ZOVIA 1/35 - ethynodiol diacetate and ethinyl estradiol tablets
Mayne Pharma Inc.

Zovia® 1/35
(Ethynodiol Diacetate and Ethinyl Estradiol Tablets USP, 1 mg/35 mcg)

Rx only

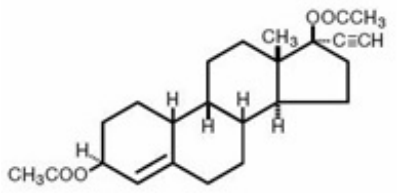
Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

DESCRIPTION

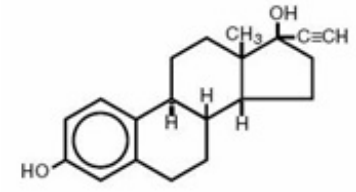
Zovia 1/35: Each pale pink tablet contains 1 mg of ethynodiol diacetate and 35 mcg of ethinyl estradiol, and the inactive ingredients include lactose monohydrate, pregelatinized starch, vitamin e, magnesium stearate, microcrystalline cellulose, croscarmellose sodium, povidone, polyvinyl alcohol, titanium dioxide, talc, polyethylene glycol/macrogol, lecithin (soya), FD&C Red #40 aluminum lake, FD&C Blue #1 aluminum lake, and FD&C yellow #6 aluminum lake. Each white tablet in the Zovia 1/35 package is a placebo containing no active ingredients and the inactive ingredients include lactose monohydrate, magnesium stearate, pregelatinized starch, titanium dioxide, polydextrose, hypromellose, triacetin, and polyethylene glycol.

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:



ethynodiol diacetate
M.W.=384.51



ethinyl estradiol
M.W.=296.41

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

Zovia 1/35 is 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 and progestogen implants and injections, depends upon the reliability with which they are used. Correct and consistent use of methods can result in lower failure rates.

Table 1. Percentage of women experiencing an unintended pregnancy during the first year of typical use and the first year of perfect use of contraception and the percentage continuing use at the end of the first year. United States.

Method (1)	% of women experiencing an unintended pregnancy within the first year of use: Typical use[A] (2)	% of women experiencing an unintended pregnancy within the first year of use: Perfect use[B] (3)	% of women Continuing Use at one Year[C] (4)
Chance [D]	85	85	
Spermicides [E]	26	6	40
Periodic abstinence	25		63
Calendar		9	
Ovulation method		3	
Sympto-thermal [F]		2	
Post-ovulation		1	
Withdrawal	19	4	
Cap [G]			
Parous women	40	26	42
Nulliparous women	20	9	56
Sponge			
Parous women	40	20	42
Nulliparous women	20	9	56
Diaphragm [G]	20	6	56
Condom [H]			
Female (Reality)	21	5	56
Male	14	3	61
Pill	5		71
Progestin only		0.5	
Combined		0.1	
IUD			
Progesterone T	2.0	1.5	81
Copper T 380A	0.8	0.6	78
LNg 20	0.1	0.1	81
Injection (Depo-Provera)	0.3	0.3	70
Implant (Norplant and Norplant-2)	0.05	0.05	88
Female sterilization	0.5	0.5	100
Male sterilization	0.15	0.10	100

Emergency Contraceptive Pills: Treatment initiated within 72 hours after unprotected intercourse reduces the risk of pregnancy by at least 75%. [I]

Lactational Amenorrhea Method: LAM is a highly effective, *temporary* method of contraception. [J]

Source: Trussell J, Contraceptive efficacy. In Hatcher RA, Trussell J, Stewart F, Cates W, Stewart GK, Kowal D, Guest F, *Contraceptive Technology: Seventeenth Revised Edition.* New York NY: Irvington Publishers, 1998, in press.[1]

(A) Among typical couples who initiate use of a method (not necessarily for the first time), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason.

(B) Among couples who initiate use of a method (not necessarily for the first time) and who use it perfectly (both consistently and correctly), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason.

(C) Among couples attempting to avoid pregnancy, the percentage who continue to use a method for one year.

(D) The percents becoming pregnant in columns (2) and (3) are based on data from populations where contraception is not used and from women who cease using contraception in order to become pregnant. Among such populations, about 89% become pregnant within one year. This estimate was lowered slightly (to 85%) to represent the percent who would become pregnant within one year among women now relying on reversible methods of contraception if they abandoned contraception altogether.

(E) Foams, creams, gels, vaginal suppositories, and vaginal film.

(F) Cervical mucus (ovulation) method supplemented by calendar in the pre-ovulatory and basal body temperature in the post-ovulatory phases.

(G) With spermicidal cream or jelly.

(H) Without spermicides.

(I) The treatment schedule is one dose within 72 hours after unprotected intercourse and a second dose 12 hours after the first dose. The Food and Drug Administration has declared the following brands of oral contraceptives to be safe and effective for emergency contraception: Ovral (1 dose is 2 white pills), Alesse (1 dose is 5 pink pills), Nordette or Levlen (1 dose is 2 light-orange pills), Lo/Ovral (1 dose is 4 white pills), Triphasil or Tri-Levlen (1 dose is 4 yellow pills).

(J) However, to maintain effective protection against pregnancy, another method of contraception must be used as soon as menstruation resumes, the frequency or duration of breastfeeds is reduced, bottle feeds are introduced, or the baby reaches six months of age.

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

● Are receiving Hepatitis C drug combinations containing

ombitasvir/paritaprevir/ritonavir, with or without dasabuvir, due to the potential for ALT elevations (see Warnings, **RISK OF LIVER ENZYME ELEVATIONS WITH CONCOMITANT HEPATITIS C TREATMENT**)

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 casecontrol 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.

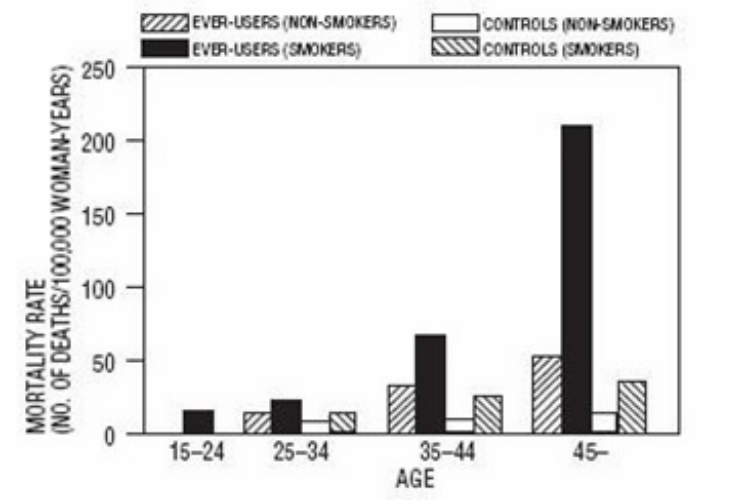
1. Thromboembolic disorders and other vascular problems.

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 hyperinsulinism.[32] Oral contraceptives have been shown to increase blood pressure among some users (see WARNING No. 10). Similar effects on risk factors have been associated with an increased risk of heart disease.

b. Thromboembolism.

An increased risk of thromboembolic and thrombotic disease associated with the use of oral contraceptives is well established.17, 33-51 Case-control studies have estimated the relative risk to be 3 for the first episode of superficial venous thrombosis, 4 to 11 for deep vein thrombosis or pulmonary embolism, and 1.5 to 6 for women with predisposing conditions for venous thromboembolic disease.[34-37, 45, 46] Cohort studies have shown the relative risk to be somewhat lower, about 3 for new cases (subjects with no past history of venous thrombosis or varicose veins) and about 4.5 for new cases requiring hospitalization.[42, 47, 48] The risk of venous thromboembolic disease associated with oral contraceptives is not related to duration of use.

A two- to seven-fold increase in relative risk of postoperative thromboembolic complications has been reported with the use of oral contraceptives.[38, 39]The relative risk of venous thrombosis in women who have predisposing conditions is about twice that of women without such medical conditions.[43] If feasible, oral contraceptives should be discontinued at least 4 weeks prior to and for 2 weeks after elective surgery of a type

associated with an increased risk of thromboembolism, and also during and following prolonged immobilization. Since the immediate postpartum period is also associated with an increased risk of thromboembolism, oral contraceptives should be started no earlier than 4 to 6 weeks after delivery in women who elect not to breast feed.

c. Cerebrovascular diseases.

Both the relative and attributable risks of cerebrovascular events (thrombotic and hemorrhagic strokes) have been reported to be increased with oral contraceptive use,[14, 17, 18, 34, 42, 46, 52-59] although, in general, the risk was greatest among older (over 35 years), hypertensive women who also smoked. Hypertension was reported to be a risk factor for both users and nonusers, for both types of strokes, while smoking increased the risk for hemorrhagic strokes.

In one large study, [52] the relative risk for thrombotic stroke was reported as 9.5 times greater in users than in nonusers. It ranged from 3 for normotensive users to 14 for users with severe hypertension.[54] The relative risk for hemorrhagic stroke was reported to be 1.2 for nonsmokers who used oral contraceptives, 1.9 to 2.6 for smokers who did not use oral contraceptives, 6.1 to 7.6 for smokers who used oral contraceptives, 1.8 for normotensive users, and 25.7 for users with severe hypertension. The risk is also greater in older women and among smokers.

d. Dose-related risk of vascular disease with oral contraceptives.

A positive association has been reported between the amount of estrogen and progestogen in oral contraceptives and the risk of vascular disease.[41, 43, 53, 59-64] A decline in serum high density lipoproteins (HDL) has been reported with many progestogens.[23-31] A decline in serum high density lipoproteins has been associated with an increased incidence of ischemic heart disease.[65] Because estrogens increase HDL-cholesterol, the net effect of an oral contraceptive depends on the balance achieved between doses of estrogen and progestogen and the nature and absolute amount of progestogens used in the contraceptives. The amount of both steroids should be considered in the choice of an oral contraceptive.

Minimizing exposure to estrogen and progestogen is in keeping with good principles of therapeutics. For any particular estrogen-progestogen combination, the dosage regimen prescribed should be one that contains the least amount of estrogen and progestogen that is compatible with a low failure rate and the needs of the individual patient. New acceptors of oral contraceptives should be started on preparations containing the lowest estrogen content that produces satisfactory results in the individual.

e. Persistence of risk of vascular disease.

There are three studies that have shown persistence of risk of vascular disease for users of oral contraceptives. In a study in the United States, the risk of developing myocardial infarction after discontinuing oral contraceptives persisted for at least 9 years for women 40-49 years old who had used oral contraceptives for 5 or more years, but this increased risk was not demonstrated in other age groups.[16] Another American study reported former use of oral contraceptives was significantly associated with increased risk of subarachnoid hemorrhage.[57] In another study, in Great Britain, the risk of developing non-rheumatic heart disease plus hypertension, subarachnoid hemorrhage, cerebral thrombosis, and transient ischemic attacks persisted for at least 6 years after discontinuation of oral contraceptives, although the excess risk was small.[14, 18, 66] It should be noted that these studies were performed with oral contraceptive

formulations containing 50 mcg or more of estrogens.

2. Estimates of mortality from contraceptive use.

One study[67] gathered data from a variety of sources that have estimated the mortality rates associated with different methods of contraception at different ages (Table 2). These estimates include the combined risk of death associated with contraceptive methods plus the risk attributable to pregnancy in the event of method failure. Each method of contraception has its specific benefits and risks. The study concluded that, with the exception of oral contraceptive users 35 and older who smoke and 40 or older who do not smoke, mortality associated with all methods of birth control is low and below that associated with childbirth. The observation of a possible increase in risk of mortality with age for oral contraceptive users is based on data gathered in the 1970's, but not reported until 1983.[67] However, current clinical practice involves the use of lower estrogen dose formulations combined with careful restriction of oral contraceptive use to women who do not have the various risk factors listed in this labeling.

Because of these changes in practice and, also, because of some limited new data that suggest that the risk of cardiovascular disease with the use of oral contraceptives may now be less than previously observed,[48,152] the Fertility and Maternal Health Drugs Advisory Committee was asked to review the topic in 1989. The Committee concluded that, although cardiovascular disease risks may be increased with oral contraceptive use after age 40 in healthy nonsmoking women (even with the newer low-dose formulations), there are greater potential health risks associated with pregnancy in older women and with the alternative surgical and medical procedures that may be necessary if such women do not have access to effective and acceptable means of contraception.

Therefore, the Committee recommended that the benefits of oral contraceptive use by healthy nonsmoking women over 40 may outweigh the possible risks. Of course, older women, as all women who take oral contraceptives, should take the lowest possible dose formulation that is effective.

Table 2. Annual number of birth-related or method-related deaths associated with control of fertility per 100,000 nonsterile women, by fertility control method according to age.[67]

	Age					
Method of control	**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
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

Adapted from Ory.[67]

3. Carcinoma of the breast and reproductive organs.

Numerous epidemiological studies have been performed on the incidence of breast, endometrial, ovarian, and cervical cancer in women using oral contraceptives. While there are conflicting reports, many studies suggest that the use of oral contraceptives is not associated with an overall increase in the risk of developing breast cancer.[17, 40, 68-78] Other studies, however, have reported an increased risk overall,[153-155] or in certain subgroups. In these studies, increased risk has been associated with long duration of use, use beginning at a young age, use before the first term pregnancy, use by those who had an early menarche, those who had a positive family history of breast cancer, or in nulliparas.[79-102, 151, 156-162] These risks have been surveyed in two books[163-164] and in review articles.[85, 99, 153, 165-167]

Some studies suggested that oral contraceptive use was associated with an increase in the risk of cervical intraepithelial neoplasia, dysplasia, erosion, carcinoma, or microglandular dysplasia in some populations of women.[17, 50, 103-115] However, there continues to be controversy about the extent to which such findings may be due to differences in sexual behavior and other factors.

In spite of many studies of the relationship between oral contraceptive use and breast and cervical cancers, a cause and effect relationship has not been established.

4. Hepatic neoplasia.

Benign hepatic adenomas and other hepatic lesions have been associated with oral contraceptive use, [116-121] although the incidence of such benign tumors is rare in the United States. Indirect calculations have estimated the attributable risk to be in the range of 3.3 cases per 100,000 for users, a risk that increases after 4 or more years of use.[120] Rupture of benign, hepatic adenomas or other lesions may cause death through intraabdominal hemorrhage. Therefore, such lesions should be considered in women

presenting with abdominal pain and tenderness, abdominal mass, or shock. About one quarter of the cases presented because of abdominal masses; up to one half had signs and symptoms of acute intraperitoneal hemorrhage.[121] Diagnosis may prove difficult.

Studies from the U.S.,[122, 150] Great Britain,[123, 124] and Italy[125] have shown an increased risk of hepatocellular carcinoma in long-term (>8 years; relative risk of 7-20) oral contraceptive users. However, these cancers are rare in the United States, and the attributable risk (the excess incidence) of liver cancers in oral contraceptive users approaches less than 1 per 1,000,000 users.

5. Risk of liver enzyme elevations with concomitant hepatitis C treatment

During clinical trials with the Hepatitis C combination drug regimen that contains ombitasvir/paritaprevir/ ritonavir, with or without dasabuvir, ALT elevations greater than 5 times the upper limit of normal (ULN) including some cases greater than 20 times the ULN, were significantly more frequent in women using ethinyl estradiol-containing medications suchs as COCs. Discontinue Zovia 1/35 prior to starting therapy with the combination drug regimen ombitasvir/paritaprevir/ritonavir, with or without dasabuvir [see Contraindications]. Zovia 1/35 can be restarted approximately 2 weeks following completion of treatment with the combination drug regimen.

6. Ocular lesions.

There have been reports of retinal thrombosis and other ocular lesions associated with the use of oral contraceptives. Oral contraceptives should be discontinued if there is unexplained, gradual or sudden, partial or complete loss of vision; onset of proptosis or diplopia; papilledema; or any evidence of retinal vascular lesions. Appropriate diagnostic and therapeutic measures should be undertaken immediately.

7. Oral contraceptive use before or during pregnancy.

Extensive epidemiological studies have revealed no increased risk of birth defects in women who have used oral contraceptives prior to pregnancy.[126, 129] The majority of recent studies also do not suggest a teratogenic effect, particularly insofar as cardiac anomalies and limb reduction defects are concerned, [126, 129] when the pill is taken inadvertently during early pregnancy.

The administration of oral contraceptives to induce withdrawal bleeding should not be used as a test for pregnancy. Oral contraceptives should not be used during pregnancy to treat threatened or habitual abortion. It is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing oral contraceptive use. If the patient has not adhered to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period and further use of oral contraceptives should be withheld until pregnancy has been ruled out. Oral contraceptive use should be discontinued if pregnancy is confirmed.

8. Gallbladder disease.

Earlier studies reported an increased lifetime relative risk of gallbladder surgery in users of oral contraceptives and estrogens.[40, 42, 53, 70] More recent studies, however, have shown that the relative risk of developing gallbladder disease among oral contraceptive users may be minimal.[130-132] The recent findings of minimal risk may be related to the use of oral contraceptive formulations containing lower doses of estrogens and progestogens.

9. Carbohydrate and lipid metabolic effects.

Oral contraceptives have been shown to cause a decrease in glucose tolerance in a significant percentage of users.[32] This effect has been shown to be directly related to estrogen dose.[133] Progestogens increase insulin secretion and create insulin resistance, the effect varying with different progestational agents.[32, 134] However, in the nondiabetic woman, oral contraceptives appear to have no effect on fasting blood glucose. Because of these demonstrated effects, prediabetic and diabetic women should be carefully observed while taking oral contraceptives.

Some women may have persistent hypertriglyceridemia while on the pill. As discussed earlier (see **WARNINGS**1a and 1d), changes in serum triglycerides and lipoprotein levels have been reported in oral contraceptive users.[23-31, 135, 136]

10. Elevated blood pressure.

An increase in blood pressure has been reported in women taking oral contraceptives[50, 53, 137-139] and this increase is more likely in older oral contraceptive users[137] and with extended duration of use.[53] Data from the Royal College of General Practitioners[138] and subsequent randomized trials have shown that the incidence of hypertension increases with increasing concentrations of progestogens.

Women with a history of hypertension or hypertension-related disease, or renal disease[139] should be encouraged to use another method of contraception. If such women elect to use oral contraceptives, they should be monitored closely and if significant elevation of blood pressure occurs, oral contraceptives should be discontinued. For most women, elevated blood pressure will return to normal after stopping oral contraceptives,[137] and there is no difference in the occurrence of hypertension among ever- and never-users.[140]

11. Headache.

The onset or exacerbation of migraine or the development of headache of a new pattern that is recurrent, persistent, or severe requires discontinuation of oral contraceptives and evaluation of the cause.

12. Bleeding irregularities.

Breakthrough bleeding and spotting are sometimes encountered in patients on oral contraceptives, especially during the first three months of use. Nonhormonal causes should be considered and adequate diagnostic measures taken to rule out malignancy or pregnancy in the event of breakthrough bleeding, as in the case of any abnormal vaginal bleeding. If a pathologic basis has been excluded, time alone or a change to another formulation may solve the problem. In the event of amenorrhea, pregnancy should be ruled out. Some women may encounter post-pill amenorrhea or oligomenorrhea, especially when such a condition was pre-existent.

PRECAUTIONS

1. Physical examination and follow-up.

It is good medical practice for all women to have annual history and physical examinations, including women using oral contraceptives. The physical examination, however, may be deferred until after initiation of oral contraceptives if requested by the

woman and judged appropriate by the clinician. The physical examination should include special reference to blood pressure, breasts, abdomen, and pelvic organs, including cervical cytology, and relevant laboratory tests. In case of undiagnosed, persistent, or recurrent abnormal vaginal bleeding, appropriate measures should be conducted to rule out malignancy. Women with a strong family history of breast cancer or who have breast nodules should be monitored with particular care.

2. Lipid disorders.

Women who are being treated for hyperlipidemias should be followed closely if they elect to use oral contraceptives. Some progestogens may elevate LDL levels and may render the control of hyperlipidemias more difficult.

3. Liver function.

If jaundice develops in any woman receiving oral contraceptives, they should be discontinued. Steroids may be poorly metabolized in patients with impaired liver function and should be administered with caution in such patients. Cholestatic jaundice has been reported after combined treatment with oral contraceptives and troleandomycin. Hepatotoxicity following a combination of oral contraceptives and cyclosporine has also been reported.

4. Fluid retention.

Oral contraceptives may cause some degree of fluid retention. They should be prescribed with caution, and only with careful monitoring, in patients with conditions that might be aggravated by fluid retention, such as convulsive disorders, migraine syndrome, asthma, or cardiac, hepatic, or renal dysfunction.

5. Emotional disorders.

Women with a history of depression should be carefully observed and the drug discontinued if depression recurs to a serious degree.

6. Contact lenses.

Contact lens wearers who develop visual changes or changes in lens tolerance should be assessed by an ophthalmologist.

7. Drug interactions.

Reduced efficacy and increased incidence of breakthrough bleeding and menstrual irregularities have been associated with concomitant use of rifampin. A similar association, though less marked, has been suggested for barbiturates, phenylbutazone, phenytoin sodium, and possibly with griseofulvin, ampicillin, and tetracyclines. Administration of troglitazone concomitantly with a combination oral contraceptive (estrogen and progestin) reduced the plasma concentrations of both hormones by approximately 30%. This could result in loss of contraceptive efficacy.

Concomitant Use with HCV Combination Therapy – Liver Enzyme Elevation

Do not co-administer Zovia 1/35 with HCV drug combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir, due to potential for ALT elevations (see Warnings, **RISK OF LIVER ENZYME ELEVATIONS WITH**

CONCOMITANT HEPATITIS C TREATMENT).

8. Laboratory test interactions.

Certain endocrine and liver function tests and blood components may be affected by oral contraceptives:

a. Increased prothrombin and factors VII, VIII, IX and X; decreased antithrombin III; increased platelet aggregability.

b. Increased thyroid binding globulin (TBG), leading to increased circulating total thyroid hormone as measured by protein-bound iodine (PBI), T4 by column or by radioimmunoassay. Free T3 resin uptake is decreased, reflecting the elevated TBG; free T4 concentration is unaltered.

c. Other binding proteins may be elevated in the serum.

d. Sex-steroid binding globulins are increased and result in elevated levels of total circulating sex steroids and corticoids; however, free or biologically active levels remain unchanged.

e. Triglycerides and phospholipids may be increased.

f. Glucose tolerance may be decreased.

g. Serum folate levels may be depressed. This may be of clinical significance if a woman becomes pregnant shortly after discontinuing oral contraceptives.

h. Increased sulfobromophthalein and other abnormalities in liver function tests may occur.

i. Plasma levels of trace minerals may be altered.

j. Response to the metyrapone test may be reduced.

9. Carcinogenesis.

(See WARNINGS.)

10. Pregnancy.

Pregnancy Category X. (See CONTRAINDICATIONS and WARNINGS.)

11. Nursing mothers.

Small amounts of oral contraceptive steroids have been identified in the milk of nursing mothers[141-143] and a few adverse effects on the child have been reported, including jaundice and breast enlargement. In addition, oral contraceptives given in the postpartum period may interfere with lactation by decreasing the quantity and quality of breast milk. If possible, the nursing mother should be advised not to use oral contraceptives, but to use other forms of contraception until she has completely weaned her child.

12. Pediatric use.

Safety and efficacy of Zovia 1/35 have been established in women of reproductive age. Safety and efficacy are expected to be the same for postpubertal adolescents under the

age of 16 and for users 16 years and older. Use of this product before menarche is not indicated.

13. Venereal diseases.

Oral contraceptives are of no value in the prevention or treatment of venereal disease. The prevalence of cervical *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in oral contraceptive users is increased several-fold.[144, 145] It should not be assumed that oral contraceptives afford protection against pelvic inflammatory disease from chlamydia.144 Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

14. General.

a. The pathologist should be advised of oral contraceptive therapy when relevant specimens are submitted.

b. Treatment with oral contraceptives may mask the onset of the climacteric. (See WARNINGS regarding risks in this age group.)

INFORMATION FOR PATIENTS

See patient labeling printed below.

ADVERSE REACTIONS

An increased risk of the following serious adverse reactions has been associated with the use of oral contraceptives (see WARNINGS):

- Thrombophlebitis and thrombosis
- Arterial thromboembolism
- Pulmonary embolism
- Myocardial infarction and coronary thrombosis
- Cerebral hemorrhage
- Cerebral thrombosis
- Hypertension
- Gallbladder disease
- Benign and malignant liver tumors, and other hepatic lesions

There is evidence of an association between the following conditions and the use of oral contraceptives, although additional confirmatory studies are needed:

- Mesenteric thrombosis
- Neuro-ocular lesions (e.g., retinal thrombosis and optic neuritis)

The following adverse reactions have been reported in patients receiving oral contraceptives and are believed to be drug-related:

- Nausea
- Vomiting
- Gastrointestinal symptoms (such as abdominal cramps and bloating)
- Breakthrough bleeding
- Spotting
- Change in menstrual flow
- Amenorrhea during or after use
- Temporary infertility after discontinuation of use
- Edema
- Chloasma or melasma, which may persist
- Breast changes: tenderness, enlargement, secretion
- Change in weight (increase or decrease)
- Change in cervical erosion or secretion
- Diminution in lactation when given immediately postpartum
- Cholestatic jaundice
- Migraine
- Rash (allergic)
- Mental depression
- Reduced tolerance to carbohydrates
- Vaginal candidiasis
- Change in corneal curvature (steepening)
- Intolerance to contact lenses

The following adverse reactions or conditions have been reported in users of oral contraceptives and the association has been neither confirmed nor refuted:

- Premenstrual syndrome
- Cataracts
- Changes in appetite
- Cystitis-like syndrome
- Headache
- Nervousness
- Dizziness
- Hirsutism
- Loss of scalp hair

- Erythema multiforme
- Erythema nodosum
- Hemorrhagic eruption
- Vaginitis
- Porphyria
- Impaired renal function
- Hemolytic uremic syndrome
- Acne
- Changes in libido
- Colitis
- Budd-Chiari syndrome
- Endocervical hyperplasia or ectropion

OVERDOSAGE

Serious ill effects have not been reported following acute ingestion of large doses of oral contraceptives by young children.[180, 181] Overdosage may cause nausea, and withdrawal bleeding may occur in females.

NON-CONTRACEPTIVE HEALTH BENEFITS

The following non-contraceptive health benefits related to the use of oral contraceptives are supported by epidemiological studies that largely utilized oral contraceptive formulations containing estrogen doses exceeding 35 mcg of ethinyl estradiol or 50 mcg of mestranol.[148, 149]

Effects on menses:

- Increased menstrual cycle regularity
- Decreased blood loss and decreased risk of iron-deficiency anemia
- Decreased frequency of dysmenorrhea

Effects related to inhibition of ovulation:

- Decreased risk of functional ovarian cysts
- Decreased risk of ectopic pregnancies

Effects from long-term use:

- Decreased risk of fibroadenomas and fibrocystic disease of the breast
- Decreased risk of acute pelvic inflammatory disease
- Decreased risk of endometrial cancer
- Decreased risk of ovarian cancer

● Decreased risk of uterine fibroids

DOSAGE AND ADMINISTRATION

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

IMPORTANT: If the Sunday start schedule is selected, the patient should be instructed to use an additional method of protection until after the first week of administration *in the initial cycle.*

The possibility of ovulation and conception prior to initiation of use should be considered.

Zovia 1/35

Dosage Schedules

The Zovia 1/35 tablet dispensers contain 21 pale pink active tablets arranged in three numbered rows of 7 tablets each, followed by a fourth row of 7 white placebo (inactive) tablets .

Days of the week are embossed on the plastic compact just above the tablets, starting with Sunday on the left.

28-Day Schedule: For a DAY 1 START, count the first day of menstrual flow as Day 1 and the first tablet (pale pink) is then taken on Day 1. For a SUNDAY START when menstrual flow begins on or before Sunday, the first tablet (pale pink) is taken on that day. With either a DAY 1 START or SUNDAY START, 1 tablet (pale pink) is taken each day at the same time for 21 days. Then the white tablets are taken for 7 days, whether bleeding has stopped or not. After all 28 tablets have been taken, whether bleeding has stopped or not, the same dosage schedule is repeated beginning on the following day.

Special notes

Spotting, breakthrough bleeding, or nausea. If spotting (bleeding insufficient to require a pad), breakthrough bleeding (heavier bleeding similar to a menstrual flow), or nausea occurs the patient should continue taking her tablets as directed. The incidence of spotting, breakthrough bleeding or nausea is minimal, most frequently occurring in the first cycle. Ordinarily spotting or breakthrough bleeding will stop within a week. Usually the patient will begin to cycle regularly within two or three courses of tablet-taking. In the event of spotting or breakthrough bleeding organic causes should be borne in mind. (See WARNING No. 12.)

Missed menstrual periods. Withdrawal flow will normally occur 2 or 3 days after the last active tablet is taken. Failure of withdrawal bleeding ordinarily does not mean that the patient is pregnant, providing the dosage schedule has been correctly followed. (See WARNING No. 7.)

If the patient has *not* adhered to the prescribed dosage regimen, the possibility of pregnancy should be considered after the first missed period, and oral contraceptives should be withheld until pregnancy has been ruled out.

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 first intermenstrual interval after discontinuing the tablets is usually prolonged;

consequently, a patient for whom a 28-day cycle is usual might not begin to menstruate for 35 days or longer. Ovulation in such prolonged cycles will occur correspondingly later in the cycle. Post-treatment cycles after the first one, however, are usually typical for the individual woman prior to taking tablets. (See WARNING No. 12.)

Missed tablets. If a woman misses taking one active tablet, the missed tablet should be taken as soon as it is remembered. In addition, the next tablet should be taken at the usual time. If two consecutive active tablets are missed in week 1 or week 2 of the dispenser, the dosage should be doubled for the next 2 days. The regular schedule should then be resumed, but an additional method of protection must be used as backup for the next 7 days if she has sex during that time or she may become pregnant.

If two consecutive active tablets are missed in week 3 of the dispenser or three consecutive active tablets are missed during any of the first 3 weeks of the dispenser, direct the patient to do one of the following: Day 1 Starters should discard the rest of the dispenser and begin a new dispenser that same day; Sunday Starters should continue to take 1 tablet daily until Sunday, discard the rest of the dispenser and begin a new dispenser that same day. The patient may not have a period this month; however, if she has missed two consecutive periods, pregnancy should be ruled out. An additional method of protection must be used as a backup for the next 7 days after the tablets are missed if she has sex during that time or she may become pregnant.

While there is little likelihood of ovulation if only one active tablet is missed, the possibility of spotting or breakthrough bleeding is increased and should be expected if two or more successive active tablets are missed. However, the possibility of ovulation increases with each successive day that scheduled active tablets are missed.

If one or more placebo tablets of Zovia 1/35 are missed, the schedule should be resumed on the eighth day after the last pale pink colored tablet was taken. Omission of placebo tablets in the 28-tablet courses does not increase the possibility of conception provided that this schedule is followed.

HOW SUPPLIED

Zovia 1/35: Each pale pink Zovia 1/35 tablet is round, biconvex, unscored, debossed with **X1** on one side and contains 1 mg of ethynodiol diacetate and 35 mcg of ethinyl estradiol.

Zovia 1/35 is packaged in cartons of three (NDC 51862-894-03) and six (NDC 51862-894-06) tablet compact dispensers. Each compact dispenser contains 21 pale pink tablets and 7 white placebo tablets. Placebo tablets are round, biconvex and have a debossed **P** on one side and **N** on the other side.

Store at 20° to 25°C (68° to 77°F). [See USP controlled room temperature.]

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BRIEF SUMMARY OF PATIENT WARNINGS

This product (like all oral contraceptives) is intended to prevent pregnancy. It does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

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 heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives are strongly advised not to smoke.

In the detailed leaflet, "What You Should Know About Oral Contraceptives," which you have received, the risks and benefits of oral contraceptives are discussed in much more detail. That leaflet also provides information on other forms of contraception. ***Please take time to read it carefully for it may have been recently revised.***

If you have any questions or problems regarding this information, contact your doctor.

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 about 1% per year when used without missing any pills. The typical failure rate of large numbers of pill users is less than 3% per year when women who miss pills are included. However, forgetting to take pills considerably increases the chances of pregnancy.

For most women, oral contraceptives are free of serious or unpleasant side effects.

However, oral contraceptive use is associated with certain serious diseases or conditions that can cause severe disability or death, though rarely. 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. The risks associated with taking oral contraceptives increase significantly if you:

● smoke, or

● have high blood pressure, diabetes, high cholesterol, or are overweight, or

● have or have had clotting disorders, heart attack, stroke, angina pectoris (chest pains on exertion), cancer of the breast or sex organs, jaundice (yellowing of the skin or whites of the eyes), or malignant (cancerous) or benign (noncancerous) liver tumors.

Women should not use oral contraceptives if they suspect they are pregnant or if they have unexplained vaginal bleeding.

Most side effects of the pill are not serious. The most common effects are nausea, vomiting, bleeding between menstrual periods, 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.

Proper use of oral contraceptives requires that they be taken under your doctor's continuing supervision, because they can be associated with serious side effects. The serious side effects of the pill occur very infrequently, especially if you are in good health and are young. However, you should know that the following medical conditions have been associated with or made worse by the pill, and that certain of the risks may persist after use of the pill has been discontinued:

1. Blood clots in the legs, arms, lungs, heart (heart attack), eyes, abdomen, or elsewhere in the body. As mentioned above, smoking increases the risk of heart attacks and strokes and subsequent serious medical consequences.

2. Stroke, due to a blood clot, or to bleeding in the brain (hemorrhage) as a result of bursting of a blood vessel. Stroke can lead to paralysis in all or part of the body, or to death.

3. Liver tumors, which may rupture and cause severe bleeding and death. A possible, but not definite, association has also been found with the pill and liver cancer. However, with or without use of the pill, liver cancers are extremely rare in the United States.

4. High blood pressure, although blood pressure ordinarily, but not always, returns to original levels when the pill is stopped.

5. Gallbladder disease, which might require surgery.

The symptoms associated with these serious side effects are discussed in the detailed leaflet given to you with your supply of pills. Notify your doctor or health care provider if you notice any unusual physical disturbances while taking the pill. In addition, you should be aware that drugs such as antiepileptics, antibiotics (especially rifampin), as well as certain other drugs, may decrease oral contraceptive effectiveness.

There is a conflict among studies regarding breast cancer and oral contraceptive use. Some studies have reported an increase in the risk of developing breast cancer, particularly at a younger age. This increased risk appears to be related to duration of use. The majority of studies have found no overall increase in the risk of developing

breast cancer. 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. There is insufficient evidence to rule out the possibility that pills may cause such cancers.

Taking the pill may provide some important non-contraceptive benefits. These include less painful menstruation, less menstrual blood loss and anemia, less risk of fibroids, pelvic infections, and noncancerous breast disease, and less risk of cancer of the ovary and of the lining of the uterus (womb).

Be sure to discuss any medical condition you may have with your health care provider. He or she will take a medical and family history before prescribing oral contraceptives and will also examine you. The physical examination may be delayed to another time if you request it and the health care provider believes that it is a good medical practice to postpone it. You should be re-examined at least once a year while taking oral contraceptives. The detailed patient information leaflet gives you further information that you should read and discuss with your health care provider.

DETAILED PATIENT LABELING:

WHAT YOU SHOULD KNOW ABOUT ORAL CONTRACEPTIVES

This product (like all oral contraceptives) is intended to prevent pregnancy. It does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

INTRODUCTION

It is important that any woman who considers using an oral contraceptive understand the risks involved. Although the oral contraceptives have important advantages over other methods of contraception, they have certain risks that no other method has. Only you and your physician can decide whether the advantages are worth these risks. This leaflet will tell you about the most important risks. It will explain how you can help your doctor prescribe the pill as safely as possible by telling him/her about yourself and being alert for the earliest signs of trouble. And it will tell you how to use the pill properly so that it will be as effective as possible. THERE IS MORE DETAILED INFORMATION AVAILABLE IN THE LEAFLET PREPARED FOR DOCTORS. Your pharmacist can show you a copy; you may need your doctor's help in understanding parts of it.

This leaflet is not a replacement for a careful discussion between you and your health care provider. 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 provider's advice with regard to regular check-ups while you are on the pill.

If you do not have any of the conditions listed below and are thinking about using oral contraceptives, to help you decide, you need information about the advantages and risks of oral contraceptives and of other contraceptive methods as well. This leaflet describes the advantages and risks of oral contraceptives. Except for sterilization, the intrauterine device (IUD), and abortion, which have their own specific risks, the only risks of other methods are those due to pregnancy should the method fail. Your doctor can answer questions you may have with respect to other methods of contraception, and further questions you may have on oral contraceptives after reading this leaflet.

WHAT ARE ORAL CONTRACEPTIVES?

The most common type of oral contraceptive, often simply called "the pill," is a combination of estrogen and progestogen, the two kinds of female hormones. The amount of estrogen and progestogen can vary, but the amount of estrogen is more important because both the effectiveness and some of the dangers of the pill have been related to the amount of estrogen. The pill works principally by preventing release of an egg from the ovary during the cycle in which the pills are taken.

EFFECTIVENESS OF ORAL CONTRACEPTIVES

The pill is one of the most effective methods of birth control. When they are taken correctly, without missing any pills, the chance of becoming pregnant is less than 1% (1 pregnancy per 100 women per year of use) when used perfectly, without missing any pills. Typical failure rates are actually about 3% per year. The chance of becoming pregnant increases with each missed pill during a menstrual cycle.

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

Percentage of women experiencing an unintended pregnancy during the first year of typical use and the first year of perfect use of contraception and the percentage continuing use at the end of the first year. United States.

Method (1)	% of women experiencing an unintended pregnancy within the first year of use		% of women Continuing Use at one Year[C]
	Typical use[A] (2)	Perfect (3)	(4)
Chance [D]	85	85	
Spermicides [E]	26	6	40
Periodic abstinence	25		63
Calendar		9	
Ovulation method		3	
Sympto-thermal [F]		2	
Post-ovulation		1	
Withdrawal	19	4	
Cap [G]			
Parous women	40	26	42
Nulliparous women	20	9	56
Sponge			
Parous women	40	20	42
Nulliparous women	20	9	56
Diaphragm [G]	20	6	56
Condom [H]			
Female (Reality)	21	5	56
Male	14	3	61
Pill	5		71
Progestin only		0.5	
Combined		0.1	
IUD			
Progesterone T	2.0	1.5	81
Copper T 380A	0.8	0.6	78
LNg 20	0.1	0.1	81
Injection (Depo-Provera)	0.3	0.3	70
Implant (Norplant and Norplant-2)	0.05	0.05	88
Female sterilization	0.5	0.5	100
Male sterilization	0.15	0.10	100

Emergency Contraceptive Pills: Treatment initiated within 72 hours after unprotected intercourse reduces the risk of pregnancy by at least 75%. [I]

Lactational Amenorrhea Method: LAM is a highly effective, *temporary* method of contraception. [J]

Source: Trussell J, Contraceptive efficacy. In Hatcher RA, Trussell J, Stewart F, Cates W, Stewart GK, Kowal D, Guest F, *Contraceptive Technology: Seventeenth Revised Edition.* New York NY: Irvington Publishers, 1998, in press. [1]

(A) Among typical couples who initiate use of a method (not necessarily for the first time), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason.

(B) Among couples who initiate use of a method (not necessarily for the first time) and who use it perfectly (both consistently and correctly), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason.

(C) Among couples attempting to avoid pregnancy, the percentage who continue to use a method for one year.

(D) The percents becoming pregnant in columns (2) and (3) are based on data from populations where contraception is not used and from women who cease using contraception in order to become pregnant. Among such populations, about 89% become pregnant within one year. This estimate was lowered slightly (to 85%) to represent the percent who would become pregnant within one year among women now relying on reversible methods of contraception if they abandoned contraception altogether.

(E) Foams, creams, gels, vaginal suppositories, and vaginal film.

(F) Cervical mucus (ovulation) method supplemented by calendar in the pre-ovulatory and basal body temperature in the post-ovulatory phases.

(G) With spermicidal cream or jelly.

(H) Without spermicides.

(I) The treatment schedule is one dose within 72 hours after unprotected intercourse and a second dose 12 hours after the first dose. The Food and Drug Administration has declared the following brands of oral contraceptives to be safe and effective for emergency contraception: Ovral (1 dose is 2 white pills), Alesse (1 dose is 5 pink pills), Nordette or Levlen (1 dose is 2 light-orange pills), Lo/Ovral (1 dose is 4 white pills), Triphasil or Tri-Levlen (1 dose is 4 yellow pills).

(J) However, to maintain effective protection against pregnancy, another method of contraception must be used as soon as menstruation resumes, the frequency or duration of breastfeeds is reduced, bottle feeds are introduced, or the baby reaches six months of age.

WHO SHOULD NOT TAKE ORAL CONTRACEPTIVES

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 heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives are strongly advised not to smoke.

Some women should not use the pill. For example, you should not take the pill if you are pregnant or think you may be pregnant. You should also not use the pill if you have any of the following conditions:

● Heart attack or stroke (blood clot or hemorrhage in the brain), currently or in the past.

● Blood clots in the legs (thrombophlebitis), lungs (pulmonary embolism), eyes, or elsewhere in the body, currently or in the past.

● Chest pain (angina pectoris), currently or in the past.

● Known or suspected breast cancer or cancer of the lining of the uterus (womb), cervix, or vagina, currently or in the past.

● Unexplained vaginal bleeding (until a diagnosis is reached by your doctor).

● Yellowing of the whites of the eyes or of the skin (jaundice) during pregnancy or during previous use of the pill.

● Liver tumor (whether cancerous or not), currently or in the past.

● Take any Hepatitis C drug combination containing obitasvir/paritaprevir/ritonavir with or without dasabuvir. This may increase levels of the liver enzyme "alanine aminotransferase" (ALT) in the blood.

● Known or suspected pregnancy (one or more menstrual periods missed).

Tell your health care provider if you have ever had any of these conditions. He or she can recommend a safer method of birth control.

OTHER CONSIDERATIONS BEFORE TAKING ORAL CONTRACEPTIVES

Tell your health care provider if you have or have had any of the following conditions, as he or she will want to watch them closely or they might cause him or her to suggest using another method of contraception:

● Breast nodules (lumps), fibrocystic disease (breast cysts), abnormal mammograms (x-ray pictures of the breast), or abnormal Pap smears

● Diabetes

● High blood pressure

●High blood cholesterol or triglycerides

● Migraine or other headaches or epilepsy

● Mental depression

● Gallbladder, heart, or kidney disease

● History of scanty or irregular menstrual periods

● Problems during a prior pregnancy

● latest post-marketing stability data summary Fibroid tumors of the womb

● History of jaundice (yellowing of the whites of the eyes or of the skin)

● Varicose veins

● Tuberculosis

● Plans for elective surgery

Women with any of these conditions should be checked often by their health care provider if they choose to use oral contraceptives.

Also, be sure to tell your doctor if you smoke or are on any medications.

RISKS OF TAKING ORAL CONTRACEPTIVES

1. Risk of developing blood clots. Blood clots and blockage of blood vessels are the most serious side effects of taking oral contraceptives. 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.

If you take oral contraceptives and need elective surgery, need to stay in bed for a prolonged illness, or have recently delivered a baby, you may be at risk of developing blood clots. You should consult your doctor about stopping oral contraceptives 3 to 4 weeks before surgery and not taking oral contraceptives for 2 weeks after surgery or during bed rest. You should also not take oral contraceptives soon after delivery of a baby. It is advisable to wait for at least 4 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 on Breast feeding in GENERAL PRECAUT IONS.)

The risk of circulatory disease in oral contraceptive users may be higher in users of high-dose pills and may be greater with longer duration of oral contraceptive use. In addition, some of these increased risks may continue for a number of years after stopping oral contraceptives. The risk of abnormal blood clotting increases with age in both users and nonusers of oral contraceptives, but the increased risk from the oral contraceptive appears to be present at all ages. For women aged 20 to 44 it is estimated that about 1 in 2,000 using oral contraceptives will be hospitalized each year because of abnormal clotting. Among nonusers in the same age group, about 1 in 20,000 would be hospitalized each year. For oral contraceptive users in general, it has been estimated that in women between the ages of 15 and 34, the risk of death due to a circulatory disorder is about 1 in 12,000 per years, whereas for nonusers the rate is about 1 in 50,000 per year. In the age group 35 to 44, the risk is estimated to be about 1 in 2,500 per year for oral contraceptive users and about 1 in 10,000 per year for nonusers.

2. Heart attacks and strokes. Oral contraceptives may increase the tendency to develop strokes (stoppage by blood clots or rupture of blood vessels of the brain) and angina pectoris and heart attacks (blockage of blood vessels of the heart). Any of these conditions can cause death or permanent disability.

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

3. Gallbladder disease. Oral contraceptive users probably have a greater risk than non-users of having gallbladder disease, although this risk may be related to pills containing high doses of estrogens.

4. Liver tumors. In rare cases, oral contraceptives can cause benign but dangerous liver tumors. These benign 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 several 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 rare.

5. Cancer of the reproductive organs and breasts. There is conflict among studies regarding breast cancer and oral contraceptive use. Some studies have reported an increase in the risk of developing breast cancer, particularly at a younger age. This increased risk appears to be related to duration of use. The majority of studies have found no overall increase in the risk of developing breast cancer. Women who use oral contraceptives and have a strong family history of breast cancer or who have had

breast nodules or abnormal mammograms should be closely followed by their doctors.

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. There is insufficient evidence to rule out the possibility that pills may cause such cancers.

ESTIMATED RISK OF DEATH FROM BIRTH CONTROL METHOD OR PREGNANCY

All methods of birth control and pregnancy are associated with a risk of developing certain diseases that 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 according to age.

	Age					
Method of control	**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
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 (7-26 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, although over the age of 40, 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) in that age group.

The suggestion that women over 40 who don't smoke should not take oral contraceptives is based on information from older high-dose pills and on less selective use of pills than is practiced today. 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. However, all women, especially older women, are cautioned to use the lowest dose pill that is effective.

WARNING SIGNALS

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

● Sharp chest pain, coughing up blood, or sudden shortness of breath (indicating a possible blood clot in the lung).

● Pain in the calf (indicating a possible blood 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, or numbness in an arm or leg (indicating a possible stroke).

● Sudden partial or complete loss of vision (indicating a possible blood clot in the blood vessels of the eye).

● Breast lumps (indicating possible breast cancer or fibrocystic disease of the breast). Ask your doctor or health care provider to show you how to examine your own breasts.

● Severe pain or tenderness or a mass in the stomach area (indicating a possible 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).

● Unusual swelling.

● Other unusual conditions.

SIDE EFFECTS OF ORAL CONTRACEPTIVES

1. Vaginal bleeding.

Spotting. This is a slight staining between your menstrual periods that may not even require a pad. Some women spot even though they take their pills exactly as directed. Many women spot although they have never taken the pills. Spotting does not mean that your ovaries are releasing an egg. Spotting may be the result of irregular pill-taking. Getting back on schedule will usually stop it.

If you should spot while taking the pills, you should not be alarmed, because spotting usually stops by itself within a few days. It seldom occurs after the first pill cycle. Consult your doctor if spotting persists for more than a few days or if it occurs after the second cycle.

Unexpected (breakthrough) bleeding. Unexpected (breakthrough) bleeding does not mean that your ovaries have released an egg. It seldom occurs, but when it does

happen it is most common in the first pill cycle. It is a flow much like a regular period, requiring the use of a pad or tampon.

If you experience breakthrough bleeding use a pad or tampon and continue with your schedule. Usually your periods will become regular within a few cycles. Breakthrough bleeding will seldom bother you again.

Consult your doctor or health care provider if breakthrough bleeding is heavy, does not stop within a week, or if it occurs after the second cycle.

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

3. Fluid retention or raised blood pressure. Oral contraceptives may cause edema (fluid retention), with swelling of the fingers or ankles. If you experience fluid retention, contact your doctor or health care provider. Some women develop high blood pressure while on the pill, which ordinarily, but not always, returns to the original levels when the pill is stopped. High blood pressure predisposes one to strokes, heart attacks, kidney disease, and other diseases of the blood vessels.

4. Melasma. A spotty darkening of the skin is possible, particularly of the face. This may persist after the pill is discontinued.

5. Other side effects. Other side effects may include nausea and vomiting, change in appetite, headache, nervousness, depression, dizziness, loss of scalp hair, rash, and vaginal infections.

If any of these, or other, side effects occur, call your doctor or health care provider.

GENERAL PRECAUTIONS

1. Missed periods and use of oral contraceptives before or during early pregnancy.

Occasionally women who are taking the pill miss periods. It has been reported to occur as frequently as several times each year in some women, depending on various factors such as age and prior history (your doctor is the best source of information about this). The pill should not be used when you are pregnant or suspect you may be pregnant. Very rarely, women who are using the pill as directed become pregnant. The likelihood of becoming pregnant is higher if you occasionally miss one or two pills. Therefore, if you miss a period you should consult your physician before continuing to take the pill. If you miss a period, especially if you have not taken the pill regularly, you should use an alternative method of contraception until pregnancy has been ruled out; if you have missed more than one pill at any time, you should immediately start using an additional method of contraception and complete your pill cycle.

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 findings have not been seen in more recent studies. Nevertheless, oral contraceptives or any other drugs should not be used during pregnancy unless clearly necessary and prescribed by your doctor. You should check with your doctor about risks to your unborn child of any medication taken during pregnancy.

2. Breast feeding.

If you are breast feeding, consult your doctor 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 doctor 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 breakthrough bleeding. Such drugs include rifampin, drugs used for epilepsy such as barbiturates (for example, phenobarbital) and phenytoin (Dilantin is one brand of this drug), phenylbutazone (Butazolidin is one brand), Rezulin (troglitazone) a hypoglycemic, and possibly certain antibiotics. You may need to use additional contraception when you take drugs that can make oral contraceptives less effective.

Oral contraceptives may have an influence upon the way other drugs act. Check with your doctor if you are taking *any* other drugs while you are on the pill.

HOW TO TAKE THE PILL

IMPORTANT POINTS TO REMEMBER

BEFORE YOU START TAKING YOUR PILLS:

1. BE SURE TO READ THESE DIRECTIONS:

● Before you start taking your pills.

● Anytime you are not sure what to do.

2. THE RIGHT WAY TO TAKE THE PILL 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.

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 the pill. The problem will usually go away. If it doesn't go away, check with your doctor or clinic.

4. 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.

5. IF YOU HAVE VOMITING OR DIARRHEA, for any reason, or IF YOU TAKE SOME MEDICINES, including some antibiotics, your pills may not work as well.

Use a backup method (such as condoms, foam, or sponge) until you check with your doctor or clinic.

6. IF YOU HAVE TROUBLE REMEMBERING TO TAKE THE PILL, talk to your doctor or clinic about how to make pill-taking easier or about using another method of birth control.

7. IF YOU HAVE ANY QUESTIONS OR ARE UNSURE ABOUT THE INFORMATION IN THIS LEAFLET, call your doctor or clinic.

BEFORE YOU START TAKING YOUR PILLS

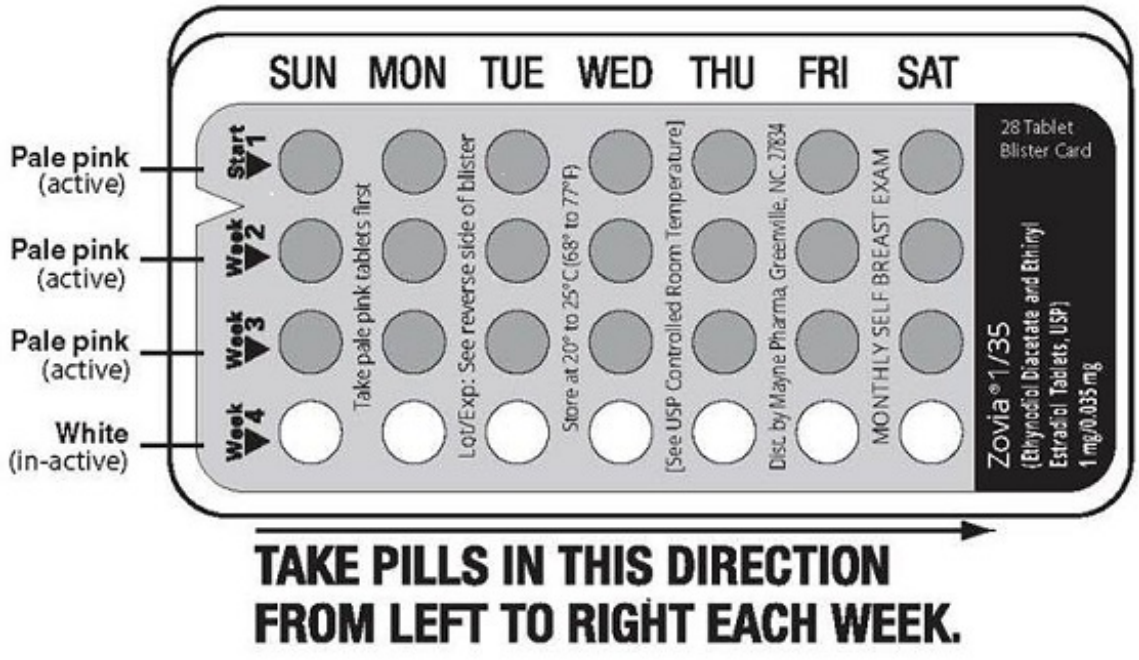
1. DECIDE WHAT TIME OF DAY YOU WANT TO TAKE YOUR PILL.

It is important to take it at about the same time every day.

2. LOOK AT YOUR PILL PACK:

Your tablet dispenser consists of a plastic compact and a blister pack containing 28 pills. The 28 tablets are arranged in four numbered rows with the days of the week embossed on the plastic compact just above the tablets, starting with Sunday on the left.

The Zovia 1/35 tablet dispenser contain 21 pale pink active tablets arranged in three numbered rows of 7 tablets each, followed by a fourth row of 7 white placebo (inactive) tablets (see graphic below).



The 28-pill pack has 21 pale pink "active" pills (with hormones) to take for 3 weeks, followed by 1 week of reminder white placebo pills (without hormones). To remove a pill press down on it with the flat of your finger. The pill will drop through a hole in the

bottom of the dispenser.

3. ALSO FIND:

● Where on the pack to start taking pills.

● In what order to take the pills (left to right).

Begin the **28-pill pack** with the first pill in Row 1 and continue across Row 1 (Start 1). Repeat for Row 2, Row 3, and finally Row 4. Take all "active" pills (pale pink) before starting Row 4.

4. BE SURE YOU HAVE READY AT ALL TIMES:

● ANOTHER KIND OF BIRTH CONTROL (such as condoms, foam, or sponge) to use as a backup in case you miss pills.

● AN EXTRA, FULL PILL PACK.

WHEN TO START THE <u>FIRST</u> PACK OF PILLS

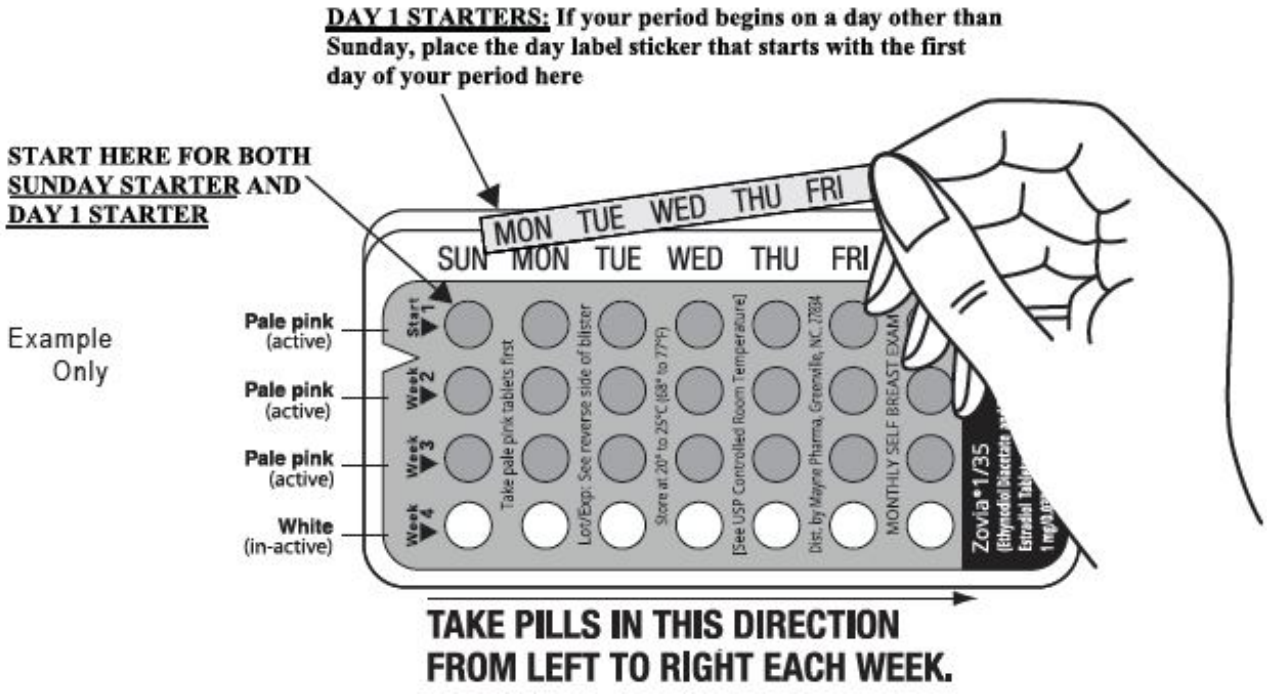
You have a choice of which day to start taking your first pack of pills. Zovia 1/35 is available in a compact blister card preset for a Sunday Start with the days of the week embossed on the plastic compact just above the tablets, starting with Sunday on the left.

Day 1 Start stickers are also provided. Decide with your doctor or clinic which is the best day for you. Pick a time of day which will be easy to remember.

DAY 1 START:

1. Pick the day label sticker that starts with the first day of your period (this is the day you start bleeding or spotting, even if it is almost midnight when the bleeding begins).

2. Place this day label sticker in the tablet dispenser over the area that has the days of the week (starting with Sunday) imprinted on the plastic compact.



Note: If the first day of your period is a Sunday, you can skip steps #1 and #2.

3. Take the first "active" pill (pale pink) of the first pack during the first 24 hours of your period.

4. You will not need to use a backup method of birth control, since you are starting the pill at the beginning of your period.

SUNDAY START:

1. Take the first "active" pill (pale pink) of the first pack on the Sunday after your period starts, even if you are still bleeding. If your period begins on Sunday, start the pack that same day.

2. Use another method of birth control as a backup method if you have sex anytime from the Sunday you start your first pack until the next Sunday (7 days). Condoms, foam, or the sponge are good backup methods of birth control.

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 between monthly periods 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 OR SWITCH YOUR BRAND OF 28-DAY PILLS:** Start the next

pack on the day after your last "reminder" pill. Do not wait any days between 28-day packs.

WHAT TO DO IF YOU MISS PILLS

If you **MISS 1**"active" pill (pale pink):

1. Take it as soon as you remember. Take the next pill at your regular time. This means you may take 2 pills in 1 day.

2. You do not need to use a backup birth control method if you have sex.

If you **MISS 2**"active" pills (pale pink) in a row in **WEEK 1 OR WEEK 2** of your pack:

1. Take 2 pills on the day you remember and 2 pills the next day.

2. Then take 1 pill a day until you finish the pack.

3. You MAY BECOME PREGNANT if you have sex in the 7 days after you miss pills. You MUST use another birth control method (such as condoms, foam, or sponge) as a backup for those 7 days.

If you **MISS 2**"active" pills (pale pink) in a row in **THE 3rd WEEK:**

1. ***If you are a Day 1 Starter:***

THROW OUT the rest of the pill pack and start a new pack that same day.

If you are a Sunday Starter:

Keep taking 1 pill every day until Sunday.

On Sunday, THROW OUT the rest of the pack and start a new pack of pills that same day.

2. You may not have your period this month but this is expected. However, if you miss your period 2 months in a row, call your doctor or clinic because you might be pregnant.

3. You MAY BECOME PREGNANT if you have sex in the 7 days after you miss pills. You MUST use another birth control method (such as condoms, foam, or sponge) as a backup for those 7 days.

If you **MISS 3 OR MORE** "active" pills (pale pink) in a row (during the first 3 weeks):

1. ***If you are a Day 1 Starter:***

THROW OUT the rest of the pill pack and start a new pack of pills that same day.

If you are a Sunday Starter:

Keep taking 1 pill every day until Sunday.

On Sunday, THROW OUT the rest of the pack and start a new pack of pills that same day.

2. You may not have your period this month but this is expected. However, if you miss your period 2 months in a row, call your doctor or clinic because you might be pregnant.

3. You MAY BECOME PREGNANT if you have sex in the 7 days after you miss pills. You MUST use another birth control method (such as condoms, foam, or sponge) as a backup for those 7 days.

A REMINDER:

If you forget any of the 7 white "reminder" pills in Week 4:

● THROW AWAY the pills you missed.

● Keep taking 1 pill each day until the pack is empty.

● You do not need a backup method.

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

● Use a BACKUP METHOD of birth control anytime you have sex.

● KEEP TAKING ONE "ACTIVE" PILL EACH DAY until you can reach your doctor or clinic.

PREGNANCY DUE TO PILL FAILURE

The incidence of pill failure resulting in pregnancy is approximately 1% (i.e., one pregnancy per 100 women per year) if taken every day as directed, but, because some women fail to follow the daily schedule, more typical failure rates are about 3%. If you become pregnant you should discuss your pregnancy with your doctor.

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 after stopping the pill.

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, pharmacist or Poison Control Center.

OTHER INFORMATION

Your health care provider will take a medical and family history before prescribing oral contraceptives and will also examine you. The physical examination may be delayed to another time if you request it and the health care provider believes that it is a good medical practice to postpone it. You should be re-examined at least once a year. Certain health problems or conditions in your medical or family history may require that your health care provider see you more frequently while you are taking the pill. 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.

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.

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

● 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

● Fibroids of the uterus (womb) 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 (womb)

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.

Keep this and all drugs out of the reach of children.

Be certain to read new revisions of this leaflet.

To report SUSPECTED ADVERSE REACTIONS, contact Mayne Pharma Toll-Free at 1-844-825-8500 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

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Greenville, NC 27834

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Iss. 07/2020 Rev.A

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

ZOVIA 1/35

ethynodiol diacetate and ethinyl estradiol tablets kit

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:51862-894

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:51862-894-01	1 in 1 PACKET	10/16/2020	
1		1 in 1 BLISTER PACK		
2	NDC:51862-894-03	3 in 1 CARTON	10/16/2020	
2		1 in 1 BLISTER PACK		
3	NDC:51862-894-06	6 in 1 CARTON	10/16/2020	
3		1 in 1 BLISTER PACK		

Quantity of Parts		
Part #	**Package Quantity**	**Total Product Quantity**
Part 1		21
Part 2		7

Part 1 of 2

ZOVIA 1/35

ethynodiol diacetate and ethinyl estradiol tablet

Product Information	
Route of Administration	ORAL

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ETHYNODIOL DIACETATE (UNII: 62H10A1236) (ETHYNODIOL - UNII:9E01C36A9S)	ETHYNODIOL DIACETATE	1 mg
ETHINYL ESTRADIOL (UNII: 423D2T571U) (ETHINYL ESTRADIOL - UNII:423D2T571U)	ETHINYL ESTRADIOL	0.035 mg

Inactive Ingredients	
Ingredient Name	**Strength**
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
STARCH, PREGELATINIZED CORN (UNII: O8232NY3SJ)	
ALPHA-TOCOPHEROL (UNII: H4N855PNZ1)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
POVIDONE (UNII: FZ989GH94E)	
POLYVINYL ALCOHOL (UNII: 532B59J990)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
TALC (UNII: 7SEV7J4R1U)	
POLYETHYLENE GLYCOL 3350 (UNII: G2M7P15E5P)	
LECITHIN, SOYBEAN (UNII: 1DI56QDM62)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	

Product Characteristics			
Color	PINK (pale pink)	**Score**	no score
Shape	ROUND	**Size**	5mm
Flavor		**Imprint Code**	X1

Contains	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA209548	10/16/2020	

Part 2 of 2

INERT

placebo tablet

Product Information

Route of Administration	ORAL

Inactive Ingredients

Ingredient Name	Strength
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
STARCH, PREGELATINIZED CORN (UNII: O8232NY3SJ)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
POLYDEXTROSE (UNII: VH2XOU12IE)	
HYPROMELLOSES (UNII: 3NXW29V3WO)	
TRIACETIN (UNII: XHX3C3X673)	
POLYETHYLENE GLYCOL 8000 (UNII: Q662QK8M3B)	

Product Characteristics

Color	WHITE	Score	no score
Shape	ROUND	Size	5mm
Flavor		Imprint Code	P;N
Contains			

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA209548	10/16/2020	

Marketing Information

Marketing	Application Number or Monograph	Marketing Start	Marketing End

Category	Citation	Date	Date
ANDA	ANDA209548	10/16/2020	

Labeler - Mayne Pharma Inc. (867220261)

Registrant - Novast Laboratories, Ltd. (527695995)

Establishment

Name	Address	ID/FEI	Business Operations
Novast Laboratories, Ltd.		527695995	analysis(51862-894) , label(51862-894) , manufacture(51862-894) , pack(51862-894)

Revised: 12/2022 Mayne Pharma Inc.