per menstrual cycle according to prescribed schedule. Tablets are then discontinued for 7 days (three weeks on, one week off).

It is recommended that Nordette-21 tablets be taken at the same time each day, preferably after the evening meal or at bedtime. During the first cycle of medication, the patient is instructed to take one Nordette-21 tablet daily for twenty-one consecutive days beginning on day five of her menstrual cycle. (The first day of menstruation is day one.) The tablets are then discontinued for one week (7 days). Withdrawal bleeding should usually occur within three days following discontinuation of Nordette-21.

(If Nordette-21 is first taken later than the fifth day of the first menstrual cycle of medication or postpartum, contraceptive reliance should not be placed on Nordette-21 until after the first seven consecutive days of administration. The possibility of ovulation and conception prior to initiation of medication should be considered.)

The patient begins her next and all subsequent 21-day courses of Nordette-21 tablets on the same day of the week that she began her first course, following the same schedule: 21 days on—7 days off. She begins taking her tablets on the 8th day after discontinuance regardless of whether or not a menstrual period has occurred or is still in progress. Any time a new cycle of Nordette-21 is started later than the 8th day, the patient should be protected by another means of contraception until she has taken a tablet daily for seven consecutive days.

If spotting or breakthrough bleeding occurs, the patient is instructed to continue on the same regimen. This type of bleeding is usually transient and without significance; however, if the bleeding is persistent or prolonged the patient is advised to consult her physician. Although the occurrence of pregnancy is highly unlikely if Nordette-21 is taken according to directions, if withdrawal bleeding does not occur, the possibility of pregnancy must be considered. If the patient has not adhered to the prescribed schedule (missed one or more tablets or started taking them on a day later than she should have) the probability of pregnancy should be considered at the time of the first missed period and appropriate diagnostic measures taken before the medication is resumed. If the patient has adhered to the prescribed regimen and misses two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen.

The patient should be instructed to take a missed tablet as soon as it is remembered. If two consecutive tablets are missed, they should both be taken as soon as remembered. The next tablet should be taken at the usual time.

Any time the patient misses one or two tablets she should also use another method of contraception until she has taken a tablet daily for seven consecutive days. If breakthrough bleeding occurs following missed tablets it will usually be transient and of no consequence. While there is little likelihood of ovulation occurring if only one or two tablets are missed, the possibility of ovulation increases with each successive day that scheduled tablets are missed. If three consecutive tablets are missed, all medication should be discontinued and the remainder of the package discarded. A new tablet cycle should be started on the 8th day after the last tablet was taken, and an alternate means of contraception should be prescribed during the seven days without tablets and until the patient has taken a tablet daily for seven consecutive days.

In the nonlactating mother, Nordette-21 may be initiated postpartum, for contraception. When the tablets are administered in the postpartum period, the increased risk of thromboembolic disease associated with the postpartum period must be considered (see "Contraindications," "Warnings," and "Precautions" concerning thromboembolic disease). It is to be noted that early resumption of ovulation may occur if Parlodel® (bromocriptine mesylate) has been used for the prevention of lactation.

HOW SUPPLIED

Nordette®-21 Tablets (0.15 mg levonorgestrel and 0.03 mg ethinyl estradiol) are available in 6 PILPAK® dispensers of 21 tablets each as follows: NDC 0008-0075, light-orange, round tablet marked "WYETH" and "75".

References available upon request.

Brief Summary Patient Package Insert: See Lo/Ovral.

DETAILED PATIENT LABELING: See Lo/Ovral.

Shown in Product Identification Section, page 336

NORDETTE®-28 ℞

[nor-det'-28]

TABLETS

(levonorgestrel and ethinyl estradiol tablets)

Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

DESCRIPTION

21 light-orange Nordette tablets, each containing 0.15 mg of levonorgestrel (*d*(-)-13 beta-ethyl-17-alpha-ethinyl-17-beta-hydroxygon-4-en-3-one), a totally synthetic progestogen, and 0.03 mg of ethinyl estradiol (19-nor-17α-pregna-1,3,5 (10)-trien-20-yne-3,17-diol), and 7 pink inert tablets. The inactive ingredients present are cellulose, D&C Red 30, FD&C Yellow 6, lactose, magnesium stearate, and polacrilin potassium.

CLINICAL PHARMACOLOGY

See NORDETTE®-21

INDICATIONS AND USAGE

See NORDETTE-21

CONTRAINDICATIONS

See NORDETTE-21

WARNINGS

See NORDETTE-21

PRECAUTIONS

See NORDETTE-21

Drug Interactions: See NORDETTE-21

Carcinogenesis: See NORDETTE-21

Nursing Mothers: See NORDETTE-21

Information for the Patient: See LO/OVRAL.

ADVERSE REACTIONS

See NORDETTE-21

OVERDOSAGE

See NORDETTE-21

NONCONTRACEPTIVE HEALTH BENEFITS

See NORDETTE-21

DOSAGE AND ADMINISTRATION

To achieve maximum contraceptive effectiveness, Nordette-28 must be taken exactly as directed and at intervals not exceeding 24 hours.

The dosage of Nordette-28 is one light-orange tablet daily for 21 consecutive days, followed by one pink inert tablet daily for 7 consecutive days, according to prescribed schedule.

It is recommended that tablets be taken at the same time each day, preferably after the evening meal or at bedtime. During the first cycle of medication, the patient is instructed to begin taking Nordette-28 on the first Sunday after the onset of menstruation. If menstruation begins on a Sunday, the first tablet (light-orange) is taken that day. One light-orange tablet should be taken daily for 21 consecutive days, followed by one pink inert tablet daily for 7 consecutive days. Withdrawal bleeding should usually occur within three days following discontinuation of light-orange tablets.

During the first cycle, contraceptive reliance should not be placed on Nordette-28 until a light-orange tablet has been taken daily for 7 consecutive days. The possibility of ovulation and conception prior to initiation of medication should be considered.

The patient begins her next and all subsequent 28-day courses of tablets on the same day of the week (Sunday) on which she began her first course, following the same schedule: 21 days on light-orange tablets—7 days on pink inert tablets. If in any cycle the patient starts tablets later than the proper day, she should protect herself by using another method of birth control until she has taken a light-orange tablet daily for 7 consecutive days.

If spotting or breakthrough bleeding occurs, the patient is instructed to continue on the same regimen. This type of bleeding is usually transient and without significance; however, if the bleeding is persistent or prolonged, the patient is advised to consult her physician. Although the occurrence of pregnancy is highly unlikely if Nordette-28 is taken according to directions, if withdrawal bleeding does not occur, the possibility of pregnancy must be considered. If the patient has not adhered to the prescribed schedule (missed one or more tablets or started taking them on a day later than she should have), the probability of pregnancy should be considered at the time of the first missed period and appropriate diagnostic measures taken before the medication is resumed. If the patient has adhered to the prescribed regimen and misses two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen.

The patient should be instructed to take a missed light-orange tablet as soon as it is remembered. If two consecutive light-orange tablets are missed, they should both be taken as soon as remembered. The next tablet should be taken at the usual time.

Any time the patient misses one or two light-orange tablets, she should also use another method of contraception until she has taken a light-orange tablet daily for seven consecutive days. If the patient misses one or more pink ta... is still protected against pregnancy provided she b... ing light-orange tablets again on the proper day. If breakthrough bleeding occurs following mis... orange tablets, it will usually be transient and of ... quence. While there is little likelihood of ovulation ... if only one or two light-orange tablets are missed, ... bility of ovulation increases with each successive ... scheduled light-orange tablets are missed. If three ... tive light-orange Nordette tablets are missed, all ... should be discontinued and the remainder of th... package discarded. A new tablet cycle should be s... the first Sunday following the last missed tablet, ... ternate means of contraception should be prescribe... the days without tablets and until the patient ha... light-orange tablet daily for 7 consecutive days.

In the nonlactating mother, Nordette-28 may be i... postpartum, for contraception. When the tablets ar... istered in the postpartum period, the increased ... thromboembolic disease associated with the po... period must be considered (see Contraindications, W... and Precautions concerning thromboembolic disease... be noted that early resumption of ovulation may ... Parlodel® (bromocriptine mesylate) has been use... prevention of lactation.

HOW SUPPLIED

Nordette®-28 Tablets (0.15 mg levonorgestrel and ... ethinyl estradiol) are available in 6 PILPAK® di... each containing 28 tablets as follows:

21 active tablets, NDC 0008-2533, light-orange, ro... marked "WYETH" and "75".

7 inert tablets, NDC 0008-0486, pink, round tablet ... "WYETH" and "486".

References available upon request.

Brief Summary Patient Package Insert: See LO/O...

DETAILED PATIENT LABELING: See LO/OVRAL.

Shown in Product Identification Section, page ...

NORPLANT® SYSTEM

(levonorgestrel implants)

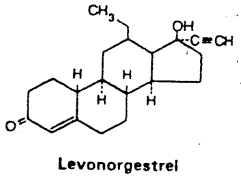
Patients should be counseled that this product ... protect against HIV infection (AIDS) and other ... transmitted diseases.

DESCRIPTION

The NORPLANT SYSTEM kit contains levonorg... plants, a set of six flexible closed capsules made of ... (dimethylsiloxane/methylvinylsiloxane copolym... containing 36 mg of the progestin levonorgestrel ... in an insertion kit to facilitate implantation. The ... are sealed with Silastic (polydimethylsiloxane) ad... sterilized. Each capsule is 2.4 mm in diameter and ... length. The capsules are inserted in a superficial ... neath the skin of the upper arm.

Information contained herewith regarding safety ... cacy was derived from studies which used two slight... ent Silastic tubing formulations. The formulation ... in the NORPLANT SYSTEM has slightly higher ... rates of levonorgestrel and at least comparable ... Evidence indicates that the dose of levonorgestrel ... by the NORPLANT SYSTEM is initially about 85 ... followed by a decline to about 50 mcg/day by 9 mo... about 35 mcg/day by 18 months with a further decl... after to about 30 mcg/day. The NORPLANT SYS... progestin-only product and does not contain estro...

Levonorgestrel, (d(-)-13-beta-ethyl-17-alpha-ethiny... hydroxygon-4-en-3-one), the active ingredient in ... PLANT SYSTEM, has a molecular weight of 312.4... following structural formula:



Levonorgestrel

CLINICAL PHARMACOLOGY

Levonorgestrel is a totally synthetic and biologic... progestin which exhibits no significant estrogen... and is highly progestational. The absolute co... conforms to that of D-natural steroids. Levonorge... subjected to a "first-pass" effect and is virtually ... available. Plasma concentrations average ap... 0.30 ng/mL over 5 years but are highly variable ... of individual metabolism and body weight.

Diffusion of levonorgestrel through the wall of ea... provides a continuous low dose of the progestin. ... blood levels are substantially below those generally ... among users of combination oral contraceptives ... the progestins norgestrel or levonorgestrel. Bec...

[illegible] given Lodine, or any other [illegible] patients with altered renal [illegible] for the development of the spe- [illegible] drugs.

[illegible] peak serum concentrations [illegible] in humans, show that the [illegible] significantly altered by acetami- [illegible], naproxen, piroxicam, [illegible] glyburide, phenytoin, and proben- [illegible] causes an increase (by [illegible] of etodolac. Although *in vivo* [illegible] to see if etodolac clearance is [illegible] of phenylbutazone, it is not [illegible] be coadministered.

[illegible] TEST INTERACTIONS

[illegible] Lodine can give a false-posi- [illegible] bilirubin (urobilin) due to the pres- [illegible] of etodolac.

[illegible], used to detect ketone bod- [illegible] false-positive findings in some [illegible] Lodine. Generally, this phenomenon [illegible] with other clinically significant [illegible] has been observed.

[illegible] with a small decrease in [illegible] clinical trials, mean decreases of 1 [illegible] in arthritic patients receiving [illegible] mg/day) after 4 weeks of therapy, [illegible] stable for up to one year of ther-

[illegible] MUTAGENESIS, AND IMPAIR-

[illegible] etodolac was observed in mice or [illegible] 15 mg/kg/day (45 to 89 mg/m^2, [illegible] periods of 2 years or 18 months, re- [illegible] not mutagenic in *in vitro* tests per- [illegible] and mouse lymphoma cells as [illegible] micronucleus test. However, data [illegible] peripheral lymphocyte test showed [illegible] in the number of gaps (3.0 to 5.3% [illegible] chromatid without dislocation) [illegible] cultures (50 to 200 μg/mL) com- [illegible] (2.0%); no other difference was [illegible] and drug-treated groups. Etodo- [illegible] of fertility in male and female [illegible] 16 mg/kg (94 mg/m^2). However, re- [illegible] fertilized eggs occurred in the 8 mg/kg

[illegible] PREGNANCY CATEGORY C

[illegible] occurrences of alterations in [illegible] found and included polydactyly, [illegible] and unossified phalanges in rats [illegible] of metatarsals in rabbits. [illegible] levels (2 to 14 mg/kg/day) close [illegible] However, the frequency and the [illegible] of these findings in initial or re- [illegible] a clear drug or dose-response

[illegible] well-controlled studies in pregnant [illegible] used during pregnancy only if the [illegible] the potential risk of the fetus. [illegible] effects of NSAIDs on parturition and [illegible] cardiovascular system with respect to [illegible], use during late pregnancy

[illegible], as with other drugs known to [illegible] synthesis, an increased incidence of [illegible], and decreased pup survival [illegible] Lodine on labor and delivery in preg-

[illegible] if Lodine is administered to a [illegible] many drugs are excreted in human [illegible] whether etodolac is excreted in human

[illegible] in children have not been estab-

[illegible]ATION

[illegible] older, no substantial differences in [illegible] the side-effect profile of Lodine [illegible] the general population. Therefore, [illegible] is generally necessary in the elderly. [illegible], caution should be exercised in [illegible] when individualizing their dosage, [illegible] when increasing the dose because [illegible] NSAID side effects less well than [illegible] PHARMACOKINETICS).

[illegible]TIONS

[illegible] for Lodine was derived from [illegible] treated with Lodine in double-blind [illegible] trials of 4 to 320 weeks in duration [illegible] surveillance studies in ap- [illegible] patients.

In clinical trials, most adverse reactions were mild and transient. The discontinuation rate in controlled clinical trials, because of adverse events, was 9% for patients treated with Lodine.

New patient complaints (with an incidence greater than or equal to 1%) are listed below by body system. The incidences were determined from clinical trials involving 465 patients with osteoarthritis treated with 300 to 500 mg of Lodine b.i.d. (i.e., 600 to 1000 mg per day).

INCIDENCE GREATER THAN OR EQUAL TO 1%—PROBABLY CAUSALLY RELATED.

Body as a whole—Chills and fever.

Digestive system—Dyspepsia (10%), abdominal pain*, diarrhea*, flatulence*, nausea*, constipation, gastritis, melena, vomiting.

Nervous system—Asthenia/malaise*, dizziness*, depression, nervousness.

Skin and appendages—Pruritus, rash.

Special senses—Blurred vision, tinnitus.

Urogenital system—Dysuria, urinary frequency.

INCIDENCE LESS THAN 1%—PROBABLY CAUSALLY RELATED (Adverse reactions reported only in worldwide postmarketing experience, not seen in clinical trials, are considered rarer and are italicized.):

Cardiovascular system—Hypertension, congestive heart failure, flushing, palpitations, syncope.

Digestive system—Thirst, dry mouth, ulcerative stomatitis, anorexia, eructation, elevated liver enzymes, *cholestatic hepatitis*, hepatitis, *cholestatic jaundice, jaundice*, PUB (i.e., peptic ulcer with or without bleeding and/or perforation) *pancreatitis*.

Hemic and lymphatic system—Ecchymosis, anemia, thrombocytopenia, bleeding time increased, *agranulocytosis, hemolytic anemia, neutropenia, pancytopenia.*

Metabolic and nutritional—Edema, serum creatinine increase, *hyperglycemia in previously controlled diabetic patients.*

Nervous system—Insomnia, somnolence.

Respiratory system—Asthma.

Skin and appendages—Angioedema, sweating, urticaria, vesiculobullous rash, *cutaneous vasculitis with purpura, Stevens-Johnson Syndrome*, hyperpigmentation, *erythema multiforme.*

Special senses—Photophobia, transient visual disturbances.

Urogenital system—*Elevated BUN, renal failure, renal insufficiency, renal papillary necrosis.*

INCIDENCE LESS THAN 1%—CAUSAL RELATIONSHIP UNKNOWN (Medical events occurring under circumstances where causal relationship to Lodine is uncertain. These reactions are listed as alerting information for physicians):

Body as a whole—Infection.

Cardiovascular system—Arrhythmias, myocardial infarction.

Digestive system—Esophagitis with or without stricture or cardiospasm, colitis.

Hemic and lympathic system—Leukopenia.

Metabolic and nutritional—Change in weight.

Nervous system—Paresthesia, confusion.

Respiratory system—Bronchitis, dyspnea, pharyngitis, rhinitis; sinusitis.

Skin and appendages—Maculopapular rash, alopecia, skin peeling, photosensitivity.

Special senses—Conjunctivitis, deafness, taste perversion.

Urogenital system—Cystitis, hematuria, leukorrhea, renal calculus, interstitial nephritis, uterine bleeding irregularities.

DRUG ABUSE AND DEPENDENCE

Lodine is a non-narcotic drug. Several predictive animal studies indicated that Lodine has no addiction potential in humans.

OVERDOSAGE

Symptoms following acute NSAID overdose are usually limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain which are generally reversible with supportive care. Gastrointestinal bleeding can occur and coma has occurred following massive ibuprofen or mefenamic-acid overdose. Hypertension, acute renal failure, and respiratory depression may occur but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following overdose.

Patients should be managed by symptomatic and supportive care following an NSAID overdose. There are no specific antidotes. Gut decontamination may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose (5 to 10 times the usual dose). This should be accomplished via emesis and/or activated charcoal (60 to 100 g in adults, 1 to 2 g/kg in children) with an osmotic cathartic. Forced diuresis, alkalinization of the urine, hemodialysis or hemoperfusion would probably not be useful due to etodolac's high protein binding.

*Drug-related patient complaints occurring in 3 to 9% of patients treated with Lodine. Drug-related patient complaints occurring in fewer than 3%, but more than 1%, are unmarked.

One case of intentional etodolac overdosage has been reported (Human Toxicol. 1988; 7:203–4). This 53-year-old female ingested from 15 to 46 two-hundred mg etodolac capsules (3 to 8.6 grams). Plasma etodolac concentrations were measured frequently over the next 4 days. At 5 hours after ingestion (3 hours after gastric lavage) the plasma etodolac level was 22 μg/mL. These plasma levels and her subsequent recovery with no signs or symptoms of etodolac toxicity were consistent with systemic absorption of 600 to 800 mg. Her laboratory tests on admission showed a prolonged prothrombin time and a false-positive urine bilirubin (attributed to the phenolic etodolac metabolites).

DOSAGE AND ADMINISTRATION

ANALGESIA

The recommended dose of Lodine for acute pain is 200 to 400 mg every 6 to 8 hours, as needed, not to exceed a total daily dose of 1200 mg. For patients weighing 60 kg or less, the total daily dose of Lodine should not exceed 20 mg/kg. For more details see INDIVIDUALIZATION OF DOSAGE.

OSTEOARTHRITIS

The recommended dose of Lodine for the management of the signs and symptoms of osteoarthritis is initially 800 to 1200 mg/day in divided doses, followed by dosage adjustment within the range of 600 to 1200 mg/day given in divided doses: 400 mg t.i.d. or b.i.d.; 300 mg q.i.d., t.i.d., or b.i.d.; 200 mg q.i.d. or t.i.d.. The total daily dose of Lodine should not exceed 1200 mg. For patients weighing 60 kg or less, the total daily dose of Lodine should not exceed 20 mg/kg. For more details see INDIVIDUALIZATION OF DOSAGE.

HOW SUPPLIED

Lodine (etodolac) is available as:

LODINE® (etodolac) Capsules

200 mg capsules (light gray with one wide red band with LODINE 200/dark gray with two narrow red bands)

—in bottles of 100, NDC 0046-0738-81

—in unit-dose packages of 100, NDC 0046-0738-99

300 mg capsules (light gray with one wide red band with LODINE 300/light gray with two narrow red bands)

—in bottles of 100, NDC 0046-0739-81

—in unit-dose packages of 100, NDC 0046-0739-99

CAPSULES IN BOTTLES

Store at 15°-30°C (59°-86°F), protected from moisture.

CAPSULES IN UNIT-DOSE PACKAGES

Store at 15°-25°C (59°-77°F), protected from moisture. For institutional use only.

Lodine® (etodolac) Tablets

400 mg tablets (yellow-orange, oval, film-coated tablet, debossed LODINE 400 on one side)

—in bottles of 100, NDC 0046-0761-81

—in unit-dose packages of 100, NDC 0046-0761-99

TABLETS IN BOTTLES

Store at 15°-30°C (59°-86°F).

TABLETS IN UNIT-DOSE PACKAGES

Store at 15°-30°C (59°-86°F)

The appearance of these capsules is a registered trademark of Wyeth-Ayerst Laboratories, Philadelphia, PA.

Caution: Federal law prohibits dispensing without prescription.

Shown in Product Identification Section, page 335

LO/OVRAL® ℞

[lōh-ōh 'vral]

Tablets

(norgestrel and ethinyl estradiol tablets)

Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

DESCRIPTION

Each LO/OVRAL tablet contains 0.3 mg of norgestrel (*dl* -13-beta-ethyl -17- alpha-ethinyl -17- beta - hydroxygon - 4- en -3-one), a totally synthetic progestogen, and 0.03 mg of ethinyl estradiol (19-nor-17α-pregna-1,3,5 (10)-trien-20-yne-3,17-diol). The inactive ingredients present are cellulose, lactose, magnesium stearate, and polacrilin potassium.

CLINICAL PHARMACOLOGY

Combination oral contraceptives act by suppression of gonadotropins. Although the primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus (which increase the difficulty of sperm entry into the uterus) and the endometrium (which reduce the likelihood of implantation).

INDICATIONS AND USAGE

Oral contraceptives are indicated for the prevention of pregnancy in women who elect to use this product as a method of contraception.

Oral contraceptives are highly effective. Table 1 lists the typical accidental pregnancy rates for users of combination oral contraceptives and other methods of contraception. The

Continued on next page

ıancy occurring before be-
ısidered. Take one tablet
ıite or light-orange tablets
tablets. Your period will
er you take the last white
ıe during the time you are
alarmed if the amount of
e. The day after you have
ı a new Pilpak of tablets
e tablets first, just as you
tablet every day without
each new Pilpak will al-
ou start tablets later than
e another method of birth
ıite or light-orange tablet

;H BLEEDING:
ı menstrual periods which
through bleeding is a flow
iring sanitary protection.
eakthrough bleeding, and
: few cycles than in later
-e usually temporary and
nt to continue taking your
ersists for more than a few

e, the chance of becoming
! pill as soon as you realize
the risk of pregnancy in-
ou skip, it is very impor-

l each contain 21 active
'ilpak. Nordette-28, Ovral-
21 active white or light-
e tablets per Pilpak.
is quite small if you miss
ılet in a cycle. Of course,
, the chance increases. If
ts (Nordette-28, Ovral-28,
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Wait four more days—
ut tablets. Then begin a
he last tablet was taken.
blets, and until you have
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ıtrol.
al-28, or Lo/Ovral-28 and
ange tablets in a row, do
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ng the last missed tablet.
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Pilpak. During the days
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ecutive days, you should
by also using another

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ıenstrual period. Tablets
every day, without inter-
or not. If bleeding is pro-
sually heavy, you should

with each tablet missed.
: you take one tablet daily
take it as soon as you re-
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ular tablet for that day at
you should use another
n to taking Ovrette until
weeks) of medication.

If more than two tablets have been missed, Ovrette should be discontinued immediately and another method of birth control used until the start of your next menstrual period. Then you may resume taking Ovrette.

At times there may be no menstrual period after a cycle of pills. Therefore, if you miss one menstrual period but have taken the pills **exactly as you were supposed to**, continue as usual into the next cycle. If you have not taken the pills correctly and miss a menstrual period, or if you are taking mini-pills and it is 45 days or more from the start of your last menstrual period, you may be pregnant and should stop taking oral contraceptives until your doctor determines whether or not you are pregnant. Until you can get to your doctor, use another form of nonhormonal contraception. If two consecutive menstrual periods are missed, you should stop taking pills until it is determined by a physician whether you are pregnant.
If you do become pregnant while using oral contraceptives, the risk to the fetus is small, on the order of no more than one per thousand. You should, however, discuss the risks to the developing child with your doctor.
3. Pregnancy due to pill failure
The incidence of pill failure resulting in pregnancy is approximately less than 1.0% if taken every day as directed, but more typical failure rates are less than 3.0%. If failure does occur, the risk to the fetus is minimal.
4. Pregnancy after stopping the pill
There may be some delay in becoming pregnant after you stop using oral contraceptives, especially if you had irregular menstrual cycles before you used oral contraceptives. It may be advisable to postpone conception until you begin menstruating regularly once you have stopped taking the pill and desire pregnancy.
There does not appear to be any increase in birth defects in newborn babies when pregnancy occurs soon after stopping the pill.
5. Overdosage
Serious ill effects have not been reported following ingestion of large doses of oral contraceptives by young children. Overdosage may cause nausea and withdrawal bleeding in females. In case of overdosage, contact your health-care provider or pharmacist.
6. Other information
Your health-care provider will take a medical and family history before prescribing oral contraceptives and will examine you. You should be reexamined at least once a year. Be sure to inform your health-care provider if there is a family history of any of the conditions listed previously in this leaflet. Be sure to keep all appointments with your health-care provider, because this is a time to determine if there are early signs of side effects of oral-contraceptive use.
Do not use the drug for any condition other than the one for which it was prescribed. This drug has been prescribed specifically for you; do not give it to others who may want birth-control pills.
HEALTH BENEFITS FROM ORAL CONTRACEPTIVES
In addition to preventing pregnancy, use of oral contraceptives may provide certain benefits. They are:
- Menstrual cycles may become more regular
- Blood flow during menstruation may be lighter, and less iron may be lost. Therefore, anemia due to iron deficiency is less likely to occur.
- Pain or other symptoms during menstruation may be encountered less frequently
- Ovarian cysts may occur less frequently
- Ectopic (tubal) pregnancy may occur less frequently
- Noncancerous cysts or lumps in the breast may occur less frequently
- Acute pelvic inflammatory disease may occur less frequently
- Oral contraceptive use may provide some protection against developing two forms of cancer: cancer of the ovaries and cancer of the lining of the uterus.

If you want more information about birth-control pills, ask your doctor or pharmacist. They have a more technical leaflet called the Professional Labeling which you may wish to read.

Shown in Product Identification Section, page 335

LO/OVRAL®-28

℞

[lōh-oh 'vral-28]
Tablets
(norgestrel and ethinyl estradiol tablets)

Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

DESCRIPTION
21 white LO/OVRAL® tablets, each containing 0.3 mg of norgestrel (*dl*-13-beta-ethyl-17-alpha-ethinyl-17-beta-hydroxygon-4-en-3-one), a totally synthetic progestogen, and 0.03 mg of ethinyl estradiol (19-nor-17α-pregna-1,3,5(10)-trien-20-yne-3,17-diol), and 7 pink inert tablets. The inactive ingredients present are cellulose, D&C Red 30, lactose, magnesium stearate, and polacrilin potassium.

CLINICAL PHARMACOLOGY
See LO/OVRAL®.

INDICATIONS AND USAGE
See LO/OVRAL.

CONTRAINDICATIONS
See LO/OVRAL.

WARNINGS
See LO/OVRAL.

PRECAUTIONS
See LO/OVRAL.
Drug Interactions: See LO/OVRAL.
Carcinogenesis: See LO/OVRAL.
Pregnancy: See LO/OVRAL.
Nursing Mothers: See LO/OVRAL.
Information for the Patient: See LO/OVRAL.

ADVERSE REACTIONS
See LO/OVRAL.

OVERDOSAGE
See LO/OVRAL.

NONCONTRACEPTIVE HEALTH BENEFITS
See LO/OVRAL.

DOSAGE AND ADMINISTRATION
To achieve maximum contraceptive effectiveness, LO/OVRAL-28 must be taken exactly as directed and at intervals not exceeding 24 hours.
The dosage of LO/OVRAL-28 is one white tablet daily for 21 consecutive days followed by one pink inert tablet daily for 7 consecutive days according to prescribed schedule. It is recommended that tablets be taken at the same time each day, preferably after the evening meal or at bedtime.
During the first cycle of medication, the patient is instructed to begin taking LO/OVRAL-28 on the first Sunday after the onset of menstruation. If menstruation begins on a Sunday, the first tablet (white) is taken that day. One white tablet should be taken daily for 21 consecutive days followed by one pink inert tablet daily for 7 consecutive days. Withdrawal bleeding should usually occur within three days following discontinuation of white tablets. During the first cycle, contraceptive reliance should not be placed on LO/OVRAL-28 until a white tablet has been taken daily for 7 consecutive days. The possibility of ovulation and conception prior to initiation of medication should be considered.
The patient begins her next and all subsequent 28-day courses of tablets on the same day of the week (Sunday) on which she began her first course, following the same schedule: 21 days on white tablets—7 days on pink inert tablets. If in any cycle the patient starts tablets later than the proper day, she should protect herself by using another method of birth control until she has taken a white tablet daily for 7 consecutive days.
If spotting or breakthrough bleeding occurs, the patient is instructed to continue on the same regimen. This type of bleeding is usually transient and without significance; however, if the bleeding is persistent or prolonged the patient is advised to consult her physician. Although the occurrence of pregnancy is highly unlikely if LO/OVRAL-28 is taken according to directions, if withdrawal bleeding does not occur, the possibility of pregnancy must be considered. If the patient has not adhered to the prescribed schedule (missed one or more tablets or started taking them on a day later than she should have), the probability of pregnancy should be considered at the time of the first missed period and appropriate diagnostic measures taken before the medication is resumed. If the patient has adhered to the prescribed regimen and misses two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen.
The patient should be instructed to take a missed white tablet as soon as it is remembered. If two consecutive white tablets are missed, they should both be taken as soon as remembered. The next tablet should be taken at the usual time.
Any time the patient misses one or two white tablets, she should also use another method of contraception until she has taken a white tablet daily for seven consecutive days. If the patient misses one or more pink tablets she is still protected against pregnancy provided she begins taking white tablets again on the proper day.
If breakthrough bleeding occurs following missed white tablets, it will usually be transient and of no consequence. While there is little likelihood of ovulation occurring if only one or two white tablets are missed, the possibility of ovulation increases with each successive day that scheduled white tablets are missed. If three consecutive white LO/OVRAL tablets are missed, all medication should be discontinued and the remainder of the 28-day package discarded. A new tablet cycle should be started on the first Sunday following the last missed tablet, and an alternate means of contraception should be prescribed during the days without tablets and until the patient has taken a white tablet daily for 7 consecutive days.

In the nonlactating mother, LO
postpartum, for contraception.
istered in the postpartum p
thromboembolic disease asso
period must be considered (see
and Precautions concerning th
be noted that early resumpti
Parlodel® (bromocriptine me
prevention of lactation.

HOW SUPPLIED
LO/OVRAL®-28 Tablets (0.3
ethinyl estradiol) are availabl
dispensers, each containing 28
21 active tablets, NDC 000
marked "WYETH" and "78".
7 inert tablets, NDC 0008-048
"WYETH" and "486".

References available upon
Brief Summary Patient Packa
DETAILED PATIENT LABELIN
Shown in Product Identif

MAZANOR®

[maz 'a-nor]
(mazindol)

DESCRIPTION
Mazanor (mazindol) is an imid
It is chemically designated as
2,3-dihydro-5H-imidazo (2,1-a)
of 2-[2'-(p-chlorobenzoyl) phe
tablets contain 1 mg mazind
present are calcium sulfate, c
stearate, povidone, and talc.

HOW SUPPLIED
Mazanor® (mazindol) Tablets,
following dosage strength in b
1 mg, NDC 0008-0071, white,
"WYETH" and "71".
Keep tightly closed.
Store below 25° C (77° F).
Dispense in tight container.
For prescribing information, u
Wyeth-Ayerst Laboratories, P.O.
19101, or contact your local Wy
Shown in Product Identifi

MEPERGAN®

[mep 'er-gan]
(meperidine HCl and promethazine HCl) Injection

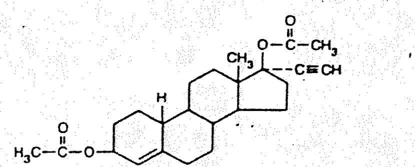
DESCRIPTION
This product is available in co
each of meperidine hydrochlori
chloride per mL with 0.1 mg ed
cium chloride, and not more th
hyde sulfoxylate, 0.25 mg sodi
phenol with sodium acetate bu

ACTIONS
Meperidine hydrochloride is a n
ple actions qualitatively simi
Phenergan®, promethazine HC
tive that has several different p
cluding antihistaminic, sedativ

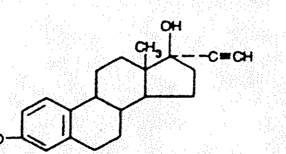
INDICATIONS
As a preanesthetic medication
are indicated. As an adjunct to l

CONTRAINDICATIONS
Hypersensitivity to meperidine
Under no circumstances should
arterial injection, due to the l
spasm and the possibility of resu
ings").
Mepergan should not be given
evidence of chemical irritation
lesions have resulted on rare oc
ous injection. The preferred par
tion is by deep, intramuscular i
Meperidine is contraindicated in
monoamine-oxidase inhibitors
received such agents within 14
Therapeutic doses of meperidine
tated unpredictable, severe, and
in patients who have received s
The mechanism of these reacti
been characterized by coma, se

Searle—Cont.



ethynodiol diacetate



ethinyl estradiol

Therapeutic class: Oral contraceptive.

CLINICAL PHARMACOLOGY

Combination oral contraceptives act primarily by suppression of gonadotropins. Although the primary mechanism of this action is inhibition of ovulation, other alterations in the genital tract, including changes in the cervical mucus (which increase the difficulty of sperm entry into the uterus) and the endometrium (which may reduce the likelihood of implantation) may also contribute to contraceptive effectiveness.

INDICATIONS AND USAGE

Demulen 1/35 and Demulen 1/50 are indicated for the prevention of pregnancy in women who elect to use oral contraceptives as a method of contraception.

Oral contraceptives are highly effective. Table 1 lists the typical accidental pregnancy rates for users of combination oral contraceptives and other methods of contraception. The efficacy of these contraceptive methods, except sterilization, depends upon the reliability with which they are used. Correct and consistent use of methods can result in lower failure rates.

Table 1. Lowest expected and typical failure rates during the first year of continuous use of a method. Percent of women experiencing an accidental pregnancy in the first year of continuous use.[1]

Method	Lowest Expected*	Typical**
No contraception	85	85
Oral contraceptives		
Combined	0.1	N/A***
Progestogen only	0.5	N/A***
Diaphragm with spermicidal cream or jelly	6	18
Spermicides alone (foam, creams, jellies and vaginal suppositories)	3	21
Vaginal sponge		
Nulliparous	6	18
Parous	9	28
IUD (medicated)		
Progesterone	2	N/A***
Copper T 380A	0.8	N/A***
Condom without spermicides	2	12
Periodic abstinence (all methods)	1-9	20
Female sterilization	0.2	0.4
Male sterilization	0.1	0.15

Adapted from Trussell et al.[1]

* The authors' best guess of the percentage of women expected to experience an accidental pregnancy among couples who initiate a method (not necessarily for the first time) and who use it consistently and correctly during the first year if they do not stop for any other reason.

** This term represents "typical" couples who initiate use of a method (not necessarily for the first time), who experience an accidental pregnancy during the first year if they do not stop for any other reason.

*** N/A—Data not available.

CONTRAINDICATIONS

Oral contraceptives should not be used in women who have the following conditions:

- Thrombophlebitis or thromboembolic disorders
- A past history of deep vein thrombophlebitis or thromboembolic disorders
- Cerebral vascular disease, myocardial infarction, or coronary artery disease, or a past history of these conditions
- Known or suspected carcinoma of the breast, or a history of this condition
- Known or suspected carcinoma of the female reproductive organs or suspected estrogen-dependent neoplasia, or a history of these conditions
- Undiagnosed abnormal genital bleeding
- History of cholestatic jaundice of pregnancy or jaundice with prior oral contraceptive use
- Past or present, benign or malignant liver tumors
- Known or suspected pregnancy

WARNINGS

Cigarette smoking increases the risk of serious cardiovascular side effects from oral contraceptive use. This risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives should be strongly advised not to smoke.

The use of oral contraceptives is associated with increased risk of several serious conditions including venous and arterial thromboembolism, thrombotic and hemorrhagic stroke, myocardial infarction, liver tumors or other liver lesions, and gallbladder disease. The risk of morbidity and mortality increases significantly in the presence of other risk factors such as hypertension, hyperlipidemia, obesity, and diabetes mellitus.

Practitioners prescribing oral contraceptives should be familiar with the following information relating to these and other risks.

The information contained herein is principally based on studies carried out in patients who used oral contraceptives with formulations containing higher amounts of estrogens and progestogens than those in common use today. The effect of long-term use of the oral contraceptives with lesser amounts of both estrogens and progestogens remains to be determined.

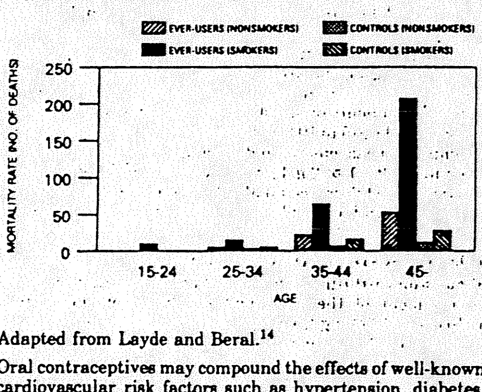
Throughout this labeling, epidemiological studies reported are of two types: retrospective case-control studies and prospective cohort studies. Case-control studies provide an estimate of the relative risk of a disease, which is defined as the *ratio* of the incidence of a disease among oral contraceptive users to that among nonusers. The relative risk (or odds ratio) does not provide information about the actual clinical occurrence of a disease. Cohort studies provide a measure of both the relative risk and the attributable risk. The latter is the *difference* in the incidence of disease between oral contraceptive users and nonusers. The attributable risk does provide information about the actual occurrence or incidence of a disease in the subject population. For further information, the reader is referred to a text on epidemiological methods.

1. Thromboembolic disorders and other vascular problems.

a. Myocardial Infarction. An increased risk of myocardial infarction has been associated with oral contraceptive use.[2-21] This increased risk is primarily in smokers or in women with other underlying risk factors for coronary artery disease such as hypertension, obesity, diabetes, and hypercholesterolemia. The relative risk for myocardial infarction in current oral contraceptive users has been estimated to be 2 to 6. The risk is very low under the age of 30. However, there is the possibility of a risk of cardiovascular disease even in very young women who take oral contraceptives.

Smoking in combination with oral contraceptive use has been reported to contribute substantially to the risk of myocardial infarction in women in their mid-thirties or older, with smoking accounting for the majority of excess cases.[22] Mortality rates associated with circulatory disease have been shown to increase substantially in smokers, especially in those 35 years of age and older among women who use oral contraceptives (see Figure 1, Table 2).

Figure 1. Circulatory disease mortality rates per 100,000 woman-years by age, smoking status, and oral contraceptive use.[14]



Adapted from Layde and Beral.[14]

Oral contraceptives may compound the effects of well-known cardiovascular risk factors such as hypertension, diabetes, hyperlipidemias, hypercholesterolemia, age, cigarette smoking, and obesity. In particular, some progestogens decrease HDL cholesterol[23-31] and cause glucose intolerance, while estrogens may create a state of hyp[illegible] traceptives have been shown to [illegible] among some users (see *Warning No.* [illegible] risk factors have been associated with [illegible] heart disease.

b. Thromboembolism. An increased [illegible] and thrombotic disease associated with [illegible] traceptives is well established.[17,[illegible]] [illegible] have estimated the relative risk to be [illegible] superficial venous thrombosis, 4 to 11 [illegible] sis or pulmonary embolism, and 1.5 to [illegible] disposing conditions for venous [illegible] ease.[34-37,45,46] Cohort studies have [illegible] be somewhat lower, about 3 for new [illegible] past history of venous thrombosis or [illegible] about 4.5 for new cases requiring [illegible] risk of venous thromboembolic disease [illegible] contraceptives is not related to duration [illegible] A two- to seven-fold increase in relative [illegible] thromboembolic complications has [illegible] use of oral contraceptives.[38,39] The [illegible] thrombosis in women who have [illegible] about twice that of women without [illegible] tions.[43] If feasible, oral contraceptives [illegible] ued at least 4 weeks prior to and for [illegible] surgery of a type associated with an [illegible] boembolism, and also during and following [illegible] bilization. Since the immediate post[illegible] associated with an increased risk of [illegible] contraceptives should be started no earlier [illegible] after delivery in women who elect [illegible]

c. Cerebrovascular diseases. Both the [illegible] able risks of cerebrovascular events [illegible] rhagic strokes) have been reported to be [illegible] contraceptive use,[14,17,18,34,[illegible]] [illegible] the risk was greatest among older [illegible] sive women who also smoked. Hypert[illegible] be a risk factor for both users and non[illegible] strokes, while smoking increased the risk [illegible] strokes.

In one large study,[52] the relative risk for [illegible] was reported as 9.5 times greater in [illegible] It ranged from 3 for normotensive users to [illegible] severe hypertension.[54] The relative risk for [illegible] stroke was reported to be 1.2 for non[illegible] contraceptives, 1.9 to 2.6 for smokers [illegible] contraceptives, 6.1 to 7.6 for smokers [illegible] traceptives, 1.8 for normotensive users, and [illegible] with severe hypertension. The risk is also [illegible] women and among smokers.

d. Dose-related risk of vascular disease [illegible] ***tives.*** A positive association has been [illegible] amount of estrogen and progestogen in [illegible] and the risk of vascular disease.[[illegible]] [illegible] serum high density lipoproteins (HDL) [illegible] with many progestogens.[23-31] A decline in [illegible] sity lipoproteins has been associated with [illegible] dence of ischemic heart disease.[illegible] [illegible] crease HDL-cholesterol, the net effect of [illegible] tive depends on the balance achieved [illegible] gen and progestogen and the nature and [illegible] progestogens used in the contraceptives. [illegible] steroids should be considered in the choice [illegible] ceptive.

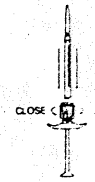
Minimizing exposure to estrogen and [illegible] ing with good principles of therapeutics. [illegible] estrogen-progestogen combination, the [illegible] scribed should be one that contains the [illegible] gen and progestogen that is compatible [illegible] rate and the needs of the individual patient. [illegible] of oral contraceptives should be started [illegible] taining the lowest estrogen content that [illegible] tory results in the individual.

e. Persistence of risk of vascular disease. [illegible] studies that have shown persistence of risk [illegible] ease for users of oral contraceptives. In [illegible] States, the risk of developing myocardial [illegible] discontinuing oral contraceptives [illegible] years for women 40–49 years old who [illegible] traceptives for 5 or more years, but this [illegible] not demonstrated in other age groups. [illegible] study reported former use of oral con[illegible] cantly associated with increased risk of [illegible] rhage.[57] In another study, in Great Britain, [illegible] oping nonrheumatic heart disease plus [illegible] arachnoid hemorrhage, cerebral thrombosis [illegible] ischemic attacks persisted for at least [illegible] tinuation of oral contraceptives, although [illegible] was small.[14,18,66] It should be noted that [illegible] performed with oral contraceptive [illegible] 50 mcg or more of estrogens.

2. Estimates of mortality from [illegible] study[67] gathered data from a variety of [illegible] estimated the mortality rates associated [illegible] methods of contraception at different [illegible] estimates include the combined risk of [illegible]

Syntex—Cont.

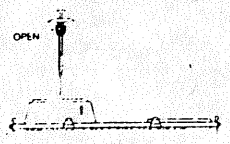
2. Hold the Injector with the open end up and fully insert the TUBEX® Sterile Cartridge-Needle Unit. Firmly tighten the ribbed collar in the direction of the "CLOSE" arrow.



3. Thread the plunger rod into the plunger of the TUBEX® Sterile Cartridge-Needle Unit until slight resistance is felt. The Injector is now ready for use in the usual manner.

To administer
Method of administration is the same as with conventional syringe. Remove needle cover by grasping it securely; twist and pull. Introduce needle into patient, aspirate by pulling back slightly on the plunger, and inject.

To remove the empty TUBEX® Cartridge-Needle Unit and dispose into a vertical needle disposal container
1. Do not recap the needle. Disengage the plunger rod.
2. Hold the Injector, needle down, over a vertical needle disposal container and loosen the ribbed collar. TUBEX® Cartridge-Needle Unit will drop into the container.



3. Discard the needle cover.

To remove the empty TUBEX® Cartridge-Needle Unit and dispose into a horizontal (mailbox) needle disposal container.
1. Do not recap the needle. Disengage the plunger rod.
2. Open the horizontal (mailbox) needle disposal container. Insert TUBEX® Cartridge-Needle Unit, needle pointing down, halfway into container. Close the container lid on cartridge. Loosen ribbed collar; TUBEX® Cartridge Unit will drop into the container.
3. Discard the needle cover.

The TUBEX® Injector is reusable and should not be discarded.
Used TUBEX® Cartridge-Needle Units should not be employed for successive injections or as multiple-dose containers. They are intended to be used only once and discarded.

NOTE: Any graduated markings on TUBEX® Sterile Cartridge-Needle Units are to be used only as a guide in mixing, withdrawing, or administering measured doses.
Wyeth does not recommend and will not accept responsibility for the use of any cartridge-needle units other than TUBEX® Cartridge-Needle Units in the TUBEX® Injector.
Directions for Use of the TUBEX® Injector have been reproduced with permission of Wyeth Laboratories.

CAUTION: Federal law prohibits dispensing without prescription.
U.S. Patent No. 4,089,969 and others.
02-2435-00-01
4/92 C14128-2
©1992 Syntex Laboratories, Inc.

TRI-NORINYL® Tablets (R)
(norethindrone and ethinyl estradiol)

BREVICON® Tablets (R)
[brev'i-kahn]
(norethindrone and ethinyl estradiol)

NORINYL® 1 + 35 Tablets (R)
[nor'i-nil]
(norethindrone and ethinyl estradiol)

NORINYL® 1 + 50 Tablets (R)
(norethindrone and mestranol)

NOR-QD® Tablets (R)
(norethindrone)
Tablets 0.35 mg.

Products of Syntex (F.P.) Inc.

DESCRIPTION

TRI-NORINYL 21-DAY Tablets provide an oral contraceptive regimen of 7 blue tablets followed by 9 yellow-green tablets and 5 more blue tablets. Each blue tablet contains norethindrone 0.5 mg and ethinyl estradiol 0.035 mg and each yellow-green tablet contains norethindrone 1 mg and ethinyl estradiol 0.035 mg.
TRI-NORINYL 28-DAY Tablets provide a continuous oral contraceptive regimen of 7 blue tablets, 9 yellow-green tablets, 5 more blue tablets, and then 7 orange tablets. Each blue tablet contains norethindrone 0.5 mg and ethinyl estradiol 0.035 mg, each yellow-green tablet contains norethindrone 1.0 mg and ethinyl estradiol 0.035 mg, and each orange tablet contains inert ingredients.
BREVICON 21-DAY Tablets provide an oral contraceptive regimen consisting of 21 blue tablets containing norethindrone 0.5 mg and ethinyl estradiol 0.035 mg.
BREVICON 28-DAY Tablets provide a continuous oral contraceptive regimen consisting of 21 blue tablets containing norethindrone 0.5 mg and ethinyl estradiol 0.035 mg and 7 orange tablets containing inert ingredients.
NORINYL 1 + 35 21-DAY Tablets provide an oral contraceptive regimen consisting of 21 yellow-green tablets containing norethindrone 1 mg and ethinyl estradiol 0.035 mg.
NORINYL 1 + 35 28-DAY Tablets provide a continuous oral contraceptive regimen consisting of 21 yellow-green tablets containing norethindrone 1 mg and ethinyl estradiol 0.035 mg and 7 orange tablets containing inert ingredients.
NORINYL 1 + 50 21-DAY Tablets provide an oral contraceptive regimen consisting of 21 white tablets containing norethindrone 1 mg and mestranol 0.05 mg.
NORINYL 1 + 50 28-DAY Tablets provide a continuous oral contraceptive regimen consisting of 21 white tablets containing norethindrone 1 mg and mestranol 0.05 mg and 7 orange tablets containing inert ingredients.
NOR-QD Tablets provide a continuous oral contraceptive regimen of one yellow norethindrone 0.35 mg tablet daily.
Norethindrone is a potent progestational agent with the chemical name 17-hydroxy-19-nor-17α-pregn-4-en-20-yn-3-one. Ethinyl estradiol is an estrogen with the chemical name 19-nor-17α-pregna-1, 3, 5(10) -trien-20-yne-3, 17-diol. Mestranol is an estrogen with the chemical name 3-methoxy-19-nor-17α-pregna-1, 3, 5(10) -trien-20-yn-17-ol.
Inactive Ingredients: Each tablet contains the following inactive ingredients: lactose, magnesium stearate, povidone, starch, and one or more of the following dyes; D&C Green No. 5, D&C Yellow No. 10, FD&C Blue No. 1, FD&C Yellow No. 6.

CLINICAL PHARMACOLOGY

Combination oral contraceptives act by suppression of gonadotrophins. Although the primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus (which increase the difficulty of sperm entry into the uterus) and the endometrium (which may reduce the likelihood of implantation).

INDICATIONS AND USAGE

Oral contraceptives are indicated for the prevention of pregnancy in women who elect to use these products as a method of contraception.
Oral contraceptives are highly effective. Table I lists the typical accidental pregnancy rates for users of combination oral contraceptives and other methods of contraception.[1] The efficacy of these contraceptive methods, except sterilization, depends upon the reliability with which they are used. Correct and consistent use of methods can result in lower failure rates.
[See table at top of next column.]

CONTRAINDICATIONS

Oral contraceptives should not be used in women who have the following conditions:
- Thrombophlebitis or thromboembolic disorders
- A past history of deep vein thrombophlebitis or thrombo-

TABLE I: LOWEST EXPECTED AND [illegible] FAILURE RATES DURING THE FIRST [illegible] CONTINUOUS USE OF A METHOD
% of Women Experiencing an Accidental [illegible] in the First Year of Continuous [illegible]

Method	Lowest Expected[a]
(No contraception)	(85)
Oral contraceptives	
combined	0.1
progestogen only	0.5
Diaphragm with spermicidal cream or jelly	3
Spermicides alone (foam, creams, jellies and vaginal suppositories)	3
Vaginal sponge	
Nulliparous	5
Multiparous	>5
IUD (medicated)	1
Condom without spermicides	2
Periodic abstinence (all methods)	2-10
Female sterilization	0.2
Male sterilization	0.1

Adapted from J. Trussell and K. Kost, Table [illegible]
[a] The authors' best guess of the percentage of [illegible] pected to experience an accidental pregnancy [illegible] ples who initiate a method (not necessarily for [illegible] time) and who use it consistently and correctly [illegible] first year if they do not stop for any other [illegible]
[b] This term represents "typical" couples who [illegible] method (not necessarily for the first time), who [illegible] an accidental pregnancy during the first year if they [illegible] stop use for any other reason. The authors [illegible] largely from the National Surveys of Family [illegible] (NSFG), 1976 and 1982.
[c] N/A—Data not available from the NSFG, NFS [illegible]
[d] Combined typical rate for both medicated and [illegible] medicated IUD. The rate for medicated IUD [illegible] available.

- Cerebral vascular or coronary artery disease
- Known or suspected carcinoma of the breast
- Carcinoma of the endometrium, and known or [illegible] estrogen-dependent neoplasia
- Undiagnosed abnormal genital bleeding
- Cholestatic jaundice of pregnancy or jaundice [illegible] pill use
- Hepatic adenomas, carcinomas or benign liver [illegible]
- Known or suspected pregnancy

WARNINGS

Cigarette smoking increases the risk of [illegible] vascular side effects from oral contraceptive [illegible] risk increases with age and with heavy smoking [illegible] more cigarettes per day) and is quite marked [illegible] over 35 years of age. Women who use oral [illegible] tives should be strongly advised not to smoke.

The use of oral contraceptives is associated with [illegible] risks of several serious conditions including myocardial infarction, thromboembolism, stroke, hepatic neoplasia, gallbladder disease, although the risk of serious [illegible] and mortality increases significantly in the presence of [illegible] underlying risk factors such as hypertension, [illegible] lipidemias, hypercholesterolemia, obesity and diabetes. Practitioners prescribing oral contraceptives should be familiar with the following information relating to these [illegible] The information contained in this package is [illegible] pally based on studies carried out in patients who [illegible] contraceptives with formulations containing [illegible] higher of estrogen.[6-11] The effects of long-term use of [illegible] lower dose formulations of both estrogens and progestogens remain to be determined.
Throughout this labeling, epidemiological studies are of two types: retrospective or case control studies and prospective or cohort studies. Case control studies provide a measure of the relative risk of a disease, a measure of the *ratio* of the incidence of a disease among users to that among nonusers, cannot be measured directly from case control studies, but the odds ratio calculated is a measure of relative risk. The relative risk does not provide information on the actual clinical occurrence of a disease. Cohort studies provide not only a measure of relative risk, but a measure of attributable risk, which is the difference in the incidence of disease between oral contraceptive users and nonusers. The attributable risk does provide information about the actual occurrence of a disease in the population.[12-13]

Parke-Davis—Cont.

(17 alpha-ethinyl-1,3,5(10)-estratriene-3,17 beta-diol), 20 mcg. Also contains acacia, NF; lactose, NF; magnesium stearate, NF; starch, NF; confectioner's sugar, NF; talc, USP. Each green tablet contains norethindrone acetate (17 alpha-ethinyl-19-nortestosterone acetate), 1.5 mg; ethinyl estradiol (17 alpha-ethinyl-1,3,5(10)-estratriene-3, 17 beta-diol), 30 mcg. Also contains acacia, NF; lactose, NF; magnesium stearate, NF; starch, NF; confectioner's sugar, NF; talc, USP; D&C yellow No. 10; FD&C yellow No. 6; FD&C blue No. 1. Each brown tablet contains microcrystalline cellulose, NF; ferrous fumarate, USP; magnesium stearate, NF; povidone, USP; sodium starch glycolate, NF; sucrose with modified dextrins.

DESCRIPTION

Loestrin **21** and Loestrin **Fe** are progestogen-estrogen combinations.

Loestrin **Fe** 1/20 and 1.5/30: Each provides a continuous dosage regimen consisting of 21 oral contraceptive tablets and seven ferrous fumarate tablets. The ferrous fumarate tablets are present to facilitate ease of drug administration via a 28-day regimen and do not serve any therapeutic purpose.

CLINICAL PHARMACOLOGY

Combination oral contraceptives act by suppression of gonadotropins. Although the primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus (which increase the difficulty of sperm entry into the uterus) and the endometrium (which reduce the likelihood of implantation).

INDICATIONS AND USAGE

Loestrin **21** and Loestrin **Fe** are indicated for the prevention of pregnancy in women who elect to use oral contraceptives as a method of contraception.

Oral contraceptives are highly effective. Table I lists the typical accidental pregnancy rates for users of combination oral contraceptives and other methods of contraception. The efficacy of these contraceptive methods, except sterilization, depends upon the reliability with which they are used. Correct and consistent use of methods can result in lower failure rates.

[See table below.]

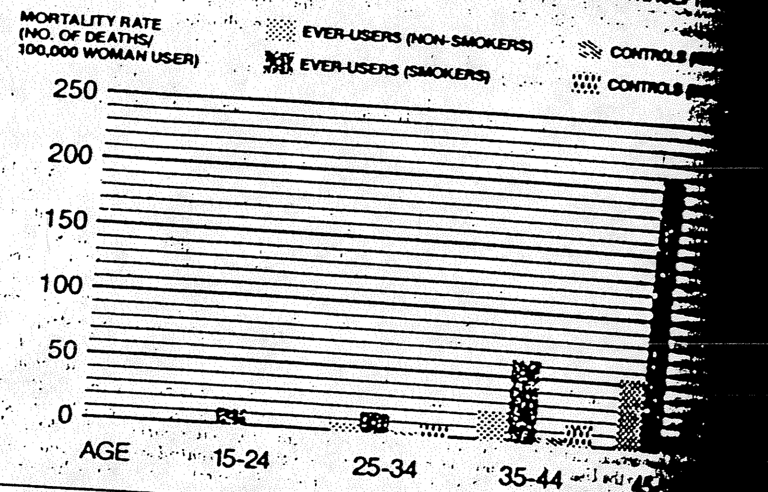
CONTRAINDICATIONS

Oral contraceptives should not be used in women who currently have the following conditions:

- Thrombophlebitis or thromboembolic disorders
- A past history of deep vein thrombophlebitis or thromboembolic disorders
- Cerebral vascular or coronary artery disease
- Known or suspected carcinoma of the breast
- Carcinoma of the endometrium or other known or suspected estrogen-dependent neoplasia
- Undiagnosed abnormal genital bleeding
- Cholestatic jaundice of pregnancy or jaundice with prior pill use
- Hepatic adenomas or carcinomas
- Known or suspected pregnancy

TABLE II

CIRCULATORY DISEASE MORTALITY RATES PER 100,000 WOMAN YEARS BY AGE, SMOKING STATUS AND ORAL CONTRACEP



Adapted from P.M. Layde and V. Beral, ref #12.

WARNINGS

Cigarette smoking increases the risk of serious cardiovascular side effects from oral contraceptive use. This risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives should be strongly advised not to smoke.

The use of oral contraceptives is associated with increased risks of several serious conditions including myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gallbladder disease, although the risk of serious morbidity or mortality is very small in healthy women without underlying risk factors. The risk of morbidity and mortality increases significantly in the presence of other underlying risk factors such as hypertension, hyperlipidemias, obesity and diabetes.

Practitioners prescribing oral contraceptives should be familiar with the following information relating to these risks.

The information contained in this package insert is principally based on studies carried out in patients who used oral contraceptives with higher formulations of estrogens and progestogens than those in common use today. The effect of long-term use of the oral contraceptives with lower formulations of both estrogens and progestogens remains to be determined.

Throughout this labeling, epidemiological studies reported are of two types: retrospective or case control studies and prospective or cohort studies. Case control studies provide a measure of the relative risk of a disease, namely, a *ratio* of the incidence of a disease among ... that among nonusers. The ... formation on the actual clinical ... hort studies provide a measure of ... the *difference* in the incidence of ... ceptive users and nonusers. The ... vide information about the ... the population (adapted from ... permission). For further ... to a text on epidemiological ...

1. Thromboembolic Disorders ... Problems.

a. Myocardial infarction

An increased risk of myoca... uted to oral contraceptive use. ... ers or women with other ... artery disease such as hyper... morbid obesity, and diabetes. ... tack for current oral contra... to be two to six (4–10). The ... of 30.

Smoking in combination with ... been shown to contribute ... myocardial infarctions in ... older with smoking ... cases (11). Mortality rates ... have been shown to increase ... the age of 35 and nonsmokers ... among women who use oral ...

[See table above.]

Oral contraceptives may ... risk factors, such as hyper... age and obesity (13). In ... known to decrease HDL ... erance, while estrogens ... ism (14–18). Oral contracep... blood pressure among ... Similar effects on risk factors ... increased risk of heart ... used with caution in ... factors.

b. Thromboembolism ...

An increased risk of thrombo... associated with the use of oral ... lished. Case control studies ... users compared to non-users ... superficial venous thrombo... sis or pulmonary embolism ... disposing conditions ... (2,3,19–24). Cohort studies ... somewhat lower, about 3 for ... cases requiring hospital... bolic disease due to oral ... length of use and disappea... A two- to four-fold increase ... thromboembolic compl... use of oral contraceptives ... thrombosis in women who ... twice that of women with... If feasible, oral contra... least four weeks prior to ... surgery of a type associated ... thromboembolism ...

TABLE I

LOWEST EXPECTED AND TYPICAL FAILURE RATES DURING THE FIRST YEAR OF CONTINUOUS USE OF A METHOD

% of Women Experiencing an Accidental Pregnancy in the First Year of Continuous Use

Method	Lowest Expected*	Typical**
(No contraception)	(89)	(89)
Oral contraceptives		3
combined	0.1	N/A***
progestin only	0.5	N/A***
Diaphragm with spermicidal cream or jelly	3	18
Spermicides alone (foam, creams, jellies and vaginal suppositories)	3	21
Vaginal sponge		
nulliparous	5	18
multiparous	>8	>28
IUD (medicated)	1	6†
Condom without spermicides	2	12
Periodic abstinence (all methods)	2–10	20
Female sterilization	0.2	0.4
Male sterilization	0.1	0.15

Adapted from J. Trussell and K. Kost, Table 11, ref. #1.

* The authors' best guess of the percentage of women expected to experience an accidental pregnancy among couples who initiate a method (not necessarily for the first time) and who use it consistently and correctly during the first year if they do not stop for any other reason.

** This term represents "typical" couples who initiate use of a method (not necessarily for the first time), who experience an accidental pregnancy during the first year if they do not stop use for any other reason.

*** N/A—Data not available

† Combined typical rate for both medicated and non-medicated IUD. The rate for medicated IUD alone is not available.

...to increase the risk of salicylate toxicity.
...: The anticoagulant effects of warfarin ...by the coadministration of 1200 mg/day of ...theless, caution should be exercised when ...that affects platelet function to the regimen ...ing oral anticoagulants.
...onists: The total body clearance of oxa... ...d by 20% in subjects who concurrently ...tic doses of cimetidine or ranitidine; no ...inetic parameter was affected. A change of ...magnitude lies within the range of normal ...unlikely to produce a clinically detectable ...outcome of therapy.
...Subjects receiving 1200 mg Daypro qd with ...bid exhibited statistically significant but ...in sitting and standing blood pressures ...Therefore, as with all NSAIDs, routine blood ...ing should be considered in these patients ...Daypro therapy.
...The coadministration of oxaprozin and ant... ...phen, or conjugated estrogens resulted in no ...ificant changes in pharmacokinetic parame... ...and/or multiple-dose studies. The interaction ...with lithium and cardiac glycosides has not ...

...mutagenesis, Impairment of fertility: In ...studies, oxaprozin administration for 2 years ...with the exacerbation of liver neoplasms ...and carcinomas) in male CD mice, but ...CD mice or rats. The significance of this ...finding to man is unknown.
...not display mutagenic potential. Results from ...forward mutation in yeast and Chinese ham... ...cells, DNA repair testing in CHO cells, mi... ...in mouse bone marrow, chromosomal ...in human lymphocytes, and cell transfor... ...in mouse fibroblast all showed no evidence of ...or cell-transforming ability.
...istration was not associated with impair... ...in male and female rats at oral doses up to ...(1180 mg/m^2); the usual human dose is ...(629 mg/m^2). However, testicular degenera... ...in beagle dogs treated with 37.5 to ...(750 to 3000 mg/m^2) of oxaprozin for ...mg/kg/day for 42 days, a finding not con... ...species. The clinical relevance of this finding ...

...Teratogenic Effects—Pregnancy Category C. ...quate or well-controlled studies in pregnant ...logy studies with oxaprozin were performed ...and rabbits. In mice and rats, no drug-related ...abnormalities were observed at 50 to 200 mg/ ...prozin (225 to 900 mg/m^2). However, in rabbits, ...formed fetuses were observed in dams treated ...mg/kg/day of oxaprozin (the usual human ...Oxaprozin should be used during pregnancy ...tial benefits justify the potential risks to the ...

...ery: The effect of oxaprozin in pregnant ...own. NSAIDs are known to delay parturition, ...closure of the fetal ductus arteriosus, and to be ...dystocia. Oxaprozin is known to have caused ...survival in rat studies. Accordingly, the use ...during late pregnancy should be avoided.
...: Studies of oxaprozin excretion in human ...been conducted; however, oxaprozin was found ...lactating rats. Since the effects of oxaprozin ...not known, caution should be exercised if ...administered to nursing women.
...: Safety and effectiveness of Daypro in chil... ...been established.
...: No adjustment of the dose of Daypro is neces... ...derly for *pharmacokinetic* reasons, although ...may need to receive a reduced dose because of ...ght or disorders associated with aging. No ...ferences in the pharmacokinetic profile for ...seen in studies in the healthy elderly. ...ted elderly patients in controlled clinical tri... ...Daypro as well as younger patients, caution ...cised in treating the elderly, and extra care ...when choosing a dose. As with any NSAID, ...likely to tolerate adverse reactions less well ...atients.

...ACTIONS

...n data were derived from patients who re... ...multidose, controlled, and open-label clini... ...om foreign marketing experience. Rates for ...in more than 1% of patients, and for most of ...events, are based on 2253 patients who took ...Daypro per day in clinical trials. Of these, ...ed for at least 1 month, 971 for at least ...6 for more than 1 year. Rates for the rarer ...ents reported from foreign marketing experience are difficult to estimate accurately and are only listed as less than 1%.

The adverse event rates below refer to the incidence in the first month of use. Most of the events were seen by this time for common adverse reactions. However, the cumulative incidence can be expected to rise with continued therapy, and some events, such as gastrointestinal bleeding (see *Warnings*), seem to occur at a constant or possibly increasing rate over time.

The most frequently reported adverse reactions were related to the gastrointestinal tract. They were nausea (8%) and dyspepsia (8%).

INCIDENCE GREATER THAN 1%: In clinical trials the following adverse reactions occurred at an incidence greater than 1% and are probably related to treatment. Reactions occurring in 3% to 9% of patients treated with Daypro are indicated by an asterisk(*); those reactions occurring in less than 3% of patients are unmarked.

Digestive system: abdominal pain/distress, anorexia, constipation*, diarrhea*, dyspepsia*, flatulence, nausea*, vomiting.

Nervous system: CNS inhibition (depression, sedation, somnolence, or confusion), disturbance of sleep.

Skin and appendages: rash*.

Special senses: tinnitus.

Urogenital system: dysuria or frequency.

INCIDENCE LESS THAN 1%:

Probable causal relationship: The following adverse reactions were reported in clinical trials at an incidence of less than 1% or were reported from foreign experience. Those reactions reported only from foreign marketing experience are in *italics*. The probability of a causal relationship exists between the drug and these adverse reactions.

Body as a whole: anaphylaxis.

Cardiovascular system: edema, blood pressure changes.

Digestive system: peptic ulceration and/or GI bleeding (see *Warnings*), liver function abnormalities including *hepatitis* (see *Precautions*), stomatitis, hemorrhoidal or rectal bleeding.

Hematologic system: anemia, thrombocytopenia, leukopenia, ecchymoses.

Metabolic system: weight gain, weight loss.

Nervous system: weakness, malaise.

Respiratory system: symptoms of upper respiratory tract infection.

Skin: pruritus, urticaria, photosensitivity.

Special senses: blurred vision, conjunctivitis.

Urogenital: *acute interstitial nephritis*, hematuria, renal insufficiency, decreased menstrual flow.

Causal relationship unknown: The following adverse reactions occurred at an incidence of less than 1% in clinical trials, or were suggested from marketing experience, under circumstances where a causal relationship could not be definitely established. They are listed as alerting information for the physician.

Cardiovascular system: palpitations.

Digestive system: alteration in taste.

Respiratory system: sinusitis, pulmonary infections.

Skin and appendages: alopecia.

Special senses: hearing decrease.

Urogenital system: increase in menstrual flow.

DRUG ABUSE AND DEPENDENCE

Daypro is a non-narcotic drug. Usually reliable animal studies have indicated that Daypro has no known addiction potential in humans.

OVERDOSAGE

No patient experienced either an accidental or intentional overdosage of Daypro in the clinical trials of the drug. Symptoms following acute overdose with other NSAIDs are usually limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain and are generally reversible with supportive care. Gastrointestinal bleeding and coma have occurred following NSAID overdose. Hypertension, acute renal failure, and respiratory depression are rare.

Patients should be managed by symptomatic and supportive care following an NSAID overdose. There are no specific antidotes. Gut decontamination may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose (5 to 10 times the usual dose). This should be accomplished via emesis and/or activated charcoal (60 to 100 g in adults, 1 to 2 g/kg in children) with an osmotic cathartic. Forced diuresis, alkalization of the urine, or hemoperfusion would probably not be useful due to the high degree of protein binding of oxaprozin.

DOSAGE AND ADMINISTRATION

Rheumatoid arthritis: The usual daily dose of Daypro in the management of the signs and symptoms of rheumatoid arthritis is 1200 mg (two 600-mg caplets) once a day. Both smaller and larger doses may be required in individual patients (see *Individualization of Dosage*).

Osteoarthritis: The usual daily dose of Daypro for the management of the signs and symptoms of moderate to severe osteoarthritis is 1200 mg (two 600-mg caplets) once a day. For patients of low body weight or with milder disease, an initial dosage of one 600-mg caplet once a day may be appropriate (see *Individualization of Dosage*).

Regardless of the indication, the dosage should be individualized to the lowest effective dose of Daypro to minimize adverse effects, and the maximum recommended total daily dose is 1800 mg (or 26 mg/kg, whichever is lower) in divided doses.

SAFETY AND HANDLING

Daypro is supplied as a solid dosage form in closed containers, is not known to produce contact dermatitis, and poses no known risk to healthcare workers. It may be disposed of in accordance with applicable local regulations governing the disposal of pharmaceuticals.

HOW SUPPLIED

Daypro 600-mg caplets are white, capsule-shaped, scored, film-coated, with DAYPRO debossed on one side and 1381 on the other side.

NDC Number	Size
0025-1381-31	bottle of 100
0025-1381-34	carton of 100 unit dose

Keep bottles tightly closed and store below 86°F (30°C). Dispense in a tight, light-resistant container with a child-resistant closure. Protect the unit dose from light.

Caution: Federal law prohibits dispensing without prescription.

2/2/93 • AO5221-2

Shown in Product Identification Section, page 329.

DEMULEN® 1/35-21 ℞
DEMULEN® 1/35-28 ℞
DEMULEN® 1/50-21 ℞
DEMULEN® 1/50-28 ℞
[*dem 'ū-len*]
(ethynodiol diacetate with ethinyl estradiol)

PRODUCT OVERVIEW

KEY FACTS

The Searle line of oral contraceptives contains two fixed-dose combination oral contraceptives (DEMULEN 1/35-21 and DEMULEN 1/35-28) containing ethynodiol diacetate (1 mg) with ethinyl estradiol (35 mcg) and two fixed-dose combination oral contraceptives (DEMULEN 1/50-21 and DEMULEN 1/50-28) containing ethynodiol diacetate (1 mg) with ethinyl estradiol (50 mcg). DEMULEN 1/35-21 and DEMULEN 1/50-21 are 21-day dosage regimens. DEMULEN 1/35-28 and DEMULEN 1/50-28 are 28-day dosage regimens (including 7 days of inert tablets). These forms are packaged in Compack® tablet dispensers.

MAJOR USE

DEMULEN 1/35 and DEMULEN 1/50 are highly effective in preventing pregnancy.

SAFETY INFORMATION

See complete safety information set forth below.

PRESCRIBING INFORMATION

DEMULEN® 1/35-21 ℞
DEMULEN® 1/35-28 ℞
DEMULEN® 1/50-21 ℞
DEMULEN® 1/50-28 ℞
[*dem 'ū-len*]
(ethynodiol diacetate with ethinyl estradiol)

DESCRIPTION

Demulen 1/35-21 and Demulen 1/35-28. Each white tablet contains 1 mg of ethynodiol diacetate and 35 mcg of ethinyl estradiol, and the inactive ingredients include calcium acetate, calcium phosphate, corn starch, hydrogenated castor oil, and povidone. Each blue tablet in the Demulen 1/35-28 package is a placebo containing no active ingredients, and the inactive ingredients include calcium sulfate, corn starch, FD&C Blue No. 1 Lake, magnesium stearate, and sucrose.

Demulen 1/50-21 and Demulen 1/50-28. Each white tablet contains 1 mg of ethynodiol diacetate and 50 mcg of ethinyl estradiol, and the inactive ingredients include calcium acetate, calcium phosphate, corn starch, hydrogenated castor oil, and povidone. Each pink tablet in the Demulen 1/50-28 package is a placebo containing no active ingredients, and the inactive ingredients include calcium sulfate, corn starch, FD&C Red No. 3, FD&C Yellow No. 6, magnesium stearate, and sucrose.

The chemical name for ethynodiol diacetate is *19-nor-17α-pregn-4-en-20-yne-3β, 17-diol diacetate*, and for ethinyl estradiol it is 19-nor-17α-pregna-1,3,5(10)-trien-20-yne-3, 17-diol. The structural formulas are as follows:

[See chemical structures at top of next column.]

Continued on next page

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... and H. Jick "Myocar- ... Therapy in Post-menopausal ... of Medicine, 294:1256–1259,
... Group, "The Coro- ... Leading to Modifications ... of the American Medical ...
... and E.W. Klein, "Pos- ... Hepatomas and Oral Con- ... 1973.
... M.M. Mahr, and H.C. ... in Young Women Ingesting ... Hemorrhage and Primary ... the American Medical Associa- ...
... and B. Benton, "Liver ... the Use of Oral Contracep- ... Medicine, 294:470–472, 1976.
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... ABOUT ESTROGENS

... produced by the ovaries. The ... kinds of estrogens. In addi- ... to make a variety of synthetic ... all these estrogens have simi- ... the same usefulness, side ... is intended to help you under- ... the risks involved in their ... safely as possible.
... important information about ... If you want to know ... or pharmacist to let you read ... the doctor.

... doctors for a number of pur-

... period of adjustment when ... produce estrogen, in order to ... symptoms of estrogen defi- ... producing estrogens, gen- ... this is called the meno-

... estrogen deficiency when a ... removed surgically before the

... are given along with a ... hormone; these combinations ... birth control pills. Patient ... taking oral contraceptives ... in this leaflet.)
... women and men.
... of the breasts after preg- ... to nurse their babies.

... OF ESTROGENS IN A PREG- ...

... PAUSE

... lives, all women eventually ... production. This usually ... may occur earlier or later. ... be removed before natu- ... producing a "surgical meno- ...
... the blood begins to decrease, ... typical symptoms: feelings of ... chest; or sudden intense epi- ... throughout the body (called "hot ... These symptoms are sometimes ... eventually develop ... "atrophic vaginitis") which ... during and after intercourse.
... to treat these symptoms of the ... considerably more than half ... menopause have only mild ... and, therefore, do not need ... need estrogens for a few ... to lower estrogen levels. ... periods longer than six ... overstimulation of the uterus ... given cyclically during each ... of pills followed by one ... (quinestrol tablets, USP) is given once daily for seven days, followed by once weekly use beginning two weeks after the start of treatment.

Sometimes, women experience nervous symptoms or depression during menopause. There is no evidence that estrogens are effective for such symptoms and they should not be used to treat them, although other treatment may be needed.

You may have heard that taking estrogens for long periods (years) after the menopause will keep your skin soft and supple and keep you feeling young. There is no evidence that this is so, however, and such long-term treatment carries important risks.

THE DANGERS OF ESTROGEN

1. *Cancer of the uterus.* If estrogens are used in the postmenopausal period for more than a year, there is an increased risk of *endometrial cancer* (cancer of the uterus). Women taking estrogens have roughly 5 to 10 times as great a chance of getting this cancer as women who take no estrogens. To put this another way, while a postmenopausal woman not taking estrogens has 1 chance in 1,000 each year of getting cancer of the uterus, a woman taking estrogens has 5 to 10 chances in 1,000 each year. For this reason *it is important to take estrogens only when you really need them.*

The risk of this cancer is greater the longer estrogens are used and also seems to be greater when larger doses are taken. For this reason *it is important to take the lowest dosage of estrogens that will control symptoms and to take it only as long as it is needed.* If estrogens are needed for longer periods of time, your doctor will want to reevaluate your need for estrogens at least every six months.

Women using estrogens should report any irregular vaginal bleeding to their doctors; although such bleeding may be of no importance, it can be an early warning of cancer of the uterus. If you have undiagnosed vaginal bleeding, you should not use estrogens until a diagnosis is made and you are certain there is no cancer of the uterus.

If you have had your uterus completely removed (total hysterectomy), there is no danger of developing cancer of the uterus.

2. *Other possible cancers.* Estrogens can cause development of other tumors in animals, such as tumors of the breast, cervix, vagina, or liver, when given for a long time. At present, there is no good evidence that women using estrogen in the menopause have an increased risk of such tumors, but there is no way yet to be sure they do not. One study raises the possibility that use of estrogen in the menopause may increase the risk of breast cancer many years later. This is a further reason to use estrogens only when clearly needed. While you are taking estrogens, it is important that you go to your doctor at least once a year for a physical examination. Also, if members of your family have had breast cancer or if you have breast nodules or abnormal mammograms (breast x-rays), your doctor may wish to carry out more frequent examinations of your breasts.

3. *Gallbladder disease.* Women who use estrogens after menopause are more likely to develop gallbladder disease requiring surgery than women who do not use estrogens. Birth control pills have a similar effect.

4. *Abnormal blood clotting.* Oral contraceptives increase the risk of blood clotting in various parts of the body. This can result in a stroke (if the clot is in the brain), a heart attack (a clot in a blood vessel of the heart), or a pulmonary embolus (a clot which forms in the legs or pelvis, then breaks off and travels to the lungs.) Any of these can be fatal.

At this time use of estrogens in the menopause is not known to cause such blood clotting, but this has not been fully studied and there could still prove to be such a risk. It is recommended that if you have had clotting in the legs or lungs or a heart attack or stroke while you were using estrogens or birth control pills, you should not use estrogens (unless they are being used to treat cancer of the breast or prostate.) If you have had a stroke or heart attack or if you have angina pectoris, estrogens should be used with great caution and only if clearly needed (for example, if you have severe symptoms of the menopause).

The larger dosages of estrogen used to prevent swelling of the breasts after pregnancy have been reported to cause clotting in the legs and lungs.

SPECIAL WARNING ABOUT PREGNANCY

You should not receive estrogen if you are pregnant. If this should occur, there is a greater than usual chance that the developing child will be born with a birth defect, although the possibility remains fairly small. A female child may have an increased risk of developing cancer of the vagina or cervix later in life (in the teens or twenties). Every possible effort should be made to avoid exposure to estrogens during pregnancy. If exposure occurs, see your doctor.

OTHER EFFECTS OF ESTROGENS

In addition to the serious known risks of estrogens previously described, estrogens have the following side effects and potential risks:

1. *Nausea and vomiting.* The most common side effect of estrogen therapy is nausea. Vomiting is less common.

2. *Effects on the breasts.* Estrogens may cause breast tenderness or enlargement and may cause the breasts to secrete a liquid. These effects are not dangerous.

3. *Effects on the uterus.* Estrogens may cause benign fibroid tumors of the uterus to enlarge.

Some women will have menstrual bleeding when estrogens are stopped. However, if the bleeding occurs on days you are still taking estrogens, you should report this to your doctor.

4. *Effects on the liver.* On rare occasions, women taking oral contraceptives develop a tumor of the liver which can rupture and bleed into the abdomen. So far, these tumors have not been reported in women using estrogens in the menopause, but you should report to your doctor immediately any swelling or unusual pain or tenderness in the abdomen.

Women with a past history of jaundice (yellowing of the skin and white parts of the eyes) may get jaundice again during estrogen use. If this occurs, stop taking estrogens and see your doctor.

5. *Other effects.* Estrogens may cause excess fluid to be retained in the body. This may make some conditions worse, such as epilepsy, migraine, heart disease, or kidney disease.

SUMMARY

Estrogens have important uses, but they have serious risks as well. You must decide, with your doctor, whether the risks are acceptable to you in view of the benefits of treatment. Except where your doctor has prescribed estrogens for use in special cases of cancer of the breast or prostate, you should not use estrogens if you have cancer of the breast or uterus, are pregnant, have undiagnosed abnormal vaginal bleeding, clotting in the legs or lungs, or have had a stroke, heart attack or angina, or clotting in the legs or lungs in the past while you were taking estrogens.

You can use estrogens as safely as possible by understanding that your doctor will require regular physical examinations while you are taking them and will try to use the smallest dosage possible and discontinue the drug as soon as possible.

Be alert for signs of trouble including:

1. Abnormal bleeding from the vagina
2. Pains in the calves or chest or sudden shortness of breath, or coughing blood (indicating possible clots in the legs, heart, or lungs)
3. Severe headache, dizziness, faintness, or changes in vision (indicating possible developing clots in the brain or eye)
4. Breast lumps (you should ask you doctor how to examine your own breasts)
5. Jaundice (yellowing of the skin)
6. Mental depression

Based on his or her assessment of your medical needs, your doctor has prescribed this drug for you. Do not give this drug to anyone else.

Storage—Store between 15°–30°C (59°–86°F).

Caution—Federal law prohibits dispensing without prescription

0437G027

Shown in Product Identification Section, page 322

LOESTRIN® 21 ℞
(Norethindrone Acetate and Ethinyl Estradiol Tablets, USP)

LOESTRIN® 21 1/20 ℞
(Each white tablet contains 1 mg norethindrone acetate and 20 mcg ethinyl estradiol.)

LOESTRIN® 21 1.5/30 ℞
(Each green tablet contains 1.5 mg norethindrone acetate and 30 mcg ethinyl estradiol.)

LOESTRIN® Fe ℞
(Norethindrone Acetate and Ethinyl Estradiol Tablets, USP and Ferrous Fumarate Tablets, USP)

LOESTRIN® Fe 1/20 ℞
(Each white tablet contains 1 mg norethindrone acetate and 20 mcg ethinyl estradiol. Each brown tablet contains 75 mg ferrous fumarate, USP)

LOESTRIN® Fe 1.5/30 ℞
(Each green tablet contains 1.5 mg norethindrone acetate and 30 mcg ethinyl estradiol. Each brown tablet contains 75 mg ferrous fumarate)

Each white tablet contains norethindrone acetate (17 alpha-ethinyl-19-nortestosterone acetate), 1 mg; ethinyl estradiol

Continued on next page

This product information was prepared in August 1993. On these and other Parke-Davis Products, information may be obtained by addressing PARKE-DAVIS, Division of Warner-Lambert Company, Morris Plains, New Jersey 07950.

Ortho—Cont.

6. Other Information
Your health care provider will take a medical and family history before prescribing oral contraceptives and will examine you. You should be reexamined at least once a year. Be sure to inform your health care provider if there is a family history of any of the conditions listed previously in this leaflet. Be sure to keep all appointments with your health care provider, because this is a time to determine if there are early signs of side effects of oral contraceptive use.

Do not use the drug for any condition other than the one for which it was prescribed. This drug has been prescribed specifically for you; do not give it to others who may want birth control pills.

HEALTH BENEFITS FROM ORAL CONTRACEPTIVES

In addition to preventing pregnancy, use of combination oral contraceptives may provide certain benefits. They are:
- menstrual cycles may become more regular
- blood flow during menstruation may be lighter and less iron may be lost. Therefore, anemia due to iron deficiency is less likely to occur.
- pain or other symptoms during menstruation may be encountered less frequently
- ectopic (tubal) pregnancy may occur less frequently
- noncancerous cysts or lumps in the breast may occur less frequently
- acute pelvic inflammatory disease may occur less frequently
- oral contraceptive use may provide some protection against developing two forms of cancer: cancer of the ovaries and cancer of the lining of the uterus.

If you want more information about birth control pills, ask your doctor or pharmacist. They have a more technical leaflet called the Professional Labeling, which you may wish to read. The Professional Labeling is also published in a book entitled *Physicians' Desk Reference*, available in many book stores and public libraries.

ORTHO PHARMACEUTICAL CORPORATION
Raritan, New Jersey 08869
Revised September 1991

TRADEMARK
631-10-030-5

Shown in Product Identification Section, page 321

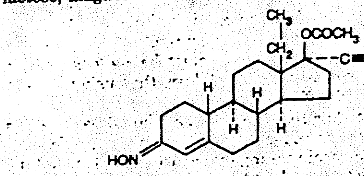
ORTHO TRI-CYCLEN™ ℞
(norgestimate/ethinyl estradiol)

DESCRIPTION

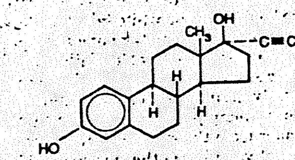
ORTHO TRI-CYCLEN (norgestimate/ethinyl estradiol) Tablets are a combination oral contraceptive. Each white tablet contains 0.180 mg of the progestational compound, norgestimate (18,19-Dinor-17-pregn-4-en-20-yn-3-one, 17-(acetyl-oxy)-13-ethyl-,oxime,(17α)-(+)-) and 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17α-pregna, 1,3,5(10)-trien-20-yne-3,17-diol). Inactive ingredients include lactose, magnesium stearate, and pregelatinized starch.

Each light blue tablet contains 0.215 mg of the progestational compound norgestimate (18,19-Dinor-17-pregn-4-en-20-yn-3-one,17-(acetyloxy)-13-ethyl-,oxime,(17α)-(+)-) with 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17α-pregna,1,3,5(10)-trien-20-yne-3,17-diol). Inactive ingredients include FD&C Blue No. 2 Aluminum Lake, lactose, magnesium stearate, and pregelatinized starch.

Each blue tablet contains 0.250 mg of the progestational compound norgestimate (18,19-Dinor-17-pregn-4-en-20-yn-3-one, 17-(acetyloxy)-13-ethyl-, oxime,(17α)-(+)-) together with 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17α-pregna,1,3,5(10)-trien-20-yne-3,17-diol). Inactive ingredients include FD&C Blue No. 2 Aluminum Lake, lactose, magnesium stearate, and pregelatinized starch.



Norgestimate



Ethinyl Estradiol

ORTHO TRI-CYCLEN is administered on a 21 day on medication, and 7 day off medication cyclic regimen.

Each green tablet in the ORTHO TRI-CYCLEN ☐ 28 package contains only inert ingredients, as follows: D&C Yellow No. 10 Aluminum Lake, FD&C Blue No. 2 Aluminum Lake, lactose, magnesium stearate, microcrystalline cellulose and pregelatinized starch.

CLINICAL PHARMACOLOGY

Combination oral contraceptives act by suppression of gonadotropins. Although the primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus (which increase the difficulty of sperm entry into the uterus) and the endometrium (which reduce the likelihood of implantation).

Norgestimate and ethinyl estradiol are well absorbed following oral administration of ORTHO TRI-CYCLEN. On the average, peak serum concentrations of norgestimate and ethinyl estradiol are observed within two hours (0.5–2.0 hr for norgestimate and 0.75–3.0 hr for ethinyl estradiol) after administration followed by a rapid decline due to distribution and elimination. Although norgestimate serum concentrations following single or multiple dosing were generally below assay detection within 5 hours, a major norgestimate serum metabolite, 17-deacetyl norgestimate, (which exhibits a serum half-life ranging from 12 to 30 hours) appears rapidly in serum with concentrations greatly exceeding that of norgestimate. The 17-deacetylated metabolite is pharmacologically active and the pharmacologic profile is similar to that of norgestimate. The ... estradiol ranged from ... Both norgestimate and ... tabolized and eliminated ... lowing administration of ^{14}C... and 37% (16–49%) of the ... eliminated in the urine ... norgestimate was not detected ... deacetyl norgestimate, a ... mate have been identified ... istration of radiolabeled ... Dinor -17- pregn-4-en-20-... (-);18,19-Dinor -5β- 17- ... ethyl,(17α), various ... gates of these metabolites ... to various hydroxylated ... sulfate conjugates.

INDICATIONS AND USAGE

ORTHO TRI-CYCLEN Tablets ... tion of pregnancy in women ... tives as a method of contracep... Oral contraceptives are highly ... typical accidental pregnancy ... oral contraceptives and other ... efficacy of these contraceptive ... depends upon the reliability ... rect and consistent use of ... rates.

[See table below.]

In four clinical trials with ORTHO ... efficacy pregnancy rate ... women-years. In total, 4,756 ... cles and a total of 42 pregnancies ... sents an overall use-efficacy ... years. One of these 4 studies ... clinical trial in which 4,633 ... Of the 2,312 patients on ORTHO ... cies were reported. This ... pregnancy rate of 0.94 per 100 ...

CONTRAINDICATIONS

Oral contraceptives should not be ... rently have the following conditions:
- Thrombophlebitis or thrombo...
- A past history of deep vein ... embolic disorders
- Cerebral vascular or coronary ...
- Known or suspected carcinoma ...
- Carcinoma of the endometrium ... pected estrogen-dependent ...
- Undiagnosed abnormal genital ...
- Cholestatic jaundice of pregnancy ... pill use
- Hepatic adenomas or carcinomas
- Known or suspected pregnancy

WARNINGS

Cigarette smoking increases the ... vascular side effects from oral ... risk increases with age and with ... more cigarettes per day) and is ... over 35 years of age. Women who ... tives are strongly advised not to ...

The use of oral contraceptives is ... risks of several serious conditions ... farction, thromboembolism, stroke, ... gallbladder disease, although the ... mortality is very small in healthy ... ing risk factors. The risk of ... creases significantly in the presence ... factors such as hypertension, ... diabetes.

Practitioners prescribing oral ... miliar with the following information ... The information contained in this ... pally based on studies carried out ... contraceptives with higher formulations ... progestogens than those in common ... long term use of the ... formulations of both estrogens ... be determined.

Throughout this labeling, ... are of two types: retrospective ... prospective or cohort studies. ... measure of the relative risk of a ... the incidence of a disease among ... that among non-users. The ... information on the actual clinical ... Cohort studies provide a measure ... is the *difference* in the incidence ... traceptive users and non-users. ... provide information about the ... in the population (adapted from ...

TABLE I: LOWEST EXPECTED AND TYPICAL FAILURE RATES DURING THE FIRST YEAR OF CONTINUOUS USE OF A METHOD
% of Women Experiencing an Accidental Pregnancy In the First Year of Continuous Use

Method	Lowest Expected*	Typical**
(No contraception)	(89)	(89)
Oral contraceptives		3
combined	0.1	N/A***
progestin only	0.5	N/A***
Diaphragm with spermicidal cream or jelly	3	18
Spermicides alone (foam, creams, jellies and vaginal suppositories)	3	21
Vaginal sponge		
nulliparous	5	18
multiparous	>8	>28
IUD (medicated)	1	6#
Condom without spermicides	2	12
Periodic abstinence (all methods)	2–10	20
Female sterilization	0.2	0.4
Male sterilization	0.1	0.15

Adapted from J. Trussel and K. Kost, Table II, ref. #1.
* The authors' best guess of the percentage of women expected to experience an accidental pregnancy among couples who initiate a method (not necessarily for the first time) and who use it consistently and correctly during the first year if they do not stop for any other reason.
** This term represents "typical" couples who initiate use of a method (not necessarily for the first time), who experience an accidental pregnancy during the first year if they do not stop use for any other reason.
*** N/A—Data not available
\# Combined typical rate for both medicated and non-medicated IUD. The rate for medicated IUD alone is not available.

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TO: Senator Judy Robson, Chairperson and Members of the Senate Human Services and Aging Committee
FROM: Gina Dennik-Champion MSN, RN, MSH and WNA Executive Director
DATE: October 6, 1999
RE: **Support for SB 182 - Requiring health insurance policies to cover contraceptive articles and services**

Good Morning Chairperson Robson and Members of the Senate Human Services and Aging Committee. My name is Gina Dennik-Champion, I am a Registered Nurse and the Executive Director for the Wisconsin Nurses Association (WNA). The WNA is the voice for professional nurses in Wisconsin.

Thank you for giving me the opportunity to share WNA's reasons for why we support SB 182 and the companion bill AB 362 which requires health insurance policies to cover contraceptive articles and services.

Contraception is a method of birth control which prevents the female egg cell or ovum and the male sperm cell from coming together during sexual intercourse. Egg fertilization or the formation of a new cell which begins the process of fetal development is not possible when contraceptive articles are utilized.
As the profession of all Registered Nurses in Wisconsin, WNA supports efforts to create a health care system that provides equitable access and quality services at affordable costs for all Wisconsin residents.

SB 182 is about contraceptive equity. This bill effectively address the need for equal coverage for prescriptive contraceptive articles and services. Enactment of this legislation is long overdue and it is WNA's hope that this can be accomplished before the start of the new millennium.

The benefits of passing SB 182 Contraceptive Equity, will create many positive outcomes which include:

- Use of a more effective method to prevent egg fertilization will be available because of increase access to insurance and provider services.

- Access to contraceptive services will assist women in planning a pregnancy.

- Increase access to contraceptive services increases a woman's access to healthcare providers which can only improve the health of the woman.

- Families will benefit from this bill because the dollars used to pay out-of-pocket for contraceptive services and articles will be used for other family needs.

WNA strongly believes that access to effective contraceptive services and articles avoid some of those tough feelings and decisions that face some women when pregnancy is the result of ineffective methods or lack thereof. This bill is about justice for women.

WNA wishes to thank the bills author Sen. Moore and her colleagues who support SB 182.

I thank you for the opportunity to present and will take any questions that you may have.

Thank you

Chair -
Senator Robson,

The sister stated Depo-Provera is ban in Canada & causes liver problems. I have checked with my company - that information is inaccurate. We have sold Depo Provera in Canada for the last 2 years. In addition it is sold in over 100 countries.

For the record - I will make that statement myself or if you prefer to make that statement from the Chair. As manufacturer of the product - mis-information should be acknowledged. I would be happy to talk to the Sister to found out how she obtained her information.

Judy Bowlby

Pharmacist & Hypnotherapist

Lon Newman

Equity in Prescription Insurance and Contraceptive Coverage

Legislators at the state and federal level who understand the importance of preventing unintended pregnancy have proposed a requirement that health insurance companies pay for contraceptives. Those of us who have supported this legislation over the past few years have emphasized:

That contraceptive use dramatically decreases abortions . . .

That contraceptive use decreases unintended pregnancies . . .

That family planning is a basic family health need . . .

That making contraceptive services accessible to women improves the economic circumstances of families

That preventing unintended pregnancy improves birth outcomes . . .

That making contraceptive services accessible to women is a matter of simple justice and equity:

Why should a woman bear the full cost of contraception or bear the child?

Is it fair that health insurers pay for Viagra and not for contraception?

And yet this legislation has failed to advance.

. . . . Last year, at the hearings in the state assembly, fourteen people and organizations testified. There were only two opponents: Wisconsin Right to Life and a representative of the insurance lobby.

What if the reasons for opposing this bill have nothing to do with reducing abortions or improving maternal health. What if the reasons for opposing this bill have nothing to do with helping families succeed, with creating equity between women and men., or even with healthier infants and healthier births? What if on the one hand the reason this legislation is opposed is political power and on the other protecting profits?

Contraception prevents abortions. There is no rational or empirical disagreement on that, so for today's testimony, I focused on what I know as an employer. What are the costs of unintended pregnancy to employers: Who pays the bills?

Remembering that 40-50% of all pregnancies in the U.S. are unintended – one of the highest rates in the industrialized world, I've developed two simple graphs to illustrate three simple points:

1. The first graph is a quick estimate of the most obvious health care costs for 100 contracepting women of reproductive age and 100 non-contracepting women of reproductive age. The contraceptive care estimate on the graph includes comprehensive preventive care . . . annual pap and pelvic exams and other related services and not simply contraceptives. The assumed rates of pregnancy for the 100 women in the non-contracepting group were the lowest estimate that I found (National Institutes of Medicine). Some recognized sources had annual pregnancy rates as high as 80% (almost double what I used in these assumptions) for sexually active women not using contraceptives. Even with low estimates of pregnancy and low estimates for the costs of childbirth, the main point is that **the annual costs of the health care provided to 100 contracepting women are much lower than the costs of the health care that would be provided to 100 non-contracepting women.**

2. The second graph is based on my own experiences as an employer. Although I have a workforce which is female, I'm sure the principle as well as the costs to other employers is much the same. **The highest cost of unintended pregnancy is in lost work days, lost productivity, substitution pay, maternity leave, worker replacement, and family and medical leave.** In fact, these costs, as the second graph attempts to illustrate, tower over cost estimates of directly providing contraceptive care **and** over the estimated costs of increased insurance premiums for covering contraceptive care.

3. In looking at these admittedly unscientific estimates, the most significant thing I realized is that under our current policies, the major cost of unintended pregnancy (absenteeism, substitution, maternity leave, even replacement of workers who don't return due to child care difficulties or costs) is paid by the employer. . . . and, right now, the costs of contraception and routine reproductive health care are paid by the women, themselves. That's why the insurance companies, unlike any other interest I can think of . . . don't profit by providing coverage for contraceptive care: **Women and employers are paying the biggest part of the "bills" now. . .**

Conclusions

If the insurance companies claim that they will raise premiums by $2.00 per month per employee to provide contraceptive benefits, the employer should accept the terms. It's worth it.

Health Insurance companies should immediately offer contraceptive coverage to their own employees. That's what I'm going to do. It's worth it.

The reason there are so many organizations that support this legislation is that almost everyone wins by providing contraceptive care:

Contraceptive coverage improves women's health;
Contraception improves opportunities for women and family income;
Providing contraceptive coverage is equitable and just;
Contraception leads to better birth outcomes and improves children's health;
Contraceptive coverage prevents abortion.

And . . . Contraceptive coverage saves money for Wisconsin's Employers . . . For Wisconsin's economy, it's worth it.

Lon Newman, President
WI Family Planning and Reproductive Health Association
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719 N Third Ave. Wausau, WI 54401
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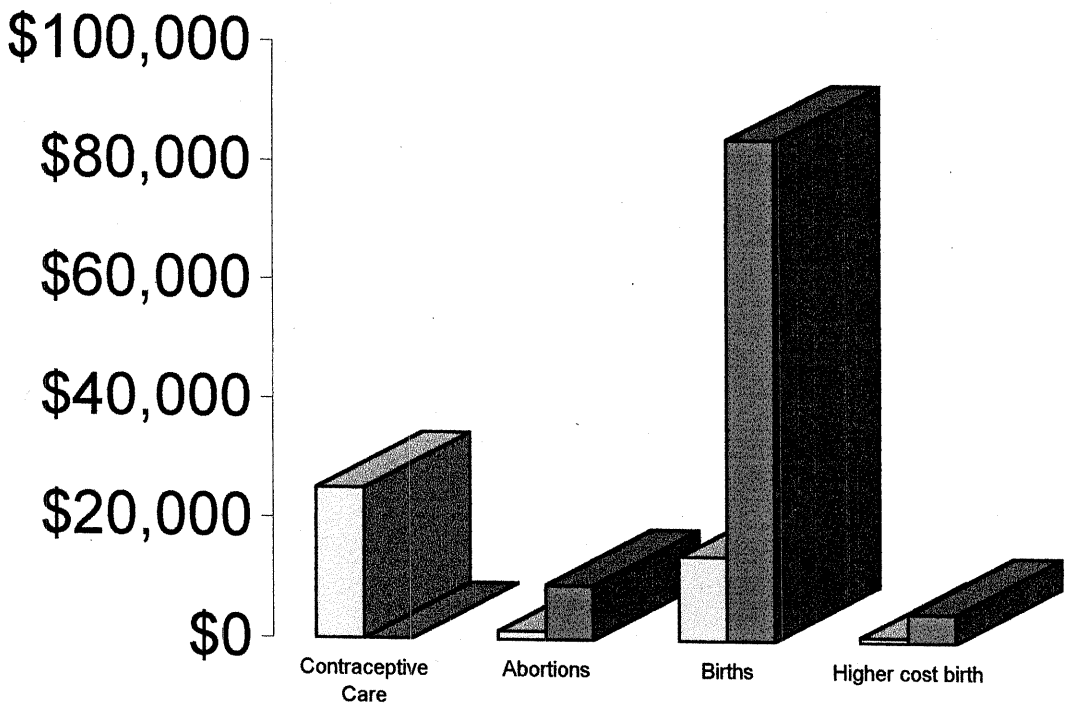
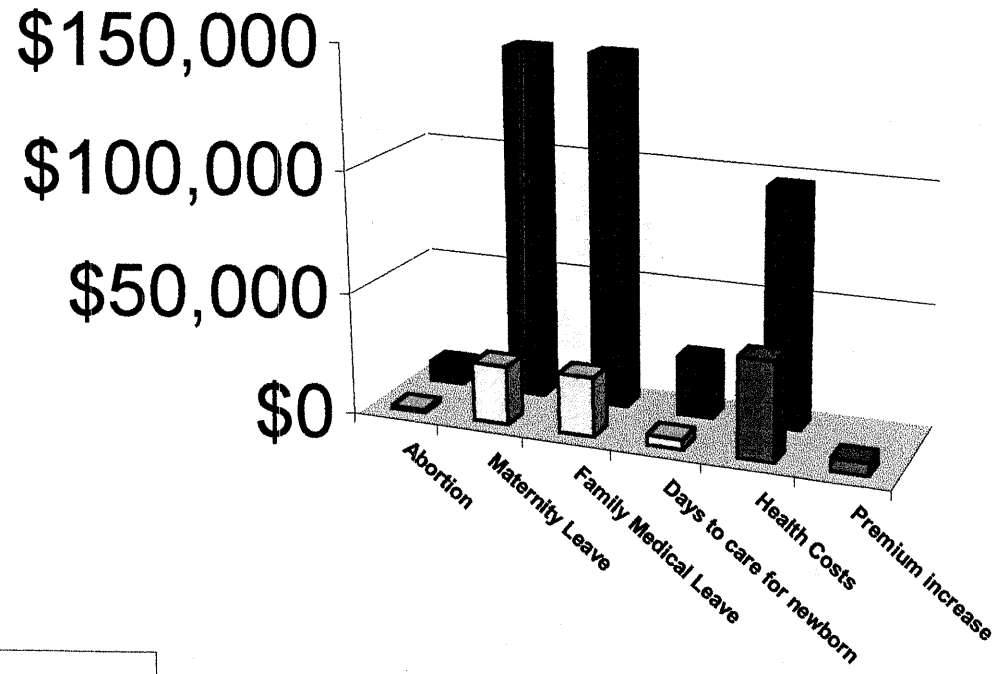
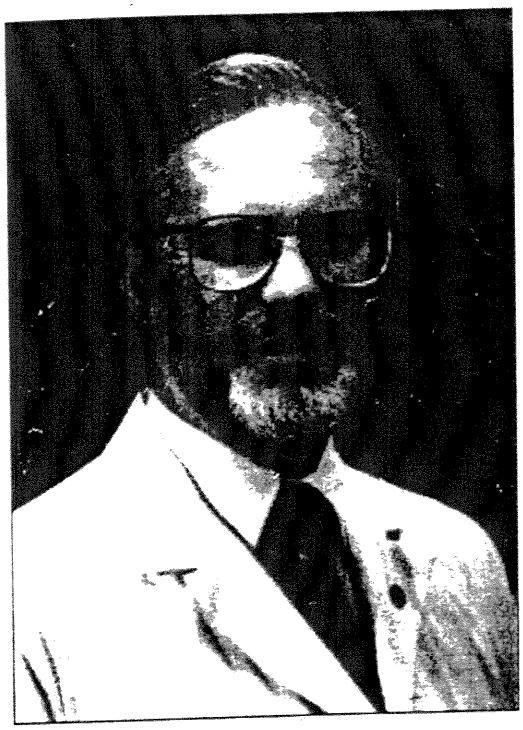
RH Costs for 100 Employees



Estimates of Absentee and Coverage Costs





The New Abortionists

Dr. Thomas Hilgers, director for Pope Paul VI for the Study of Human Reproduction in Omaha, Nebraska.

The following is an intriguing examinination of those chemical abortions that masquerade as contraceptives. This presentation explores these crucial topics from both a spiritual and a scientific perspective. Dr. Thomas Hilgers is an OB/GYN physician, Larry Frieders is the Vice-President of Pharmacists for Life. The interviewer is Denny Hartford, director of Vital Signs Ministries.

HARTFORD: Dr. Hilgers, can we begin by discussing first of all why Christians should be concerned about what I've referred to as the "new abortionists"?

HILGERS: For a number of years chemical abortifacients have been available and, in fact, used extensively. But for the most part, people, not just Christians, but people of all faiths and backgrounds haven't been aware of it. There's a profound amount of ignorance out there with regard to the abortion effects of birth control pills and other chemicals that are on the market.

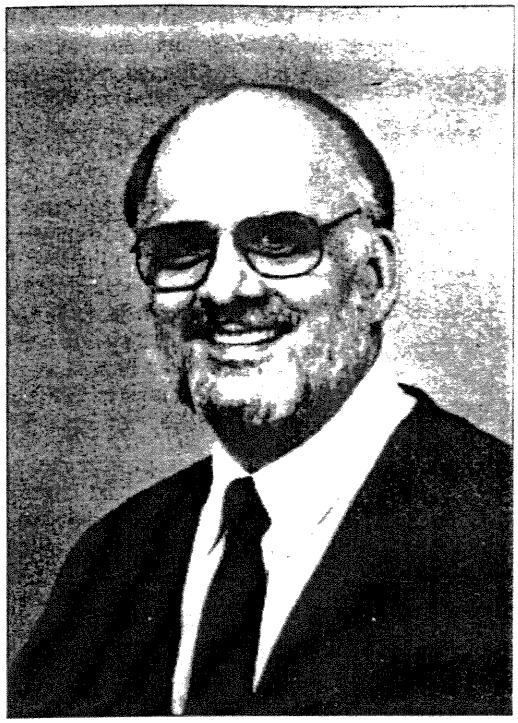
HARTFORD: Larry, I know that in your role as a professional pharmacist you agree that there is a tremendous amount of confusion and even misinformation on this subject. What do you think are some of the initial problems that we have to address with the issue?

FRIEDERS: Well, when you look at the literature and the information that's available on the birth control pill, for example, you find that the facts are there. The package inserts, the Physicians Desk Reference, a variety of sources of information—all very specifically state what these oral contraceptives do. They are indicated only for the prevention of pregnancy. And there are three mechanisms of how the birth control pills work, and they're quite well established; they've been known for years. The most commonly portrayed method is that it interferes with ovulation. So if you don't have a viable egg being produced, you're not going to get pregnant—this action is certainly a type of contraception. However, when that fails, and it does fail, the "back-up mechanisms" by which pregnancies are avoided come into play. Obviously, the one "back-up mechanism" that we're most concerned with is the one that changes the woman's body in such a way that if there is a new life, that tiny human loses the ability to implant and then grow and be nourished by the mother. The facts are clear—we've all known them intellectually. I learned them in school. I had to answer those questions on my state board pharmacy exam. The problem was getting that knowledge from my intellect down to where it became part of who I am. I had to accept the fact that I was participating in the sale and distribution of a product that was, in fact, causing the loss of life. So it's not that the knowledge isn't there, but rather that there's something keeping that knowledge from descending from one's intellect, down into the area of your heart where you can recognize the awesome tragedies that are happening.

HARTFORD: Dr. Hilgers, when we mention chemical abortion many people will think of RU-486 or they may even think of a third world country with some witch doctor or native medicine practitioner giving an expectant mother drugs for abortion. But, the issue is much, much broader. We're talking about a whole new generation of drugs that are killing unborn children.

HILGERS: Indeed. Of course, the use of oral contraceptives and intrauterine devices are the main two abortifacients that have been here in the United States for many, many years. I wrote a paper, 20 years ago now, detailing the abortifacient effects of the intrauterine device. The basic facts about life or death involved in that issue have not changed at all. And what Mr. Frieders has said about the long-standing knowledge of the birth control pills' adverse effects on the lining of the uterus is certainly true. Now we've seen the recent FDA approval of Norplant, one of the newer implantable, so-called "contraceptives" which has as one of its primary mechanisms the disturbance of the lining of the uterus. When this lining is injured, it is done for the specific purpose of destroyinq the new life that is created if conception occurs—and with Norplant ovulation [and conception] probably occurs an alarming percentage of the time.

Chemical abortion in contemporary culture. An interview with Dr. Thomas Hilgers & Larry Frieders



Larry Frieders, vice-president of Pharmacists for Life.

HARTFORD: Larry, in order to understand these things fully,we may have to go back to some basic biology, specifically the scientific facts surrounding the beginning of human life. What is conception? And at what point in the process of the development of the child do these drugs and devices actually interfere to end a human life?

FRIEDERS: The science is actually pretty well known. There is only one point in time when a new life is created. And that's when there are 23 chromosomes from mom and 23 chromosomes from dad that come together, miraculously, and create a new cell containing 46 chromosomes. It is an organism unlike any that's ever existed in the past and totally unlike anything that will ever exist again. It is a human being.

Now, during the seven to ten days that this new life is progressing down the fallopian tube, it is growing in size continuously — it is doubling and doubling and doubling, until it reaches a point where it needs to attach to the mother's uterus in order to gain additional nourishment from her blood supply. But at no time does this still very tiny human child ever become part of the woman's body. Nor is the mother part of the child. The mother is providing nourishment, and providing a safe and warm place for the baby to survive. The blood supplies are totally different. They do not share chemical activities of the body. Mother may be sick; baby may be healthy; there is not a one-to-one relationship. So at no time does baby become a part of mom. That's the physiology that so obviously contradicts the rhetoric of abortion when people are talking merely about the rights of women. That little life is not a part of the mother; therefore, the mother does not have a moral right to have the other person killed.

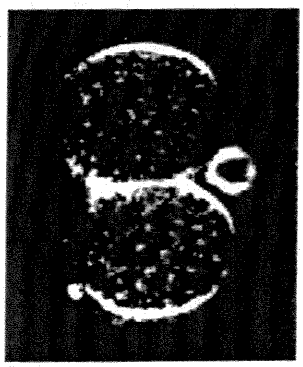
HARTFORD: Dr. Hilgers, at what point then do we see the drugs interrupting this process? I know that the American Medical Association attempted a few years ago to actually redefine conception in order to allow for an easier acceptance of these drugs. Could you discuss that and tell us exactly how abortions are occurring through the use of abortifacient chemicals?

HILGERS: The chemical abortions we are speaking of here take place at the point where implantation occurs, that is, in the lining of the uterus. That is, as Mr. Frieders said, seven to nine days following conception. And, yes, the American Medical Association and other organizations did try and redefine the beginning of human life specifically to help sell abortifacient devices and drugs. What they did was reject the traditionally-accepted and scientifically-authenticated definition (namely, conception) and substitute a belief that life did not "begin" until implantation or even later. It was a purely political decision, and obviously it was not based on fact.

The redefinition of the beginning of life was actually done to redefine abortion in hopes that these devices like the IUD and drugs like birth control pills would no longer be thought of as abortive. It's interesting to note that, the redefinition began in the sixties with the intrauterine device and the concerns about the religious groups in Pakistan and India particularly - which are non-Christian religions but which have a deep respect for life and are very much opposed to abortion. The manufacturers of the devices and their friends were worried these devices would not be well accepted in these cultures, and so the "sales pitch" ignored science and centered on changing language instead.

HARTFORD: What we are learning here is that the developing human child, created as Christians testify in the image and likeness of God, is in effect left homeless, not being able to implant in the uterus and is thus left to die an ignoble and secret death. Through the chemicals and the IUDs, we therefore have the termination of a life—we have an abortion. Gentlemen, why is this not common knowledge? You both have said that this information has been around, that it is in black and white in the Physicians Desk Reference and even in the literature of the manufacturers. Why then is there so much misinformation even from Christian physicians, the clergy, and others about these crucial matters?

HILGERS: I must say that a large amount of it comes from the physicians themselves. Physicians, for the most part, have simply denied that these devices are



". . . it is doubling, and doubling, and doubling."

abortive. With regard to the birth control pill, for example, they will argue that most of the time they act as contraceptives, which is probably true. But at the same time they deny that at least some of the time they are clearly abortive. This denial has become a part of their practice to the extent where it is no longer a part of their ethical sensitivity. When talking to women about any of these devices and chemicals, their presentation avoids telling the patient about the possibility that they might be abortive. So the physicians, in order to justify their own practices, have kept this information from people. Part of our responsibility is to bring that information to people so they can begin to look at this more carefully and make moral and ethically-true decisions.

HARTFORD: Larry, I know that you have undergone a spiritual conversion when it comes to dealing with chemical abortion. In your own practice you came to the decision that you no longer were going to merely oppose so-called birth control pills in an abstract way, but you were not going to sell them in your store. Could you tell us briefly how that conversion occurred in your life?

FRIEDERS: Well, Denny, I'm happy to talk about that. My thinking was first challenged around 1986 or 1987. At that time there had been a convict executed in Texas, and I read a letter to the editor in one of the pharmacy journals from a person who was condemning the act of using medicines, things that are supposed to heal, to kill. You see, they have to have a pharmacist prepare the compound and administer it. The person who wrote this letter of opposition was a man named Bo Kuhar, who I learned was the President of a group called Pharmacists for Life. I contacted him about that issue. In subsequent conversations, he made me aware of the fact that involvement with birth control pills also created alarming moral problems.

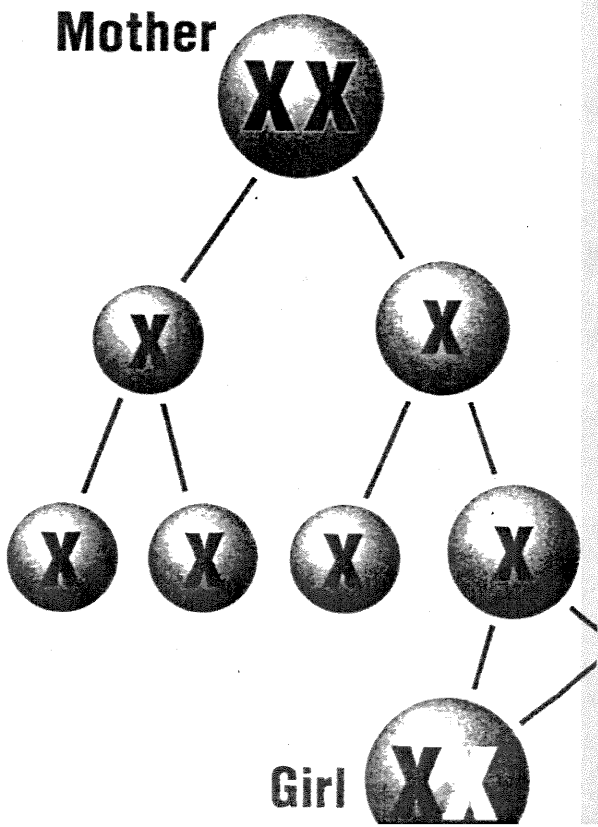
Even though I knew the science in an intellectual sense, the ramifications of the truth started to become clearer to me. At that time I was still selling birth control pills. I figured even if they were bad, if customers don't buy them from me they'll buy them from someone else, and it's not my job to impose my morality on these customers, etc., etc.—all the line of basically illogical rhetoric that people use. But I had people praying for me, and I was attending church on a regular basis at that time. It became more and more obvious that the more I sold these things, the more I felt torn. I knew I was doing something contrary to my Christian beliefs.

Then I was put in touch with more pharmacists who had the same experience and who had stopped selling the pills. Mr. Kuhar stopped selling them in his store. A fellow named Paul Reckenbauck in Ohio discontinued the sale of them in his store. Another fellow named Phil Brooks and I contacted them all and talked to them. Not once did anybody order me to stop, they all kindly said that was a decision that was mine to make. They all did say, however, that they would pray for me. They promised to ask God for wisdom and courage for me. The last conversation I had was in a small prayer group just sitting around talking with some people, and someone said, "Well you know what you have to do." So we discontinued the sale. We were filling anywhere between 100-200 prescriptions a month for the pill, and we prepared a letter to physicians and customers letting everyone know what we were going to do and when we were going to do it, and then we did it!

The first contact I had with someone coming for a birth control pill was a young family, a newly married Jewish couple. They tentatively handed me their prescription, and I thought "This is it; this is my first consultation telling someone I can't do this." So I got my packet of information, and I asked the young couple to go with me to my desk area in the back. I began to explain to them why I no longer sold the pills, and I had my information on natural family planning that I was ready to offer, when the young girl broke down sobbing almost hysterically. At that time I felt I had perhaps made a mistake. I shot up a quick prayer —"Lord, this is not a good start for this change in my life. It could have been easier, couldn't it?" But, as it turns out, the girl explained that her mother had breast cancer, and her aunt had died of cancer. She did not have all the knowledge, but she believed that birth control pills somehow had contributed to certain types of cancers. And so she had been really afraid of them. The tears were actually tears of relief, and she was very happy to know that somebody said "I don't think you ought to take these things." After that point it was all easy. I had critics call and complain; I had letters written; but essentially it got easier.

HARTFORD: Dr. Hilgers, many people would say that Mr. Frieders, overreacted in his decision not to sell any birth control pills. They might argue that their own doctor prescribes birth control pills but only the types that do not endanger the unborn. Are there any birth control pills out there that do not have this potential to abort a developing child?

HILGERS: Denny, there are none! At my last count in looking at the Physicians Desk Reference, which



is the big book that all doctors possess which describes all the medicines that are on the market, there were 44 different types of birth control pills. You see, when we talk about the birth control pill we are not talking about the same pill. At least 44 different ones exist, and they have different concentrations of chemicals that make them work. None of these so-called birth control pills have a mechanism which is completely contraceptive. Put the other way around, all birth control pills available have a mechanism which disturbs or disintegrates the lining of the uterus to the extent that the possibility of abortion exists when break-through ovulation occurs.

HARTFORD: Regarding the chances of "breakthrough" ovulation, Dr. Hilgers, just how high could that figure be?

HILGERS: I would say that most birth control pills on the market have anywhere from a four percent to ten percent chance of allowing "breakthrough" ovulation. There are pills called mini-pills which contain only a progesterone-like hormone where the percentage of ovulations are probably more in the 50 to 60 percent range. But those are not used as commonly. So, the most common birth control pill probably is in the range of two to ten percent.

HARTFORD: It can hardly be disputed that local pastors encounter a dramatically different attitude to children in their premarital counseling than what existed even a generation ago. I'm sure that both of you have encountered this in your own fields as well. You certainly have had to deal with men and women who expect from you advice on birth control. Dr. Hilgers, how do you deal with what is, at its base, an anti-child bias? What do you say to them?

HILGERS: Denny, my job is rather easy in this respect because in about two minutes I can describe for them how a woman's body itself can tell them with remarkable accuracy when she is fertile and when she is not fertile. For the most part, my patients are like men and women throughout the West: that is, they are unaware of the inherent dangers of birth control pills and devices.

People often have this notion that's been sold for many years that the much-derided "calendar rhythm" method of some forty years ago doesn't work. But that's irrelevant to a discussion of modern methods. Indeed, contemporary methods of natural family planning, which carefully define the times of a woman's fertility and infertility are very, very effective for both achieving and avoiding pregnancy.

So, again Denny, my job is pretty easy because it involves good news about their health, their emotional and spiritual lives, and their responsibilities. They're often rather startled because nobody's ever told them this before, but generally they are very happy to learn the facts, and we then build on that secure foundation.

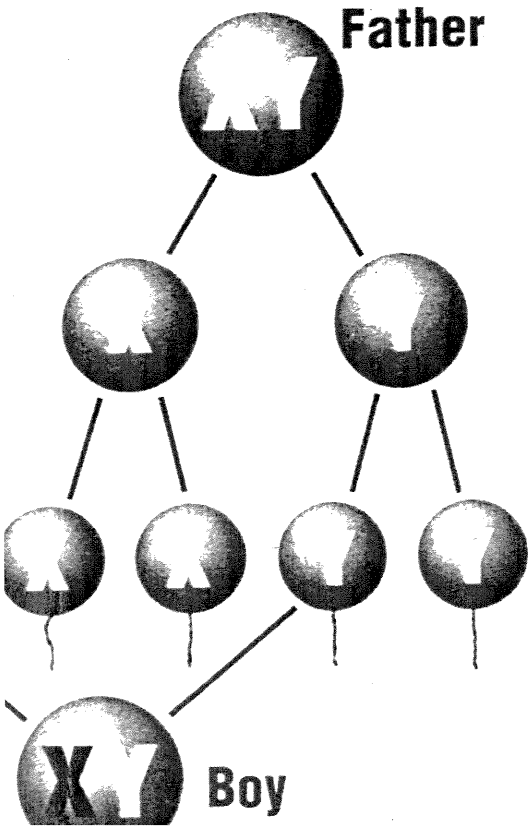
HARTFORD: Your advice must be unlike that of many OB/GYN doctors, is it not?

HILGERS: I'm afraid so. It has occurred to me recently that birth control pills are probably the major medicine that gynecologists prescribe. People usually think of the pill as just for contraceptive purposes, but doctors prescribe them for ovarian cysts, to eliminate unusual bleeding, to regulate the cycle when the cycle might be too long or too short, to treat endometriosis, to treat pre-menstrual tension syndrome, and so on. There's a variety of conditions that bring a patient into the gynecologist, and that doctor will often put them on the birth control pill to solve it. But you see the birth control pill doesn't solve any of that. It only suppresses the system - it only covers it up or disguises the underlying cause of all these different kinds of problems. This is a tremendous tragedy.

Since I haven't been involved in the prescription of birth control pills for many years, I have instead been studying all of this, so that now we can offer genuine treatments for these disorders. By using a health-maintenance system, we can tell if women have ovarian cysts, we can tell if they have unusual bleeding, and what the causes are. If they have premenstrual syndrome, for instance, we can cooperatively treat their menstrual cycles and ovulation cycles in a way that's not merely suppressive or, worse yet, actually destructive. So it's a whole new way, really, of practicing medicine and it is very exciting and very rewarding. It uses the skills and talents that I've spent a lot of time trying to learn over many years in a way that's really constructive to my patients.

HARTFORD: Larry, you also take a position on the pill which is unpopular with many in your profession. You argue effectively, however, that since the pill is not a medicine, it is actually a strange thing for pharmacists to prescribe.

FRIEDERS: You're right, Dr. Hilgers' point is a very important one. Not one of the maladies for which the pill is commonly prescribed is documented in the official literature or in the package inserts. So to use those pills for something other than its only indication, which, of course, is to prevent pregnancy, is to



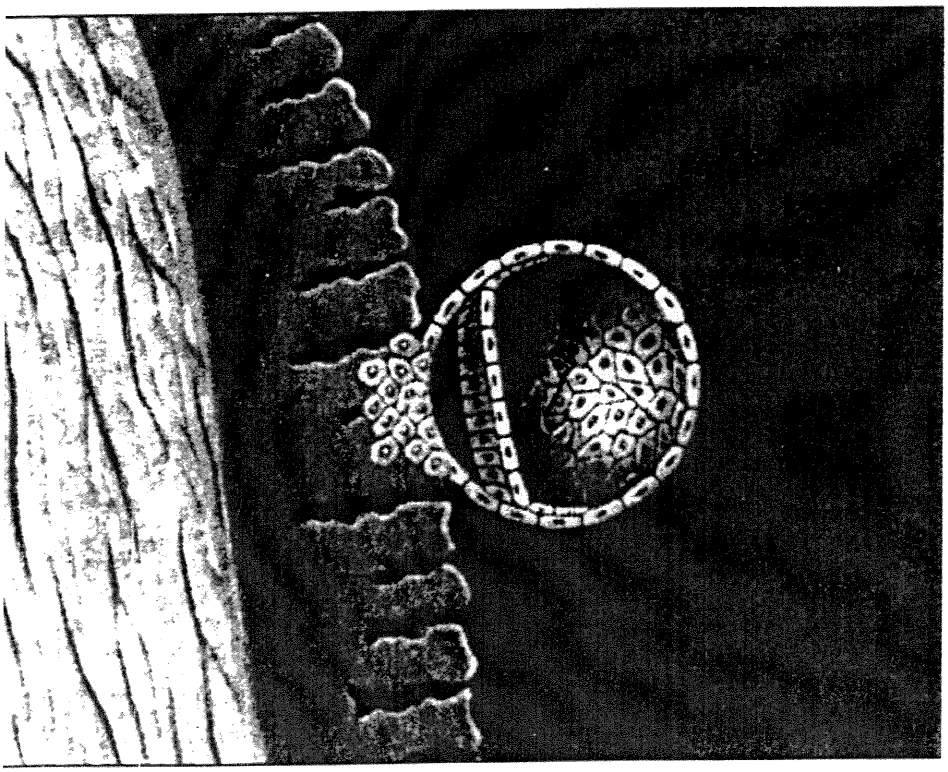
use it inappropriately and, one might argue in this litigious society might even be to use it illegally. Again, the FDA is very specific about what the pill can be used for, and there's only one indication. So it puts the pharmacist in an unusual situation. Here we are dispensing things in good faith, on the orders of a doctor, and in some cases the drugs are being used inappropriately.

HARTFORD: What about the commercial strength of the birth control industry? The dollars involved here must be incredible.

FRIEDERS: Well, look, you have 28 little pills; they're very small and I'm sure that they do not cost much to make. However, they sell for around $20 or more. I've extrapolated that and it runs to about 3 or 3 1/2 billion dollars a year in the United States. So we're up against a very large financial interest indeed. I would think gross profits on these products are probably in the range of 75% or more. So when you make a decision not to sell pills, or when you make a decision not to prescribe pills, or, for that matter, when you make a decision to unequivocally avoid using the pill, you are opening yourself up to an awful lot of powerful criticism. And what you become to your peers then is a very powerful mirror. Once somebody sees you responding positively to the truth, in step with the will of the Lord, it hurts them. And they can turn that hurt into anger and, before long, they're coming after you!

Denny Hartford of Vital Signs Ministries, an evangelical pro-life agency engaged in educational services.

HARTFORD: So, one of the reasons for the misinformation and the confusion, is that we're actually opposing a very powerful and entrenched industry—over a 3 billion dollar a year industry. Obviously, there is a very lucrative market there that the industry doesn't want disturbed.



A developing vesicule implants itself on the uterus wall.

HILGERS: It influences the medical professional's practice significantly, Denny. Several years ago I did a study on the amount of advertising dollars that went into the professional journals. We looked at the five major journals of obstetrics and gynecology. Twenty-five percent of all the advertising in those journals was provided by the contraceptive industry. Millions of dollars go to those journals to support those advertisements, and of course support the journals and the staff which, in turn, promote contraceptives in their reporting and editorial policy. The numbers of dollars and the international contraceptive industrialization that has gone on in the last 25 or 30 years is really incredible. This is really big-time business, there's no question about that.

HARTFORD: Debra Evans, a prominent evangelical author who deals extensively with medical ethics in her work, made the statement recently that it's going to be very difficult to picket a woman's medicine cabinet. Her point was to emphasize the tremendous difficulties facing the pro-life community as they seek to protect the unborn from the waves of chemical abortion that are now upon us. It seems that groups like Pharmacists for Life, and researchers and physicians like yourself, Dr. Hilgers, may well end up being key warriors in a new battle for the sanctity of human life.

HILGERS: Over the last several years the threat posed by RU-486, which has been talked about a lot and is recognized by everybody as an abortive chemical, is that it will change the whole abortion industry to a microscopic abortion industry and actually eliminate the need for surgical abortions. The sort of odd thing about that is this microscopic abortion business has been around for a long time. And our role, it seems to me, is primarily to provide education, but also to be able to provide moral leadership to our colleagues. Men and women need to understand that Christian decision making must be in full accord with the truth. Education is very important, because, as we've said, we're looking at a profound amount of ignorance on these issues.

HARTFORD: Gentleman, let me quickly sum up here. Through surgical abortion, just in the United States alone, we are destroying over 4,000 children every day. Churches have begun to decry the violence, the barbaric inhumanity represented by the knives and suction machines of the abortionists. However, what we have learned here is that the devil is destroying other innocent victims but through more secret and subtle ways. Make no mistake; however, what we have been exploring here is also abortion. It is no less sinister a crime, not only against man, but certainly against God even though the weapons employed are the more socially-acceptable ones of chemicals or devices.

We want to encourage Christians before God, to look very carefully at both the scientific and the spiritual evidence, and make certain that your personal and public witness to the sanctity of all human life is comprehensive. If there has been sin, confess to the forgiving Christ of the cross and sin no more. If there has been cowardice and ignorance, forsake them now and walk in the healing light and love of the Savior. Human life is not something with which we can gamble. ■

WORD GAMES PEOPLE PLAY ABO

Not too long ago, as medical history is measured, a group of physicians launched their campaign against abortion with this resolution:

"In questions of abstract right, the medical profession do not acknowledge such words as expediency, time service [cowardice]. We are the physician guardians of women, we alone, thus far, of their offspring. The case is here of life or death—the life or death of thousands—and it depends, almost wholly, upon ourselves. As a profession we are unanimous in our condemnation of the crime [which is] no simple offense against public morality and decency, no mere misdemeanor, no attempt on the life of the mother, but the wanton and murderous destruction of her child."[1]

This document served as a pro-life manifesto for years, not only for this group but for society as a whole. Its adoption was unanimous. The place: Louisville, Ky. The year: 1859. The group: The American Medical Association.

BY EUGENE F. DIAMOND, M.D.

The advent of advocate science

Since 1859, scientific investigation has *strengthened* the facts upon which the AMA's original anti-abortion position was based. For instance, Oscar Hertwig demonstrated in 1875 that human life begins with the union of sperm and egg (an event referred to until only recently by the basically interchangable terms *fertilization* or *conception*). Hertwig's pioneering work encouraged medical societies worldwide to work toward outlawing abortion, which was becoming more practical with the introduction of anesthesia and antiseptics.[2]

As in-vitro fertilization (IVF) was perfected, the pro-abortion claim "we don't know when life begins" became obsolete and ludicrous. So abortion advocates took another tack, claiming that IVF showed "conception is not an event, but a process." Their objective was not to clarify anything—the goal of legitimate science—but to confuse the issues. For if no one can fix a point when conception has occurred, the principle that life deserves protection from conception onward has no real meaning.

Even a non-scientist knows that life itself is a process comprised of events. Scientifically speaking, this process is an observable continuum that begins at fertilization (conception) and ends with death. Nonetheless, IVF has provided a window into the very early elements of this process, as follows:

1. The sperm head gets to the surface of the ovum and emits an enzyme that opens a path for the genetic material of the sperm (pronucleus) to enter the ovum.

2. The sperm's pronucleus makes its way to the ovum's pronucleus (12 hours).

3. The pronuclei fuse to form a zygote (2 hours).

4. The nucleus reproduces itself and divides into two daughter cells (18 hours).

The total process is 32 hours or less. When it "begins" is subject to interpretation. But whatever point you use, the process is clearly over long *before* abortion, either surgical or chemical, is usually considered. So this argument does not strengthen the pro-abortion case.

Medical newspeak

Another pro-abortion strategy has been to redefine "contraceptive" (and, by inference, "conception"). Prior to 1976, a "contraceptive" was understood to be an agent that prevented the union of sperm and ovum. In 1976, The American College of Obstetricians and Gynecologists (ACOG), realizing that this definition didn't help its political agenda, arbitrarily changed the definition.

A contraceptive now meant anything that prevented *implantation of the blastocyst*, which occurs six or seven days after fertilization. Conception, as defined by *Dorland's Illustrated Medical Dictionary* (27th Edition), became: "the onset of pregnancy, marked by implantation of the blastocyst."

The hidden agenda in ACOG's redefinition of "contraceptive" was to blur the distinction between agents preventing fertilization and those preventing implantation of the week-old embryo. Specifically, abortifacients such as IUDs, combination pills, minipills, progestin-only pills, injectables such as Pro-vera and, more recently, implantables such as Norplant, all are contraceptives by this definition.

The next strategy was to invent a new term, "pre-embryo," to make it possible to dispose of frozen embryos after in-vitro fertilization. The term "embryo" traditionally has defined the first eight weeks of intrauterine development. The term "pre-embryo" was first popularized in the Tennessee frozen embryo case, when Junior L. Davis sued to force his wife to destroy embryos prepared for in-vitro fertilization.[3]

Both the attending physician, Dr. Ray King, and the legal expert in the case, John A. Robertson, referred to the frozen embryos as "pre-embryos." The judge pointed out, however, that in all of his notes, Dr. King had used the term "embryo" to describe what he now wished to formalize as a "pre-embryo." Similarly, Mr. Robertson, testifying as to the status of what he called "pre-embryos," had in all of his previous legal writings referred to the same stages of human development as "embryos."

The invention of the term "pre-embryo" correlates with the redefinition of contraception. The so-called "pre-embryo" is said to become an "embryo" at the time of (surprise!) implantation.

Straining at gnats, swallowing camels

Abortion advocates have demonstrated a willingness to utilize any artifice that will confuse the status of the early developing human being. Perhaps you have heard some of the following assertions:

WARS

T THE BEGINNING OF LIFE

Some zygotes become hydatiform moles or ovarian teratomas; therefore not all zygotes deserve protection.

But as Jerome Lejeune has[1] demonstrated, neither of these tumors is of zygotic origin. The hydatiform mole is derived entirely from paternal germ cell material, and the ovarian teratoma is derived from chromosomal material entirely of maternal origin.[2]

Sometimes two embryos re-combine into a single being; therefore, the uniqueness of embryos is questionable.[3]

Such combination of embryos in mice has been demonstrated in the laboratory.[4] In order to effect such combination, however, the zona pellucida must be removed from each embryo by either a proteolytic enzyme or a mechanical process. The two embryos, devoid of their zona pellucida, must then be squeezed together through a micropipette to achieve combination of embryos.

But the function of the zona pellucida is to prevent contiguous embryos from combining. In order for this to occur in nature, two embryos in the same state of development would have to lose their zona pellucidae simultaneously. There is no convincing evidence that this actually occurs in human beings.

Identical twinning means a zygote is not always a unique individual.

Twinning of individuals with identical genotypes can occur after fertilization. It has recently been suggested that, because twinning is possible prior to gastrulation, abortion prior to gastrulation would not be murdering in a moral sense because "there is no individual to be the personal referent of such an action."[7]

The zygote, however, is either one individual human being or potentially two individual human beings of identical genetic makeup. Is murder mitigated because we do not know whether we are killing one individual or two? It would seem more reasonable to say that moral culpability is *increased* by the possibility that one might be killing two rather than one human being. If I burn down my enemy's house intending only to kill him, but find out that his identical twin brother has also died in the fire, am I more or less guilty of murder?

So, when does life begin?

Prior to 1973 (when *Roe* v. *Wade* became law), embryology and obstetrics textbooks stated unequivocally, "Life begins with the fertilization of the ovum by the spermatozoa."[8]

Furthermore, the "life" in question was obviously viewed as uniquely and indisputably human. "The zygote thus formed represents the beginning of life for a new unique individual."[9]

Even as recently as 1981, when a United States Senate Judiciary Subcommittee invited both sides of the abortion issue to testify on the question of when life begins, the vast majority concurred with these selected statements. From the official record of the hearing:[10]

"By all the criteria of modern molecular biology, life is present from the moment of conception."–Professor Hymie Gordon, Mayo Clinic

"It is scientifically correct to say that an individual human life begins at conception. . . . Our laws, one function of which is to help preserve the lives of our people, should be based on accurate scientific data."–Professor Micheline Matthews-Roth, Harvard University Medical School

"This straightforward biological fact (the beginning of life is conception) should not be distorted to serve sociological, political, or economic goals."–Dr. Watson A. Bowes, University of Colorado Medical School

Only one expert witness, Leon Rosenberg, M.D., said, "Science has no criteria for determining humanness." On a purely semantic level, this statement was patently untrue. Scientifically speaking, it is preposterous, for if true, the speaker, himself, would not be able to "prove" his own humanness.[11]

Humanness is not a philosophical or theological issue, but it is determined—as is dogness, mouseness or snakeness—by the genetic makeup of the individual involved, from the moment of conception. No woman, after all, has ever given birth to a carrot or a cat or anything other than a being endowed with humanness.

The pro-abortion movement has achieved monumental political success by distorting language, muddying issues and withholding the truth from the public, with the tacit assistance of the media. The central themes of the pro-life movement are irrefutable and should be asserted categorically and without ambiguity. Words in this war are important tools that must not be dulled by sloppy thinking or intentional sabotage. They stand for facts, and the facts give witness to the truth. ■

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1 From "Report on Criminal Abortion," *The Transactions of the American Medical Association* (1859) 12:76-77.

2 Franklin E. Payne, Jr. *Biblical Medical Ethics* (Milford, Mich.: Mott Media, 1985), 143-147.

3 *Davis v. Davis*, Fifth Judicial Court, Tennessee, No. E-14196, Sept. 21, 1989 (Young, W. Dale, Presiding.)

4 Jerome Lejeune, "On the Nature of Man: Alfred Award Lecture," *Child & Family*, 13:151, 1974.

5 Haring, B. "New Dimensions of Responsible Parenthood," *Theological Studies*, 37:420, 1976.

6 B. Mintz, "Experimental Genetic Mosaicism," *Journal of Experimental Zoology*, 157:273, 1964.

7 T. Shannon and A. Wolter, "Reflections on the Moral Status of the Pre-Embryo," *Theological Studies*, 51:603, 1990.

8 See Leslie Arey, *Embryology*, 6th ed. (Philadelphia: W. B. Saunders Co., 1954); cits. J. C. Beadles, Patten, *Human Embryology*, 3rd ed. (New York: McGraw Hill, 1968).

9 Louis Hellman, "Gametogenesis to Implantation," *Biology of Gestation*, vol. 1 of N.S. Assali (New York: Academic Press, 1968), 76.

10 Report, Subcommittee on Separation of Powers to Senate Judiciary Committee, S-158, 97th Congress, 1st Session, 1981. Cited by Randy Alcorn, *Pro-life Answers to Pro-choice Arguments* (Portland, Ore.: Multnomah Press, 1992), 40-41.

11 Franklin E. Payne, Jr. *Op. Cit.*, 147.