

bleeding is persistent or prolonged, the patient is advised to consult her health care professional. The possibility of ovulation increases with each successive day that scheduled yellow tablets are missed. 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. Hormonal contraception must be discontinued if pregnancy is confirmed.

The risk of pregnancy increases with each tablet missed. For additional patient instructions regarding missed tablets, see the **WHAT TO DO IF YOU MISS PILLS** section in the **DETAILED PATIENT LABELING** below.

LYBREL may be initiated no earlier than day 28 postpartum in the nonlactating mother or after a second-trimester abortion due to the increased risk for thromboembolism (see **CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS** concerning thromboembolic disease). The patient should be advised to use a nonhormonal back-up method for the first 7 days of tablet-taking. However, if intercourse has already occurred, pregnancy should be excluded before the start of combined oral contraceptive use or the patient must wait for her first menstrual period.

In the case of first-trimester abortion, if the patient starts LYBREL immediately, additional contraceptive measures are not needed.

HOW SUPPLIED

LYBREL[®] (90 mcg levonorgestrel and 20 mcg ethinyl estradiol) Tablets are available in a ClickCase[®], NDC 0008-1117-30 containing:

28 round, yellow biconvex, film-coated tablet debossed with “W” on one side and “1117” on the other side.

Store at up to 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature].

United States Patent Numbers: 6,500,814; D497,803S

References available upon request.

Brief Summary Patient Package Insert

This product (like all oral contraceptives) is intended to prevent pregnancy. Oral contraceptives do not protect against transmission of HIV (AIDS) and other sexually transmitted diseases (STDs) such as chlamydia, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis.

Oral contraceptives, also known as “birth-control pills” or “the pill,” are taken to prevent pregnancy, and when taken correctly, have a failure rate of approximately 1-2% per year (1 to 2 pregnancies per 100 women per year of use) when used without missing any pills. The average failure rate of large numbers of pill users is approximately 5% per year (5 pregnancies per 100 women per year of use) when women who miss pills are included. However, forgetting to take pills considerably increases the chances of pregnancy.

LYBREL is a birth-control pill that is taken every day. When you take LYBREL, the lining of your uterus does not undergo the changes needed for menstruation, and therefore you do not have regular menstrual periods. You are likely to have unscheduled or unplanned bleeding or spotting when you start to use LYBREL. The number of days each month with unscheduled bleeding and spotting usually decreases over time for the majority of women. When using LYBREL, the convenience of having no regular menstrual periods should be weighed against the inconvenience of unscheduled or unplanned breakthrough bleeding and spotting.

For the majority of women, oral contraceptives can be taken safely. However, there are some women who are at high risk of developing certain serious diseases that can be life-threatening or may cause temporary or permanent disability or death. The risks associated with taking oral contraceptives increase significantly if you:

- smoke
- have high blood pressure, diabetes, high cholesterol, or a tendency to form blood clots, or are obese
- have or have had clotting disorders, heart attack, stroke, angina pectoris, cancer of the breast or sex organs, jaundice, malignant or benign liver tumors, or major surgery with prolonged immobilization
- have headaches with neurological symptoms

You should not take the pill if you suspect you are pregnant or have unexplained vaginal bleeding.

Although cardiovascular disease risks may be increased with oral contraceptive use in healthy, non-smoking women over 40 (even with the newer low-dose formulations), there are also greater potential health risks associated with pregnancy in older women.

Cigarette smoking increases the risk of serious adverse effects on the heart and blood vessels from oral contraceptive use. This risk increases with age and with the amount of smoking (15 or more cigarettes per day has been associated with a significantly increased risk) and is quite marked in women over 35 years of age. Women who use oral contraceptives should not smoke.

Most side effects of the pill are not serious. The most common such effects are nausea, vomiting, unscheduled bleeding, weight gain, breast tenderness, and difficulty wearing contact lenses. These side effects, especially nausea and vomiting, may subside within the first three months of use.

The serious side effects of the pill occur very infrequently, especially if you are in good health and do not smoke. However, you should know that the following medical conditions have been associated with or made worse by the pill:

1. Blood clots in the legs (thrombophlebitis), lungs (pulmonary embolism), stoppage or rupture of a blood vessel in the brain (stroke), blockage of blood vessels in the heart (heart attack and angina pectoris) or other organs of the body. As mentioned above,

smoking increases the risk of heart attacks and strokes and subsequent serious medical consequences. Women with migraine also may be at increased risk of stroke with pill use.

2. Liver tumors, which may rupture and cause severe bleeding. A possible, but not definite, association has been found with the pill and liver cancer. However, liver cancers are extremely rare. The chance of developing liver cancer from using the pill is thus even rarer.
3. High blood pressure, although blood pressure usually returns to normal when the pill is stopped.

The symptoms associated with these serious side effects are discussed in the detailed leaflet given to you with your supply of pills. Notify your health care provider if you notice any unusual physical disturbances while taking the pill. In addition, drugs such as rifampin, as well as some anticonvulsants and some antibiotics, herbal preparations containing St. John's Wort (*Hypericum perforatum*), and HIV/AIDS drugs may decrease oral contraceptive effectiveness.

Various studies give conflicting reports on the relationship between breast cancer and oral contraceptive use.

Oral contraceptive use may slightly increase your chance of having breast cancer diagnosed, particularly if you started using hormonal contraceptives at a younger age.

After you stop using hormonal contraceptives, the chances of having breast cancer diagnosed begin to go down, and disappear 10 years after stopping use of the pill. It is not known whether this slightly increased risk of having breast cancer diagnosed is caused by the pill. It may be that women taking the pill were examined more often, so that breast cancer was more likely to be detected.

You should have regular breast examinations by a health care professional and examine your own breasts monthly. Tell your health care professional if you have a family history of breast cancer or if you have had breast nodules or an abnormal mammogram. Women who currently have or have had breast cancer should not use oral contraceptives because breast cancer is usually a hormone-sensitive tumor.

Some studies have found an increase in the incidence of cancer of the cervix in women who use oral contraceptives. However, this finding may be related to factors other than the use of oral contraceptives.

Taking the pill provides some important noncontraceptive benefits. These include less painful menstruation, fewer pelvic infections, and fewer cancers of the ovary and the lining of the uterus.

Be sure to discuss any medical condition you may have with your health care provider. Your health care provider will take a medical and family history before prescribing oral contraceptives and will examine you. The physical examination may be delayed to another time if you request it, and the health care provider believes that it is appropriate to postpone it. You should be reexamined at least once a year while taking oral contraceptives. The detailed patient information

leaflet gives you further information which you should read and discuss with your health care provider.

What You Should Know About Your Menstrual Cycle When You Use LYBREL

You are likely to have unscheduled or unplanned bleeding or spotting when you start to use LYBREL. The number of days each month with bleeding or spotting usually decreases over time in the majority of women. In a study of LYBREL, about 5 out of 10 women had 7 or more days of bleeding or spotting while using their third 28-day pill pack of LYBREL. The number of women with 7 or more days of bleeding or spotting decreased to 3 out of 10 women during the use of their seventh pill pack. Among women who continued to use LYBREL for one year, about 6 out of 10 women had no bleeding or spotting during their last month of use.

Do not stop taking LYBREL because of bleeding or spotting as this will increase your chance of getting pregnant. If the spotting or bleeding continues for more than 7 consecutive days or if the bleeding is heavy, call your health care provider.

Can I Get Pregnant While Taking LYBREL?

You are not likely to get pregnant if you take LYBREL at the same time everyday as directed by your health care provider. Because regular monthly bleeding does not occur on LYBREL, it may be difficult to recognize if you get pregnant. If you suspect that you may be pregnant, or if you have symptoms of pregnancy such as nausea/vomiting or unusual breast tenderness, you should have a pregnancy test and you should contact your health care professional. Stop taking LYBREL if you are pregnant.

Instructions for the Patient

HOW TO TAKE LYBREL

Important Points to Remember

Before You Start Taking LYBREL:

1. **BE SURE TO READ THESE DIRECTIONS:**

Before you start taking LYBREL.

And

Anytime you are not sure what to do.

2. **THE RIGHT WAY TO TAKE LYBREL IS TO TAKE ONE PILL EVERY DAY AT THE SAME TIME.**

If you miss pills, you could get pregnant. This includes starting the pack late. The more pills you miss, the more likely you are to get pregnant. See “WHAT TO DO IF YOU MISS PILLS” below.

3. **MANY WOMEN HAVE SPOTTING OR LIGHT BLEEDING, OR MAY FEEL SICK TO THEIR STOMACH DURING THE FIRST 1-3 PACKS OF PILLS.**

If you feel sick to your stomach, do not stop taking LYBREL. This will usually go away. If it doesn't go away, check with your health care professional.

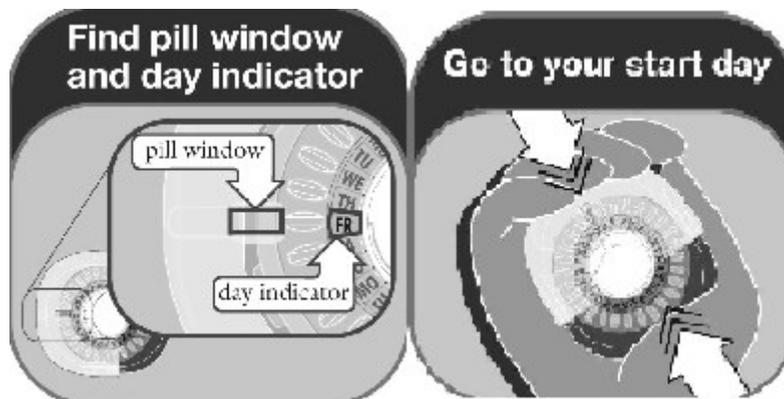
4. **MOST WOMEN HAVE SPOTTING OR BLEEDING DURING THE FIRST FEW MONTHS OF TAKING LYBREL.** Do not stop taking your pills even if you are having

bleeding or spotting. If the bleeding or spotting lasts for more than 7 consecutive days, talk to your health care provider.

5. **MISSING PILLS CAN ALSO CAUSE SPOTTING OR LIGHT BLEEDING**, even when you make up these missed pills.
On the days you take 2 pills to make up for missed pills, you could also feel a little sick to your stomach.
6. **IF YOU VOMIT** (within 4 hours after you take your pill), you should follow the instructions for **WHAT TO DO IF YOU MISS PILLS**. **IF YOU HAVE DIARRHEA** or **IF YOU TAKE SOME MEDICINES**, including some antibiotics, your pills may not work as well.
Use a back-up nonhormonal method (such as condoms and/or spermicide) until you check with your health care professional.
7. **IF YOU HAVE TROUBLE REMEMBERING TO TAKE *LYBREL***, talk to your health care professional about how to make pill-taking easier or about using another method of birth control.
8. **IF YOU HAVE ANY QUESTIONS OR ARE UNSURE ABOUT THE INFORMATION IN THIS LEAFLET**, call your health care professional.

BEFORE YOU START TAKING *LYBREL*

1. **DECIDE WHAT TIME OF DAY YOU WANT TO TAKE YOUR PILL**. It is important to take your pill at the **SAME TIME** every day.
2. **LOOK AT YOUR *LYBREL* DISPENSER**. The pill pack has 28 “active” yellow pills (with hormones).
3. Follow these 3 steps to set your *LYBREL* case to your starting day:
 - a. Look at your ClickCase[®] dispenser. Find the pill window and day indicator. Place the case lengthwise in the palm of your hand, so that the pill window and day indicator are visible.



- b. Make note of the day that lines up with the window. If the desired start day is not aligned with the window, firmly squeeze the ends of the case together until it clicks. Then fully RELEASE. Keep clicking and releasing until you reach the desired start day.
- c. To take your pill, firmly squeeze the ends of the case together until it clicks; do NOT release. Turn the case over, and allow the pill to drop out into your other hand. Before releasing, turn the case back over, then fully RELEASE, and the next day's pill automatically advances.



4. BE SURE YOU HAVE READY AT ALL TIMES:

ANOTHER KIND OF NONHORMONAL BIRTH CONTROL (such as condoms and/or spermicide) to use as a back-up in case you miss pills.

AN EXTRA, FULL PILL PACK.

WHEN TO START THE *FIRST* PACK OF *LYBREL*

Day 1 Start

1. Take the first “active” yellow pill of the first pack during the *first 24 hours of your period*.
2. You will not need to use a back-up nonhormonal method of birth control, since you are starting the pill at the beginning of your period.

WHAT TO DO DURING THE MONTH

1. TAKE ONE PILL AT THE SAME TIME EVERY DAY UNTIL THE PACK IS EMPTY.
Do not skip pills even if you are spotting or bleeding or feel sick to your stomach (nausea).
Do not skip pills even if you do not have sex very often.
2. WHEN YOU FINISH A PACK
Start the next pack on the day after your last pill. **Do not wait any days between packs.**

IF YOU SWITCH FROM ANOTHER BRAND OF COMBINATION PILLS:

When switching from a 21 pill pack: Start LYBREL on the first day of your period (withdrawal bleed). Be sure that no more than 7 days pass between the last day of your 21-day pack and your first LYBREL pill.

When switching from a 28 pill pack (21 active and 7 inactive pills, or 24 active and 4 inactive pills): Start LYBREL on the first day of your period (withdrawal bleed). Be sure that no more than 7 days pass after the last active pill and your first LYBREL pill.

IF YOU SWITCH FROM ANOTHER TYPE OF BIRTH CONTROL

When switching from other types of birth control such as pills containing only a progestin (progestin only pill or POP), an injection, or an implant, your health care professional will provide you with instructions for when to start LYBREL.

WHAT TO DO IF YOU MISS PILLS

Combination oral contraceptives may not be as effective if you miss pills. Instructions for what to do if you miss pills are provided in the following table.

# of pills missed in a row	What to do when you miss a pill(s)
1 missed pill	<ul style="list-style-type: none">• Take the missed pill as soon as you remember. <p style="text-align: center;">THEN</p> <ul style="list-style-type: none">• Take the next pill at your regular time. This means you may take 2 pills in 1 day.• You COULD BECOME PREGNANT if you have sex during the 7 days after you restart your pills. You MUST use a nonhormonal birth-control method (such as condoms and/or spermicide) as a back-up for those 7 days.

# of pills missed in a row	What to do when you miss a pill(s)
<p>2 missed pills</p> <p>and remembered on the day of the second missed pill</p>	<ul style="list-style-type: none"> • Take 2 missed pills on the day you remember. The following day you are back on schedule to take 1 pill a day. <p>For example, you take your pills in the morning and you missed 1 pill on Monday and 1 on Tuesday. On Tuesday evening you remembered that you missed your Monday and Tuesday pills. You take the 2 missed pills on Tuesday evening and on Wednesday morning you're back on schedule and you take 1 pill.</p> <ul style="list-style-type: none"> • You COULD BECOME PREGNANT if you have sex during the 7 days after you restart your pills. You MUST use a nonhormonal birth-control method (such as condoms and/or spermicide) as a back-up for those 7 days.
<p>2 missed pills</p> <p>and remembered on the day after the second pill is missed</p>	<ul style="list-style-type: none"> • Take 2 missed pills on the day you remember. The next day you take 2 pills. The following day you are back on schedule to take your pills. <p>For example, you take your pills in the morning and you missed 1 pill on Monday and 1 on Tuesday. On Wednesday morning you remembered that you missed your Monday and Tuesday pills. You take the 2 missed pills on Wednesday morning and 2 pills on Thursday morning. On Friday morning you're back on schedule and you take 1 pill.</p> <ul style="list-style-type: none"> • You COULD BECOME PREGNANT if you have sex during the 7 days after you restart your pills. You MUST use a nonhormonal birth-control method (such as condoms and/or spermicide) as a back-up for those 7 days.
<p>3 or more missed pills</p>	<ul style="list-style-type: none"> • Contact your health care professional for further advice. Keep taking one pill every day until you reach your health care professional. Do not take the missed pills. • You COULD BECOME PREGNANT if you have sex during the 7 days after you restart your pills. You MUST use a nonhormonal birth-control method (such as condoms and/or spermicide) as a back-up for those 7 days.

FINALLY, IF YOU ARE STILL NOT SURE WHAT TO DO ABOUT THE PILLS YOU HAVE MISSED

Use a BACK-UP NONHORMONAL BIRTH-CONTROL METHOD anytime you have sex.

PREGNANCY AFTER STOPPING THE PILL

If you do not desire pregnancy, you should use another method of birth-control immediately after stopping LYBREL. You can get pregnant within days after stopping LYBREL.

For additional information see “Detailed Patient Labeling.”

DETAILED PATIENT LABELING

This product (like all oral contraceptives) is intended to prevent pregnancy. Oral contraceptives do not protect against transmission of HIV (AIDS) and other sexually transmitted diseases (STDs) such as chlamydia, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis.

INTRODUCTION

Any woman who considers using oral contraceptives (the “birth-control pill” or “the pill”) should understand the benefits and risks of using this form of birth control. This leaflet will give you much of the information you will need to make this decision and will also help you determine if you are at risk of developing any of the serious side effects of the pill. It will tell you how to use the pill properly so that it will be as effective as possible. However, this leaflet is not a replacement for a careful discussion between you and your health care professional. You should discuss the information provided in this leaflet with him or her, both when you first start taking the pill and during your revisits. You should also follow your health care professional's advice with regard to regular check-ups while you are on the pill.

LYBREL is a birth-control pill that is taken every day. When you take LYBREL, the lining of your uterus does not undergo the changes needed for menstruation, and therefore you do not have regular menstrual periods. You are likely to have unscheduled or unplanned bleeding or spotting when you start to use LYBREL. The number of days each month with unscheduled bleeding and spotting usually decreases over time for the majority of women. When using LYBREL, the convenience of having no regular menstrual periods should be weighed against the inconvenience of unscheduled or unplanned breakthrough bleeding and spotting.

EFFECTIVENESS OF ORAL CONTRACEPTIVES

Oral contraceptives or “birth-control pills” or “the pill” are used to prevent pregnancy and are more effective than other nonsurgical methods of birth control. When they are taken correctly, without missing any pills the chance of becoming pregnant is approximately 1-2% per year (1 to 2 pregnancies per 100 women per year of use). Average failure rates are approximately 5% per year (5 pregnancies per 100 women per year of use) when women who miss pills are included. The chance of becoming pregnant increases with each missed pill.

In comparison, average failure rates for other methods of birth control during the first year of use are as follows:

IUD: 0.1-2%	Female condom alone: 21%
Depo-Provera [®] (injectable progestogen): 0.3%	Cervical cap
Norplant [®] System (levonorgestrel implants): 0.05%	Never given birth: 20%
Diaphragm with spermicides: 20%	Given birth: 40%
Spermicides alone: 26%	Periodic abstinence: 25%
Male condom alone: 14%	No methods: 85%

WHO SHOULD NOT TAKE ORAL CONTRACEPTIVES

Although cardiovascular disease risks may be increased with oral contraceptive use in healthy, non-smoking women over 40 (even with the newer low-dose formulations), there are also greater potential health risks associated with pregnancy in older women.

Cigarette smoking increases the risk of serious adverse effects on the heart and blood vessels from oral contraceptive use. This risk increases with age and with the amount of smoking (15 or more cigarettes per day has been associated with a significantly increased risk) and is quite marked in women over 35 years of age. Women who use oral contraceptives should not smoke.

Some women should not use the pill. For example, you should not take the pill if you have any of the following conditions:

- History of heart attack or stroke.
- Blood clots in the legs (thrombophlebitis), lungs (pulmonary embolism), or eyes.
- History of blood clots in the deep veins of your legs.
- Hereditary or acquired blood clotting disorders
- Chest pain (angina pectoris).
- Known or suspected breast cancer or cancer of the lining of the uterus, cervix or vagina, or certain hormonally-sensitive cancers.
- Unexplained vaginal bleeding (until a diagnosis is reached by your health care professional).
- Liver tumor (benign or cancerous) or active liver disease.

- Yellowing of the whites of the eyes or of the skin (jaundice) during pregnancy or during previous use of the pill.
- Known or suspected pregnancy.
- A need for surgery with prolonged bedrest.
- Heart valve or heart rhythm disorders that may be associated with formation of blood clots.
- Diabetes affecting your circulation.
- Headaches with neurological symptoms such as aura.
- Uncontrolled high blood pressure.
- Allergy or hypersensitivity to any of the components of LYBREL (levonorgestrel and ethinyl estradiol tablets).

Tell your health care professional if you have had any of these conditions. Your health care professional can recommend another method of birth control.

OTHER CONSIDERATIONS BEFORE TAKING ORAL CONTRACEPTIVES

Tell your health care professional if you or any family member has ever had:

- Breast nodules, fibrocystic disease of the breast, an abnormal breast X-ray or mammogram.
- Diabetes.
- Elevated cholesterol or triglycerides.
- High blood pressure.
- A tendency to form blood clots.
- Migraine or other headaches or epilepsy.
- Depression.
- Gallbladder, liver, heart, or kidney disease.
- History of scanty or irregular menstrual periods.

Women with any of these conditions should be checked often by their health care professional if they choose to use oral contraceptives. Also, be sure to inform your health care professional if you smoke or are on any medications.

RISKS OF TAKING ORAL CONTRACEPTIVES

LYBREL is a non-cyclic oral contraceptive that provides a low daily dose of estrogen and progestin; however, LYBREL provides women with more hormonal exposure on a yearly basis (13 additional weeks of hormone intake per year) than conventional cyclic oral contraceptives containing the same strength of synthetic estrogens and similar strength of progestins.

1. Risk of Developing Blood Clots

Blood clots and blockage of blood vessels are the most serious side effects of taking oral contraceptives and can cause death or serious disability. In particular, a clot in the legs can cause thrombophlebitis and a clot that travels to the lungs can cause a sudden blocking of the vessel carrying blood to the lungs. Rarely, clots occur in the blood vessels of the eye and may cause blindness, double vision, or impaired vision.

Users of combination oral contraceptives have a higher risk of developing blood clots compared to non-users. This risk is highest during the first year of combination oral contraceptive use.

If you take oral contraceptives and need elective surgery, need to stay in bed for a prolonged illness or injury, or have recently delivered a baby, you may be at risk of developing blood clots. You should consult your health care professional about stopping oral contraceptives three to four weeks before surgery and not taking oral contraceptives for two weeks after surgery or during bed rest. You should also not take oral contraceptives soon after delivery of a baby or after a midtrimester pregnancy termination. It is advisable to wait for at least four weeks after delivery if you are not breast-feeding. If you are breast-feeding, you should wait until you have weaned your child before using the pill. (See also the section **While Breast-Feeding in GENERAL PRECAUTIONS.**)

The risk of blood clots is greater in users of combination oral contraceptives compared to nonusers. This risk may be higher in users of high-dose pills (those containing 0.05 mg or more of estrogen) and may also be greater with longer use. In addition, some of these increased risks may continue for a number of years after stopping combination oral contraceptives. The risk of abnormal blood clotting increases with age in both users and nonusers of combination oral contraceptives, but the increased risk from the oral contraceptive appears to be present at all ages.

The excess risk of blood clots is highest during the first year a woman ever uses a combined oral contraceptive. This increased risk is lower than blood clots associated with pregnancy. The use of combination oral contraceptives also increases the risk of other clotting disorders, including heart attack and stroke. Blood clots in veins cause death in 1% to 2% of cases. The risk of clotting is further increased in women with other conditions. Examples include: smoking, high blood pressure, abnormal lipid levels, certain inherited or acquired clotting disorders, obesity, surgery or injury, recent delivery or second trimester abortion, prolonged inactivity or bedrest. If possible, combination oral contraceptives should be stopped before surgery and during prolonged inactivity or bedrest.

Cigarette smoking increases the risk of serious cardiovascular events. This risk increases with age and amount of smoking and is quite pronounced in women over 35. Women who use

combination oral contraceptives should be strongly advised not to smoke. If you smoke you should talk to your health care professional before taking combination oral contraceptives.

2. Heart Attacks and Strokes

Oral contraceptives may increase the tendency to develop strokes or transient ischemic attacks (blockage or rupture of blood vessels in the brain), and angina pectoris and heart attacks (blockage of blood vessels in the heart). Any of these conditions can cause death or serious disability.

Smoking greatly increases the possibility of suffering heart attacks and strokes. Furthermore, smoking and the use of oral contraceptives greatly increase the chances of developing and dying of heart disease.

Women with migraine (especially migraine/headache with neurological symptoms such as aura) who take oral contraceptives also may be at higher risk of stroke and must not use combination oral contraceptives (see section **WHO SHOULD NOT TAKE ORAL CONTRACEPTIVES**).

3. Gallbladder Disease

Oral contraceptive users probably have a greater risk than nonusers of having gallbladder disease, although this risk may be related to pills containing high doses of estrogens. Oral contraceptives may worsen existing gallbladder disease or accelerate the development of gallbladder disease in women previously without symptoms.

4. Liver Tumor

In rare cases, oral contraceptives can cause benign but dangerous liver tumors. These benign liver tumors can rupture and cause fatal internal bleeding. In addition, a possible but not definite association has been found with the pill and liver cancers in two studies in which a few women who developed these very rare cancers were found to have used oral contraceptives for long periods. However, liver cancers are extremely rare. The chance of developing liver cancer from using the pill is thus even rarer.

5. Cancer of the Reproductive Organs and Breasts

Various studies give conflicting reports on the relationship between breast cancer and oral contraceptive use.

Oral contraceptive use may slightly increase your chance of having breast cancer diagnosed, particularly if you started using hormonal contraceptives at a younger age.

After you stop using hormonal contraceptives, the chances of having breast cancer diagnosed begin to go down, and disappear 10 years after stopping use of the pill. It is not known whether this slightly increased risk of having breast cancer diagnosed is caused by the pill. It may be that women taking the pill were examined more often, so that breast cancer was more likely to be detected.

You should have regular breast examinations by a health care professional and examine your own breasts monthly. Tell your health care professional if you have a family history of breast cancer or if you have had breast nodules or an abnormal mammogram. Women who currently

have or have had breast cancer should not use oral contraceptives because breast cancer is usually a hormone-sensitive tumor.

Some studies have found an increase in the incidence of cancer of the cervix in women who use oral contraceptives. However, this finding may be related to factors other than the use of oral contraceptives.

6. Lipid Metabolism and Pancreatitis

There have been reports of increases of blood cholesterol and triglycerides in users of combination oral contraceptives. Increases in triglycerides have led to inflammation of the pancreas (pancreatitis) in some cases.

Estimated Risk of Death from a Birth-Control Method or Pregnancy

All methods of birth control and pregnancy are associated with a risk of developing certain diseases which may lead to disability or death. An estimate of the number of deaths associated with different methods of birth control and pregnancy has been calculated and is shown in the following table.

Annual Number of Birth-Related or Method-Related Deaths Associated with Control of Fertility per 100,000 Nonsterile Women, by Fertility-Control Method and According to Age

Method of control and outcome	15-19	20-24	25-29	30-34	35-39	40-44
No fertility-control methods*	7.0	7.4	9.1	14.8	25.7	28.2
Oral contraceptives						
nonsmoker**	0.3	0.5	0.9	1.9	13.8	31.6
Oral contraceptives						
smoker**	2.2	3.4	6.6	13.5	51.1	117.2
IUD**	0.8	0.8	1.0	1.0	1.4	1.4
Condom*	1.1	1.6	0.7	0.2	0.3	0.4
Diaphragm/spermicide*	1.9	1.2	1.2	1.3	2.2	2.8
Periodic abstinence*	2.5	1.6	1.6	1.7	2.9	3.6

* Deaths are birth-related

**Deaths are method-related

In the above table, the risk of death from any birth-control method is less than the risk of childbirth, except for oral contraceptive users over the age of 35 who smoke and pill users over the age of 40 even if they do not smoke. It can be seen in the table that for women aged 15 to 39, the risk of death was highest with pregnancy (7 to 26 deaths per 100,000 women, depending on age). Among pill users who do not smoke, the risk of death was always lower than that associated with pregnancy for any age group, except for those women over the age of 40, when

the risk increases to 32 deaths per 100,000 women, compared to 28 associated with pregnancy at that age. However, for pill users who smoke and are over the age of 35, the estimated number of deaths exceeds those for other methods of birth control. If a woman is over the age of 40 and smokes, her estimated risk of death is four times higher (117/100,000 women) than the estimated risk associated with pregnancy (28/100,000 women) in that age group.

The suggestion that women over 40 who do not smoke should not take oral contraceptives is based on information from older high-dose pills. An Advisory Committee of the FDA discussed this issue in 1989 and recommended that the benefits of oral contraceptive use by healthy, nonsmoking women over 40 years of age may outweigh the possible risks. Older women, as all women, who take oral contraceptives, should take an oral contraceptive which contains the least amount of estrogen and progestogen that is compatible with the individual patient needs.

WARNING SIGNALS

If any of these adverse effects occur while you are taking oral contraceptives, call your health care professional immediately:

- Sharp chest pain, coughing of blood, or sudden shortness of breath (indicating a possible clot in the lung).
- Pain in the calf (indicating a possible clot in the leg).
- Crushing chest pain or heaviness in the chest (indicating a possible heart attack).
- Sudden severe headache or vomiting, dizziness or fainting, disturbances of vision or speech, weakness, or numbness in an arm or leg (indicating a possible stroke).
- Sudden partial or complete loss of vision (indicating a possible clot in the eye).
- Breast lumps (indicating possible breast cancer or fibrocystic disease of the breast; ask your health care professional to show you how to examine your breasts).
- Severe pain or tenderness in the stomach area (indicating a possibly ruptured liver tumor).
- Difficulty in sleeping, weakness, lack of energy, fatigue, or change in mood (possibly indicating severe depression).
- Jaundice or a yellowing of the skin or eyeballs, accompanied frequently by fever, fatigue, loss of appetite, dark-colored urine, or light-colored bowel movements (indicating possible liver problems).

SIDE EFFECTS OF ORAL CONTRACEPTIVES

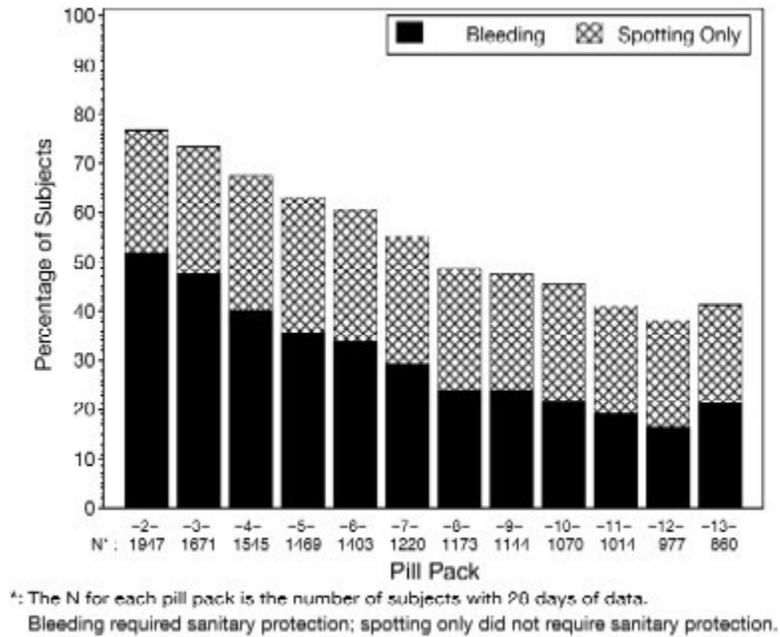
1. Unscheduled Bleeding and Spotting

Unscheduled bleeding or spotting is likely to occur while you are taking LYBREL. Unscheduled bleeding or spotting occurs most often during the first seven pill packs of LYBREL use. It tends to decrease with subsequent pill packs of use, but may occur after you have been taking LYBREL for some time. In a study of LYBREL, 60% of women had bleeding and/or spotting

during the sixth pill pack of use. Bleeding and/or spotting decreased to 48% during pill pack 9, and to 41% during pill pack 13. In this study, the percentage of women who discontinued treatment, at least in part, due to unscheduled bleeding or spotting was 18%.

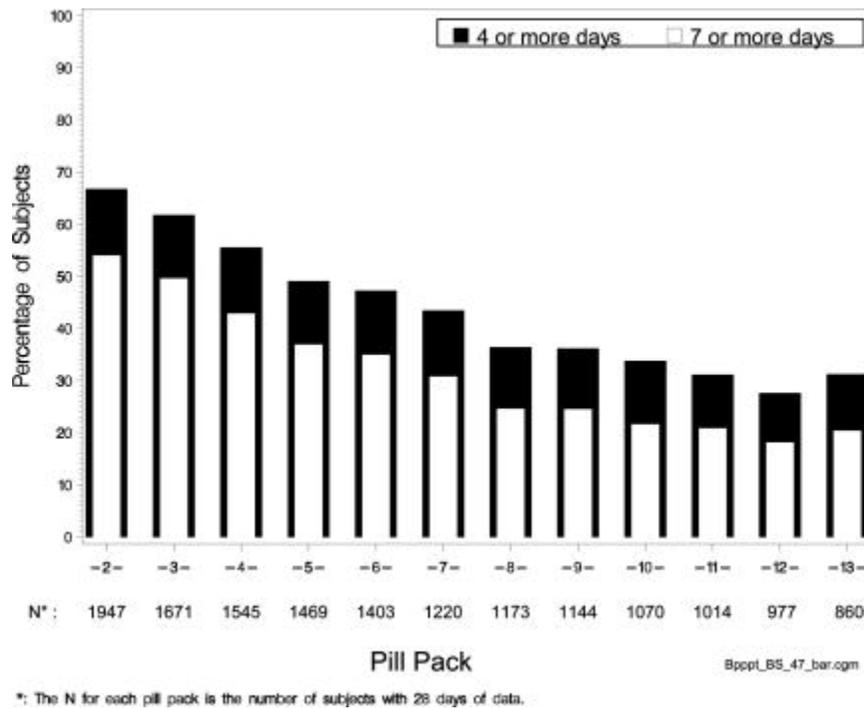
The following figure shows by pill pack, the percentage of women using LYBREL in a North American study, who experienced unscheduled bleeding or spotting only.

Percentage of Subjects Reporting Bleeding or Spotting Only per Pill Pack



The following figure shows the percentage of women using LYBREL in a North American study who had 4 or more and 7 or more days of bleeding and/or spotting during each pill pack. During pill pack 2, 67% of women experienced 4 or more days of bleeding and/or spotting and 54% of these women experienced 7 or more days of bleeding and/or spotting. During the final pill pack of use of LYBREL (pill pack 13), these percentages were 31% and 20%, respectively.

Percentage of Subjects Reporting Greater Than or Equal to 4 or 7 Days of Bleeding and/or Spotting per Pill Pack (Study 313-NA)



It is important to continue taking your pills at the same time each day according to your daily routine, even if you are having unscheduled bleeding or spotting. If the unscheduled bleeding and/or spotting continue for an extended period of time (for example, 7 consecutive days) or if the bleeding is heavy, contact your health care professional.

2. Contact Lenses

If you wear contact lenses and notice a change in vision or an inability to wear your lenses, contact your health care professional.

3. Fluid Retention

Oral contraceptives may cause edema (fluid retention) with swelling of the fingers or ankles and may raise your blood pressure. If you experience fluid retention, contact your health care professional.

4. Melasma

A spotty darkening of the skin is possible, particularly of the face.

5. Other Side Effects

Other side effects may include nausea, breast tenderness, change in appetite, headache, nervousness, depression, dizziness, loss of scalp hair, rash, vaginal infections, inflammation of the pancreas, and allergic reactions.

If these or any other side effects bother you, contact your health care professional.

GENERAL PRECAUTIONS

1. Use of Oral Contraceptives Before or During Early Pregnancy

Because regular monthly bleeding does not occur on LYBREL, an unexpected pregnancy may be difficult to recognize. If you suspect you may be pregnant, or if you have symptoms of pregnancy such as nausea/vomiting or unusual breast tenderness, a pregnancy test should be performed and you should contact your health care professional. Stop taking LYBREL if you are pregnant. Pregnancy is unlikely if the pill is taken as directed.

There is no conclusive evidence that oral contraceptive use is associated with an increase in birth defects, when taken inadvertently during early pregnancy. Previously, a few studies had reported that oral contraceptives might be associated with birth defects, but these studies have not been confirmed. Nevertheless, oral contraceptives should not be used during pregnancy. You should check with your health care professional about risks to your unborn child of any medication taken during pregnancy.

2. While Breast-Feeding

If you are breast-feeding, consult your health care professional before starting oral contraceptives. Some of the drug will be passed on to the child in the milk. A few adverse effects on the child have been reported, including yellowing of the skin (jaundice) and breast enlargement. In addition, oral contraceptives may decrease the amount and quality of your milk. If possible, do not use oral contraceptives while breast-feeding. You should use another method of contraception since breast-feeding provides only partial protection from becoming pregnant and this partial protection decreases significantly as you breast-feed for longer periods of time. You should consider starting oral contraceptives only after you have weaned your child completely.

3. Laboratory Tests

If you are scheduled for any laboratory tests, tell your health care professional you are taking birth-control pills. Certain blood tests may be affected by birth-control pills.

4. Drug Interactions

Certain drugs may interact with birth-control pills to make them less effective in preventing pregnancy or cause an increase in unscheduled bleeding. Such drugs include rifampin, drugs used for epilepsy such as barbiturates (for example, phenobarbital) and phenytoin (Dilantin[®] is one brand of this drug), primidone (Mysoline[®]), topiramate (Topamax[®]), carbamazepine (Tegretol[®] is one brand of this drug), phenylbutazone (Butazolidin[®] is one brand), some drugs used for HIV or AIDS such as ritonavir (Norvir[®]), modafinil (Provigil[®]) and possibly certain antibiotics (such as ampicillin and other penicillins, and tetracyclines), and herbal products containing St. John's Wort (*Hypericum perforatum*). You may also need to use a nonhormonal method of contraception during any pill pack in which you take drugs that can make oral contraceptives less effective.

You may be at higher risk for a specific type of liver dysfunction if you take troleandomycin and oral contraceptives at the same time.

You should inform your health care professional about all medicines you are taking, including nonprescription products.

5. Sexually Transmitted Diseases

This product (like all oral contraceptives) is intended to prevent pregnancy. It does not protect against transmission of HIV (AIDS) and other sexually transmitted diseases such as chlamydia, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis.

What You Should Know About Your Menstrual Cycle When You Use LYBREL

You are likely to have unscheduled or unplanned bleeding or spotting when you start to use LYBREL. The number of days each month with bleeding or spotting usually decreases over time in the majority of women. In a study of LYBREL, about 5 out of 10 women had 7 or more days of bleeding or spotting while using their third 28-day pill pack of LYBREL. The number of women with 7 or more days of bleeding or spotting decreased to 3 out of 10 women during the use of their seventh pill pack. Among women who continued to use LYBREL for one year, about 6 out of 10 women had no bleeding or spotting during their last month of use.

Do not stop taking LYBREL because of bleeding or spotting as this will increase your chance of getting pregnant. If the spotting or bleeding continues for more than 7 consecutive days or if the bleeding is heavy, call your health care provider.

Can I Get Pregnant While Taking LYBREL?

You are not likely to get pregnant if you take LYBREL at the same time everyday as directed by your health care provider. Because regular monthly bleeding does not occur on LYBREL, it may be difficult to recognize if you get pregnant. If you suspect that you may be pregnant, or if you have symptoms of pregnancy such as nausea/vomiting or unusual breast tenderness, you should have a pregnancy test and you should contact your health care professional. Stop taking LYBREL if you are pregnant.

HOW TO TAKE LYBREL

Important Points to Remember

Before You Start Taking LYBREL:

1. **BE SURE TO READ THESE DIRECTIONS:**

Before you start taking LYBREL.

And

Anytime you are not sure what to do.

2. **THE RIGHT WAY TO TAKE LYBREL IS TO TAKE ONE PILL EVERY DAY AT THE SAME TIME.**

If you miss pills, you could get pregnant. This includes starting the pack late. The more pills you miss, the more likely you are to get pregnant. See “WHAT TO DO IF YOU MISS PILLS” below.

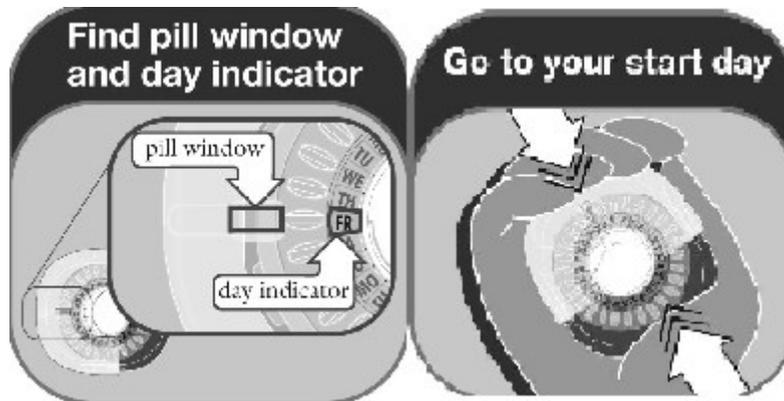
3. **MANY WOMEN HAVE SPOTTING OR LIGHT BLEEDING, OR MAY FEEL SICK TO THEIR STOMACH DURING THE FIRST 1-3 PACKS OF PILLS.**

If you feel sick to your stomach, do not stop taking LYBREL. This will usually go away. If it doesn't go away, check with your health care professional.

4. MOST WOMEN HAVE SPOTTING OR BLEEDING DURING THE FIRST FEW MONTHS OF TAKING *LYBREL*. Do not stop taking your pills even if you are having bleeding or spotting. If the bleeding or spotting lasts for more than 7 consecutive days, talk to your health care provider.
5. MISSING PILLS CAN ALSO CAUSE SPOTTING OR LIGHT BLEEDING, even when you make up these missed pills.
On the days you take 2 pills to make up for missed pills, you could also feel a little sick to your stomach.
6. IF YOU VOMIT (within 4 hours after you take your pill), you should follow the instructions for WHAT TO DO IF YOU MISS PILLS. IF YOU HAVE DIARRHEA or IF YOU TAKE SOME MEDICINES, including some antibiotics, your pills may not work as well.
Use a back-up nonhormonal method (such as condoms and/or spermicide) until you check with your health care professional.
7. IF YOU HAVE TROUBLE REMEMBERING TO TAKE *LYBREL*, talk to your health care professional about how to make pill-taking easier or about using another method of birth control.
8. IF YOU HAVE ANY QUESTIONS OR ARE UNSURE ABOUT THE INFORMATION IN THIS LEAFLET, call your health care professional.

BEFORE YOU START TAKING *LYBREL*

1. DECIDE WHAT TIME OF DAY YOU WANT TO TAKE YOUR PILL. It is important to take your pill at the SAME TIME every day.
2. LOOK AT YOUR *LYBREL* DISPENSER. The pill pack has 28 “active” yellow pills (with hormones).
3. Follow these 3 steps to set your *LYBREL* case to your starting day:
 - a. Look at your ClickCase[®] dispenser. Find the pill window and day indicator. Place the case lengthwise in the palm of your hand, so that the pill window and day indicator are visible.



- b. Make note of the day that lines up with the window. If the desired start day is not aligned with the window, firmly squeeze the ends of the case together until it clicks. Then fully RELEASE. Keep clicking and releasing until you reach the desired start day.
- c. To take your pill, firmly squeeze the ends of the case together until it clicks; do NOT release. Turn the case over, and allow the pill to drop out into your other hand. Before releasing, turn the case back over, then fully RELEASE, and the next day's pill automatically advances.



4. BE SURE YOU HAVE READY AT ALL TIMES:

ANOTHER KIND OF NONHORMONAL BIRTH CONTROL (such as condoms and/or spermicide) to use as a back-up in case you miss pills.

AN EXTRA, FULL PILL PACK.

WHEN TO START THE *FIRST* PACK OF LYBREL

Day 1 Start

1. Take the first “active” yellow pill of the first pack during the *first 24 hours of your period*.

2. You will not need to use a back-up nonhormonal method of birth control, since you are starting the pill at the beginning of your period.

WHAT TO DO DURING THE MONTH

1. TAKE ONE PILL AT THE SAME TIME EVERY DAY UNTIL THE PACK IS EMPTY.
Do not skip pills even if you are spotting or bleeding or feel sick to your stomach (nausea).
Do not skip pills even if you do not have sex very often.

2. WHEN YOU FINISH A PACK

Start the next pack on the day after your last pill. **Do not wait any days between packs.**

IF YOU SWITCH FROM ANOTHER BRAND OF COMBINATION PILLS:

When switching from a 21 pill pack: Start LYBREL on the first day of your period (withdrawal bleed). Be sure that no more than 7 days pass between the last day of your 21-day pack and your first LYBREL pill.

When switching from a 28 pill pack (21 active and 7 inactive pills, or 24 active and 4 inactive pills): Start LYBREL on the first day of your period (withdrawal bleed). Be sure that no more than 7 days pass after the last active pill and your first LYBREL pill.

IF YOU SWITCH FROM ANOTHER TYPE OF BIRTH CONTROL

When switching from other types of birth control such as pills containing only a progestin (progestin only pill or POP), an injection, or an implant, your health care professional will provide you with instructions for when to start LYBREL.

WHAT TO DO IF YOU MISS PILLS

Combination oral contraceptives may not be as effective if you miss pills. Instructions for what to do if you miss pills are provided in the following table.

# of pills missed in a row	What to do when you miss a pill(s)
1 missed pill	<ul style="list-style-type: none"> • Take the missed pill as soon as you remember. <p style="text-align: center;">THEN</p> <ul style="list-style-type: none"> • Take the next pill at your regular time. This means you may take 2 pills in 1 day. • You COULD BECOME PREGNANT if you have sex during the 7 days after you restart your pills. You MUST use a nonhormonal birth-control method (such as condoms and/or spermicide) as a back-up for those 7 days.

# of pills missed in a row	What to do when you miss a pill(s)
<p>2 missed pills</p> <p>and remembered on the day of the second missed pill</p>	<ul style="list-style-type: none"> • Take 2 missed pills on the day you remember. The following day you are back on schedule to take 1 pill a day. <p>For example, you take your pills in the morning and you missed 1 pill on Monday and 1 on Tuesday. On Tuesday evening you remembered that you missed your Monday and Tuesday pills. You take the 2 missed pills on Tuesday evening and on Wednesday morning you're back on schedule and you take 1 pill.</p> <ul style="list-style-type: none"> • You COULD BECOME PREGNANT if you have sex during the 7 days after you restart your pills. You MUST use a nonhormonal birth-control method (such as condoms and/or spermicide) as a back-up for those 7 days.
<p>2 missed pills</p> <p>and remembered on the day after the second pill is missed</p>	<ul style="list-style-type: none"> • Take 2 missed pills on the day you remember. The next day you take 2 pills. The following day you are back on schedule to take your pills. <p>For example, you take your pills in the morning and you missed 1 pill on Monday and 1 on Tuesday. On Wednesday morning you remembered that you missed your Monday and Tuesday pills. You take the 2 missed pills on Wednesday morning and 2 pills on Thursday morning. On Friday morning you're back on schedule and you take 1 pill.</p> <ul style="list-style-type: none"> • You COULD BECOME PREGNANT if you have sex during the 7 days after you restart your pills. You MUST use a nonhormonal birth-control method (such as condoms and/or spermicide) as a back-up for those 7 days.
<p>3 or more missed pills</p>	<ul style="list-style-type: none"> • Contact your health care professional for further advice. Keep taking one pill every day until you reach your health care professional. Do not take the missed pills. • You COULD BECOME PREGNANT if you have sex during the 7 days after you restart your pills. You MUST use a nonhormonal birth-control method (such as condoms and/or spermicide) as a back-up for those 7 days.

FINALLY, IF YOU ARE STILL NOT SURE WHAT TO DO ABOUT THE PILLS YOU HAVE MISSED

Use a BACK-UP NONHORMONAL BIRTH-CONTROL METHOD anytime you have sex.

KEEP TAKING ONE PILL EACH DAY until you can reach your health care professional.

PREGNANCY DUE TO PILL FAILURE

The incidence of pill failure resulting in pregnancy is approximately 1-2% per year (1 to 2 pregnancies per 100 women per year of use) if taken every day as directed, but the average failure rate is approximately 5% per year (5 pregnancies per 100 women per year of use) including women who do not always take the pill exactly as directed without missing any pills. If you do become pregnant, the risk to the fetus is minimal, but you should stop taking your pills and discuss the pregnancy with your health care professional.

PREGNANCY AFTER STOPPING THE PILL

If you do not desire pregnancy, you should use another method of birth-control immediately after stopping LYBREL. A pregnancy can occur within days after stopping LYBREL.

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

OVERDOSAGE

Overdosage may cause nausea, vomiting, breast tenderness, dizziness, abdominal pain, and fatigue/drowsiness. Withdrawal bleeding may occur in females. In case of overdosage, contact your health care professional or pharmacist.

OTHER INFORMATION

Your health care professional will take a medical and family history before prescribing oral contraceptives and will examine you. The physical examination may be delayed to another time if you request it and the health care professional believes that it is appropriate to postpone it. You should be reexamined at least once a year. Be sure to inform your health care professional 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 professional, 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, some information suggests that the use of oral contraceptives provide certain other benefits. The benefits are:

- Decreased blood loss, and less iron may be lost. Therefore, anemia due to iron deficiency is less likely to occur.
- Pain or other cycle-related symptoms may occur 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 health care professional or pharmacist. They have a more technical leaflet called the Professional Labeling which you may wish to read.



This product's label may have been updated. For current package insert and further product information, please visit www.wyeth.com or call our medical communications department toll-free at 1-800-934-5556.



United States Patent Numbers: 6,500,814; D497,803S

Wyeth®

Wyeth Pharmaceuticals Inc.
Philadelphia, PA 19101

(Update W10522C006)
(Update ET Number)
(Update Rev Date)