DESOGEN® Tablets

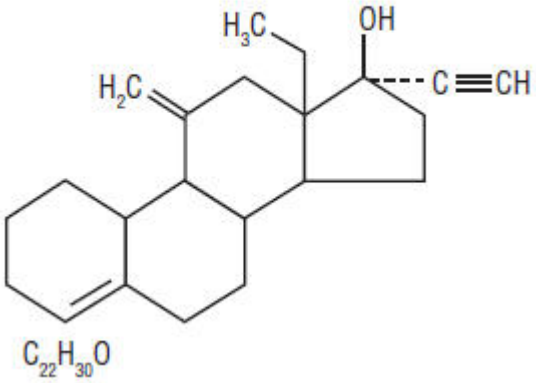
(desogestrel and ethinyl estradiol tablets USP)

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

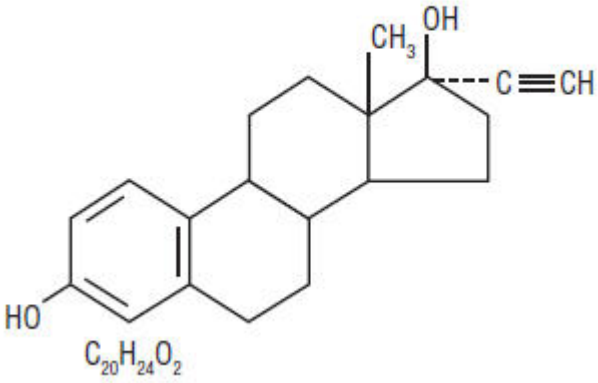
DESCRIPTION

DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP) provides an oral contraceptive regimen of 21 white round tablets each containing 0.15 mg desogestrel (13-ethyl-11-methylene-18,19-dinor-17 alpha-pregn-4-en-20-yn-17-ol) and 0.03 mg ethinyl estradiol (19-nor-17 alpha-pregna-1,3,5 (10)-trien-20-yne-3,17-diol). Inactive ingredients include vitamin E, corn starch, povidone, stearic acid, colloidal silicon dioxide, lactose, hydroxypropyl methylcellulose, polyethylene glycol, titanium dioxide, and talc. DESOGEN® also contains 7 green round tablets containing the following inert ingredients: lactose, corn starch, magnesium stearate, FD&C Blue No. 2 aluminum lake, ferric oxide, hydroxypropyl methylcellulose, polyethylene glycol, titanium dioxide, and talc. The molecular weights for desogestrel and ethinyl estradiol are 310.48 and 296.40, respectively. The structural formulas are as follows:

DESOGESTREL



ETHINYL ESTRADIOL



CLINICAL PHARMACOLOGY

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

Receptor-binding studies, as well as studies in animals, have shown that etonogestrel, the biologically active metabolite of desogestrel, combines high progestational activity with minimal intrinsic androgenicity. The relevance of this latter finding in humans is unknown.

Pharmacokinetics

Absorption

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

In the third cycle of use after a single dose of DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP), maximum concentrations of etonogestrel of 2805±1203 pg/mL (mean±SD) are reached at 1.4±0.8 hours. The area under the curve ($AUC_{0-\infty}$) is 33,858±11,043 pg/mL•hr after a single dose. At steady state, attained from at least day 19 onwards, maximum concentrations of 5840±1667 pg/mL are reached at 1.4±0.9 hours. The minimum plasma levels of etonogestrel at steady state are 1400±560 pg/mL. The AUC_{0-24} at steady state is 52,299±17,878 pg/mL•hr. The mean $AUC_{0-\infty}$ for etonogestrel at single dose is significantly lower than the mean AUC_{0-24} at steady state. This indicates that the kinetics of etonogestrel are non-linear due to an increase in binding of etonogestrel to SHBG in the cycle, attributed to increased SHBG levels which are induced by the daily administration of ethinyl estradiol. SHBG levels increased significantly in the third treatment cycle from day 1 (150±64 nmol/L) to day 21 (230±59 nmol/L).

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

In the third cycle of use after a single dose of DESOGEN®, maximum concentrations of ethinyl estradiol of 95±34 pg/mL are reached at 1.5±0.8 hours. The $AUC_{0-\infty}$ is 1471±268 pg/mL•hr after a single dose. At steady state, attained from at least day 19 onwards, maximum ethinyl estradiol concentrations of 141±48 pg/mL are reached at about 1.4±0.7 hours. The minimum serum levels of ethinyl estradiol at steady state are 24±8.3 pg/mL. The AUC_{0-24}, at steady state is 1117±302 pg/mL•hr. The mean $AUC_{0-\infty}$ for ethinyl estradiol following a single dose during treatment cycle 3 does not significantly differ from the mean AUC_{0-24} at steady state. This finding indicates linear kinetics for ethinyl estradiol.

Distribution

Etonogestrel, the active metabolite of desogestrel, was found to be 98% protein bound, primarily to sex hormone-binding globulin (SHBG). Ethinyl estradiol is primarily bound to plasma albumin. Ethinyl estradiol does not bind to SHBG, but induces SHBG synthesis. Desogestrel, in combination with ethinyl estradiol, does not counteract the estrogen-induced increase in SHBG, resulting in lower serum levels of free testosterone.

Metabolism

Desogestrel: Desogestrel is rapidly and completely metabolized by hydroxylation in the intestinal mucosa and on first pass through the liver to etonogestrel. *In vitro* data suggest an important role for the cytochrome P450 CYP2C9 in the bioactivation of desogestrel. Further metabolism of etonogestrel into 6β-hydroxy, etonogestrel and 6β-13-ethyl-dihydroxylated metabolites as major metabolites is catalyzed by CYP3A4. Other metabolites (i.e., 3α-OH-desogestrel, 3β-OH-desogestrel, and 3α-OH-5α-H-

desogestrel) also have been identified and these metabolites may undergo glucuronide and sulfate conjugation.

Ethinyl estradiol: Ethinyl estradiol is subject to a significant degree of presystemic conjugation (phase II metabolism). Ethinyl estradiol, escaping gut wall conjugation, undergoes phase I metabolism and hepatic conjugation (phase II metabolism). Major phase I metabolites are 2-OH-ethinyl estradiol and 2-methoxy-ethinyl estradiol. Sulfate and glucuronide conjugates of both ethinyl estradiol and phase I metabolites, which are excreted in bile, can undergo enterohepatic circulation.

Excretion
Etonogestrel and ethinyl estradiol are primarily eliminated in urine, bile and feces. The elimination half-life of etonogestrel is approximately 38±20 hours at steady state. The elimination half-life of ethinyl estradiol is 26±6.8 hours at steady state.

Special Populations

Race
There is no information to determine the effect of race on the pharmacokinetics of DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP).

Hepatic Insufficiency
No formal studies were conducted to evaluate the effect of hepatic disease on the disposition of DESOGEN®. However, steroid hormones may be poorly metabolized in patients with impaired liver function (see PRECAUTIONS).

Renal Insufficiency
No formal studies were conducted to evaluate the effect of renal disease on the disposition of DESOGEN®.

Drug–Drug Interactions
Interactions between desogestrel/ethinyl estradiol and other drugs have been reported in the literature (see PRECAUTIONS).

INDICATIONS AND USAGE

DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP) is indicated for the prevention of pregnancy in women who elect to use this product as a method of contraception.

CONTRAINDICATIONS

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

- Thrombophlebitis or thromboembolic disorders
- A past history of deep vein thrombophlebitis or thromboembolic disorders
- Cerebral vascular or coronary artery disease (current or history)
- Valvular heart disease with thrombogenic complications

- Inherited or acquired hypercoagulopathies
- Severe hypertension
- Diabetes with vascular involvement
- Headaches with focal neurological symptoms
- Major surgery with prolonged immobilization
- Known or suspected carcinoma of the breast (or personal history of breast cancer)
- Carcinoma of the endometrium or other known or suspected estrogen-dependent neoplasia
- Undiagnosed abnormal genital bleeding
- Cholestatic jaundice of pregnancy or jaundice with prior hormonal contraceptive use
- Hepatic tumors (benign or malignant) or active liver disease
- Known or suspected pregnancy
- Smoke, if over age 35 (see Boxed Warning and WARNINGS)
- Hypersensitivity to any of the components of DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP)
- 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

WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS
Cigarette smoking increases the risk of serious cardiovascular events from combination oral contraceptive (COC) use. This risk increases with age, particularly in women over 35 years of age, and with the number of cigarettes smoked. For this reason, COCs are contraindicated in women who are over 35 years of age, and smoke. (See CONTRAINDICATIONS.)

The use of oral contraceptives is associated with increased risks of several serious conditions including venous and arterial thrombotic and thromboembolic events (such as myocardial infarction, thromboembolism, and stroke), hepatic neoplasia, gallbladder disease, and hypertension, although the risk of serious morbidity or mortality is very small in healthy women without underlying risk factors. The risk of morbidity and mortality increases significantly in the presence of other underlying risk factors such as certain inherited thrombophilias, hypertension, hyperlipidemias, obesity, and diabetes. Practitioners prescribing oral contraceptives should be familiar with the following information relating to these risks.

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

Throughout this labeling, epidemiologic studies reported are of two types: retrospective or case control studies and prospective or cohort studies. Case control studies provide a measure of the relative risk of a disease, namely, a *ratio* of the incidence of a disease among oral contraceptive users to that among non-users. The relative risk does not provide information on the actual clinical occurrence of a disease. Cohort studies provide a measure of attributable risk, which is the *difference* in the incidence of disease between oral contraceptive users and non-users. The attributable risk does provide information about the actual occurrence of a disease in the population (Adapted from refs. 2 and 3 with the authors' permission). For further information, the reader is referred to a text on epidemiologic methods.

1. THROMBOEMBOLIC DISORDERS AND OTHER VASCULAR PROBLEMS

An increased risk of thromboembolic and thrombotic disease associated with the use of oral contraceptives is well established. Case control studies have found the relative risk of users compared to non-users 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. Cohort studies have shown the relative risk to be somewhat lower, about 3 for new cases and about 4.5 for new cases requiring hospitalization. The risk of VTE is highest during the first year of COC use and when restarting hormonal contraception following a break of four weeks or longer. The risk of thromboembolic disease due to COCs gradually disappears after use is discontinued.

Several epidemiologic studies indicate that third generation oral contraceptives, including those containing desogestrel, are associated with a higher risk of venous thromboembolism than certain second generation oral contraceptives. In general, these studies indicate an approximate two-fold increased risk, which corresponds to an additional 1–2 cases of venous thromboembolism per 10,000 women-years of use. However, data from additional studies have not shown this two-fold increase in risk.

A two- to four-fold increase in relative risk of post-operative thromboembolic complications has been reported with the use of oral contraceptives. The relative risk of venous thrombosis in women who have predisposing conditions is twice that of women without such medical conditions. If feasible, oral contraceptives should be discontinued at least four weeks prior to and for two weeks after elective surgery of a type associated with an increase in risk of thromboembolism and during and following prolonged immobilization. Since the immediate postpartum period is associated with an increased risk of thromboembolism, oral contraceptives should be started no earlier than four to six weeks after delivery in women who elect not to breast-feed.

Use of COCs also increases the risk of arterial thromboses such as strokes and myocardial infarctions, especially in women with other risk factors for these events.

COCs have been shown to increase both the relative and attributable risks of cerebrovascular events (thrombotic and hemorrhagic strokes). In general, the risk is greatest among older (>35 years of age), hypertensive women who also smoke.

2. CARCINOMA OF THE REPRODUCTIVE ORGANS AND BREASTS

Numerous epidemiologic studies have been performed on the incidence of breast, endometrial, ovarian, and cervical cancer in women using oral contraceptives. Although the risk of breast cancer may be slightly increased among current users of oral contraceptives (RR = 1.24), this excess risk decreases over time after oral contraceptive discontinuation and by 10 years after cessation the increased risk disappears. The risk does not increase with duration of use, and no relationships have been found with dose or type of steroid. The patterns of risk are also similar regardless of a woman's reproductive history or her family breast cancer history. The subgroup for whom risk has been found to be significantly elevated is women who first used oral contraceptives before age 20, but because breast cancer is so rare at these young ages, the number of cases attributable to this early oral contraceptive use is extremely small. Breast cancers diagnosed in current or previous oral contraceptive users tend to be less advanced clinically than in never-users. Women who currently have or have had breast cancer should not use oral contraceptives because breast cancer is a hormone-sensitive tumor.

Some studies suggest that combination oral contraceptive use has been associated with an increase in the risk of cervical intra-epithelial neoplasia in some populations

of women. 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.

3. HEPATIC NEOPLASIA

Benign hepatic adenomas are associated with oral contraceptive use, although the incidence of benign tumors is rare in the United States. Indirect calculations have estimated the attributable risk to be in the range of 3.3 cases/100,000 for users, a risk that increases after four or more years of use especially with oral contraceptives of higher dose. Rupture of rare, benign, hepatic adenomas may cause death through intra-abdominal hemorrhage.

Studies from Britain have shown an increased risk of developing hepatocellular carcinoma in long-term (>8 years) oral contraceptive users. However, these cancers are extremely rare in the US and the attributable risk (the excess incidence) of liver cancers in oral contraceptive users approaches less than one per million users.

4. 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 such as COCs. Discontinue DESOGEN® prior to starting therapy with the combination drug regimen ombitasvir/paritaprevir/ritonavir, with or without dasabuvir (see CONTRAINDICATIONS). DESOGEN® can be restarted approximately 2 weeks following completion of treatment with the combination drug regimen.

5. OCULAR LESIONS

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

6. ORAL CONTRACEPTIVE USE BEFORE OR DURING EARLY PREGNANCY

Extensive epidemiologic studies have revealed no increased risk of birth defects in women who have used oral contraceptives prior to pregnancy. Studies also do not suggest a teratogenic effect, particularly in so far as cardiac anomalies and limb reduction defects are concerned when oral contraceptives are 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. If the patient has not adhered to the prescribed schedule, the possibility of pregnancy should be considered at the first missed period. Oral contraceptive use should be discontinued if pregnancy is confirmed.

7. GALLBLADDER DISEASE

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

8. CARBOHYDRATE AND LIPID METABOLIC EFFECTS

Oral contraceptives have been shown to cause a decrease in glucose tolerance in a significant percentage of users. Oral contraceptives containing greater than 75 micrograms of estrogen cause hyperinsulinism, while lower doses of estrogen cause less glucose intolerance. Progestogens increase insulin secretion and create insulin resistance, this effect varying with different progestational agents. However, in the non-diabetic woman, oral contraceptives appear to have no effect on fasting blood glucose. Because of these demonstrated effects, prediabetic and diabetic women should be carefully monitored while taking oral contraceptives.

A small proportion of women will have persistent hypertriglyceridemia while on the pill. Changes in serum triglycerides and lipoprotein levels have been reported in oral contraceptive users.

9. ELEVATED BLOOD PRESSURE

Women with severe hypertension should not be started on hormonal contraceptives. An increase in blood pressure has been reported in women taking oral contraceptives and this increase is more likely in older oral contraceptive users and with continued use. Data from the Royal College of General Practitioners 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 diseases, or renal disease should be encouraged to use another method of contraception. If 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. There is no difference in the occurrence of hypertension between ever- and never-users.

10. HEADACHE

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

11. BLEEDING IRREGULARITIES

Breakthrough bleeding and spotting are sometimes encountered in patients on oral contraceptives, especially during the first three months of use. If bleeding persists or recurs, non-hormonal causes should be considered and adequate diagnostic measures taken to rule out malignancy or pregnancy, as in the case of any abnormal vaginal bleeding. If pathology has been excluded, time 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.

12. ECTOPIC PREGNANCY

Ectopic as well as intrauterine pregnancy may occur in contraceptive failures.

PRECAUTIONS

1. SEXUALLY TRANSMITTED DISEASES

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

2. 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.

3. 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.

In patients with familial defects of lipoprotein metabolism receiving estrogen-containing preparations, there have been case reports of significant elevations of plasma triglycerides leading to pancreatitis.

4. LIVER FUNCTION

If jaundice develops in any woman receiving oral contraceptives, the medication should be discontinued. The hormones in DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP) may be poorly metabolized in patients with impaired liver function.

5. 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 which might be aggravated by fluid retention.

6. EMOTIONAL DISORDERS

Women with a history of depression should be carefully observed and the drug discontinued if depression recurs to a serious degree. Patients becoming significantly depressed while taking oral contraceptives should stop the medication and use an alternate method of contraception in an attempt to determine whether the symptom is drug related. Women with a history of depression should be carefully observed and the drug discontinued if depression recurs to a serious degree.

7. CONTACT LENSES

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

8. DRUG INTERACTIONS

Consult the labeling of all concurrently-used drugs to obtain further information about interactions with hormonal contraceptives or the potential for enzyme alterations.

Effects of Other Drugs on Combined Oral Contraceptives

Substances decreasing the plasma concentrations of COCs and potentially diminishing the efficacy of COCs:

Drugs or herbal products that induce certain enzymes, including cytochrome P450 3A4 (CYP3A4), may decrease the plasma concentrations of COCs and potentially diminish the effectiveness of COCs or increase breakthrough bleeding. Some drugs or herbal products that may decrease the effectiveness of hormonal contraceptives include phenytoin, barbiturates, carbamazepine, bosentan, felbamate, griseofulvin, oxcarbazepine, rifampicin, topiramate, rifabutin, rufinamide, aprepitant, and products containing St. John's wort. Interactions between hormonal contraceptives and other drugs may lead to breakthrough bleeding and/or contraceptive failure. Counsel women to use an alternative non-hormonal method of contraception or a back-up method when enzyme inducers are used with COCs, and to continue back-up non-hormonal contraception for 28 days after discontinuing the enzyme inducer to ensure contraceptive reliability.

Colesevelam:

Colesevelam, a bile acid sequestrant, given together with a COC, has been shown to significantly decrease the AUC of ethinyl estradiol (EE). The drug interaction between the contraceptive and colesevelam was decreased when the two drug products were given 4 hours apart.

Substances increasing the plasma concentrations of COCs:

Co-administration of atorvastatin or rosuvastatin and certain COCs containing EE increase AUC values for EE by approximately 20-25%. Ascorbic acid and acetaminophen may increase plasma EE concentrations, possibly by inhibition of conjugation. Concomitant administration of strong or moderate CYP3A inhibitors, such as itraconazole, voriconazole, fluconazole, grapefruit juice, or ketoconazole may increase plasma estrogen and/or progestin concentrations.

Since desogestrel is mainly metabolized by the cytochrome P450 2C9 enzyme (CYP2C9) to form etonogestrel, the active progestin, there is a possibility of interaction with CYP2C9 substrates or inhibitors (such as: ibuprofen, piroxicam, naproxen, phenytoin, fluconazole, diclofenac, tolbutamide, glipizide, celecoxib, sulfamethoxazole, isoniazid, torsemide, irbesartan, losartan, and valsartan). The clinical relevance of these interactions is unknown.

Human immunodeficiency virus (HIV)/ Hepatitis C Virus (HCV) **protease inhibitors *and nonnucleoside reverse transcriptase inhibitors:***

Significant changes in the plasma concentrations of estrogen and /or progestin have been noted in some cases of co-administration with HIV protease inhibitors (decrease [e.g., nelfinavir, ritonavir, darunavir/ritonavir, (fos)amprenavir/ritonavir, lopinavir/ritonavir, and tipranavir/ritonavir] or increase [e.g., indinavir and atazanavir/ritonavir]) /HCV protease inhibitors (decrease [e.g., boceprevir and telaprevir]) or with non-nucleoside reverse transcriptase inhibitors (decrease [e.g., nevirapine and efavirenz] or increase [e.g., etravirine]). These changes may be clinically relevant in some cases.

Concomitant Use with HCV Combination Therapy – Liver Enzyme Elevation: Do not co-administer DESOGEN® 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**).

Effects of Combined Oral Contraceptives on Other Drugs
COCs containing EE may inhibit the metabolism of other compounds (e.g., cyclosporine, prednisolone, theophylline, tizanidine, and voriconazole) and increase their plasma concentrations. COCs have been shown to decrease plasma concentrations of acetaminophen, clofibric acid, morphine, salicylic acid, and temazepam. A significant decrease in plasma concentration of lamotrigine has been shown, likely due to induction of lamotrigine glucuronidation. This may reduce seizure control; therefore, dosage adjustments of lamotrigine may be necessary.

Women on thyroid hormone replacement therapy may need increased doses of thyroid hormone because the serum concentrations of thyroid-binding globulin increase with use of COCs.

9. INTERACTIONS WITH LABORATORY TESTS

The use of contraceptive steroids may influence the results of certain laboratory tests, such as coagulation factors, lipids, glucose tolerance, and binding proteins.

10. CARCINOGENESIS

See WARNINGS section.

11. PREGNANCY

There is little or no increased risk of birth defects in women who inadvertently use COCs during early pregnancy. Epidemiologic studies and meta-analyses have not found an increased risk of genital or non-genital birth defects (including cardiac anomalies and limb reduction defects) following exposure to low dose COCs prior to conception or during early pregnancy.

Do not use COCs to induce withdrawal bleeding as a test for pregnancy. Do not use COCs during pregnancy to treat threatened or habitual abortion.

12. NURSING MOTHERS

Advise the nursing mother to use other forms of contraception, when possible, until she has weaned her child. COCs can reduce milk production in breastfeeding mothers. This is less likely to occur once breastfeeding is well-established; however, it can occur at any time in some women. Small amounts of oral contraceptive steroids and/or metabolites are present in breast milk.

13. PEDIATRIC USE

Safety and efficacy of DESOGEN® has been established in women of reproductive age. Efficacy is 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.

14. GERIATRIC USE

This product has not been studied in postmenopausal women and is not indicated in this population.

INFORMATION FOR THE PATIENT

See Patient Labeling Printed Below

ADVERSE REACTIONS

The following serious adverse reactions with the use of COCs are discussed elsewhere in the labeling:

- Serious cardiovascular events and stroke (see Boxed Warning and WARNINGS)
- Vascular events (see WARNINGS)
- Liver disease (see WARNINGS and PRECAUTIONS)

Possibly related adverse events that have been reported in clinical trials or observational studies with Desogen or CHC users in general are as follows:

Common events:

- Depressed mood, mood altered
- Headache
- Nausea, abdominal pain
- Breast tenderness, breast pain
- Weight increased

Uncommon events

- Fluid retention
- Libido decreased
- Migraine
- Vomiting
- Diarrhea
- Rash, urticaria
- Breast enlargement

Rare events:

- Hypersensitivity
- Libido increased
- Contact Lens intolerance
- Erythema nodosum, erythema multiforme
- Vaginal discharge
- Breast discharge
- Weight decreased

OVERDOSAGE

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

DOSAGE AND ADMINISTRATION

To achieve maximum contraceptive effectiveness, DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP) must be taken exactly as directed, at the same time every day, and at intervals not exceeding 24 hours. DESOGEN® may be initiated using either a Sunday start or a Day 1 start.

NOTE: Seven different "day label strips" are provided to accommodate the selected start regimen. The patient should place the self-adhesive "day label strip" that corresponds to her starting day on the blister card above the first row of tablets.

DURING THE FIRST CYCLE OF USE:

IMPORTANT: The possibility of ovulation and conception prior to initiation of use of DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP) should be considered. A woman can begin to take DESOGEN® either on the first Sunday after the onset of her menstrual period (Sunday Start) or on the first day of her menstrual period (Day 1 Start). When switching from another oral contraceptive, DESOGEN® should be started on the same day that a new pack of the previous oral contraceptive would have been started.

SUNDAY START

When initiating a Sunday start regimen, another method of contraception, such as condoms or spermicide, should be used for the first 7 consecutive days of taking DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP).

Using a Sunday start, tablets are taken daily without interruption as follows: The first white tablet should be taken on the first Sunday after menstruation begins (if menstruation begins on Sunday, the first white tablet is taken on that day). Tablets are then taken sequentially following the arrows marked on the blister card. One white tablet is taken daily for 21 days, followed by 1 green (inactive) tablet daily for 7 days. For all subsequent cycles, the patient then begins a new 28-tablet regimen on the next day (Sunday) after taking the last green (inactive) tablet. [If switching from a different Sunday Start oral contraceptive, the first DESOGEN® tablet should be taken on the same day that a new pack of the previous oral contraceptive would have been started.]

If a patient misses 1 white (active) tablet in Weeks 1, 2, or 3, she should take the missed tablet as soon as she remembers. If the patient misses 2 consecutive white tablets in Week 1 or Week 2, the patient should take 2 tablets the day she remembers and 2 tablets the next day; thereafter, the patient should resume taking 1 tablet daily until she finishes the cycle pack. The patient should be instructed to use a back-up method of birth control (such as condoms or spermicide) if she has intercourse in the 7 days after she restarts her pills. If the patient misses 2 consecutive white tablets in the third week or misses 3 or more white tablets in a row at any time during the cycle, the patient should keep taking 1 white tablet daily until the next Sunday. On Sunday the patient should throw out the rest of that cycle pack and start a new cycle pack that same day. The patient should be instructed to use a back-up method of birth control if she has intercourse in the 7 days after restarting her pills.

Complete instructions to facilitate patient counseling on proper pill usage can be found in Detailed or Brief Patient Labeling ("How to Take the Pill" section).

DAY 1 START

Counting the first day of menstruation as "Day 1", the first white tablet should be taken on the first day of menstrual bleeding. Tablets are then taken sequentially without interruption as follows: One white tablet daily for 21 days, then one green (inactive)

tablet daily for 7 days. For all subsequent cycles, the patient then begins a new 28-tablet regimen on the next day after taking the last green (inactive) tablet. [If switching directly from another oral contraceptive, the first white tablet should be taken on the same day that a new pack of the previous oral contraceptive would have been started.]

If a patient misses 1 white tablet, she should take the missed tablet as soon as she remembers. If the patient misses 2 consecutive white tablets in Week 1 or Week 2, the patient should take 2 tablets the day she remembers and 2 tablets the next day; thereafter, the patient should resume taking 1 tablet daily until she finishes the cycle pack. The patient should be instructed to use a back-up method of birth control (such as condoms or spermicide) if she has intercourse in the 7 days after she restarts her pills. If the patient misses 2 consecutive white tablets in the third week or misses 3 or more white tablets in a row at any time during the cycle, the patient should throw out the rest of that cycle pack and start a new cycle pack that same day. The patient should be instructed to use a back-up method of birth control if she has intercourse in the 7 days after restarting her pills.

Complete instructions to facilitate patient counseling on proper pill usage can be found in Detailed or Brief Patient Labeling ("How to Take the Pill" section).

ADDITIONAL INSTRUCTIONS FOR BOTH SUNDAY AND DAY 1 STARTS

If Spotting or Breakthrough Bleeding Occurs

Breakthrough bleeding, spotting, and amenorrhea are frequent reasons for patients discontinuing oral contraceptives. In breakthrough bleeding, as in all cases of irregular bleeding from the vagina, non-functional causes should be considered. In undiagnosed persistent or recurrent abnormal bleeding from the vagina, adequate diagnostic measures are indicated to rule out pregnancy or malignancy. If both pregnancy and pathology have been excluded, time or a change to another preparation may solve the problem. Changing to an oral contraceptive with a higher estrogen content, while potentially useful in minimizing menstrual irregularity, should be done only if necessary since this may increase the risk of thromboembolic disease.

Use of DESOGEN® in the Event of a Missed Menstrual Period

1. 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 DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP) use should be discontinued if pregnancy is confirmed.
2. If the patient has adhered to the prescribed regimen and misses two consecutive periods, pregnancy should be ruled out. DESOGEN® should be discontinued if pregnancy is confirmed.

Use of DESOGEN® Postpartum

The use of DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP) for contraception may be initiated 4 to 6 weeks postpartum in women who elect not to breast-feed. When the tablets are administered during the postpartum period, the increased risk of thromboembolic disease associated with the postpartum period must

be considered (see CONTRAINDICATIONS and WARNINGS concerning Thromboembolic Disorders. See also PRECAUTIONS for Nursing Mothers).

If the patient starts on DESOGEN® postpartum, and has not yet had a period, she should be instructed to use another method of contraception until a white tablet has been taken daily for 7 consecutive days.

HOW SUPPLIED

DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP) contains 21 round white tablets and 7 round green tablets in a blister card. Each white tablet (debossed with "T_5R" on one side and "Organon" on the other side) contains 0.15 mg desogestrel and 0.03 mg ethinyl estradiol. Each green tablet (debossed with "K_2H" on one side and "Organon" on the other side) contains inert ingredients.

Box of 1 NDC 0052-0261-08

Storage: Store below 30°C (86°F).

Manufactured for: Merck Sharp & Dohme Corp., a subsidiary of
MERCK & CO., INC., Whitehouse Station, NJ 08889, USA

Active tablets manufactured by: N.V. Organon, Oss, The Netherlands
Inert tablets manufactured by: N.V. Organon, Oss, The Netherlands

For patent information: www.merck.com/product/patent/home.html

The entities above are all subsidiaries of **Merck & Co., Inc.**, Whitehouse Station, NJ 08889, USA.

Revised: XX/XXXX

uspi-8276a-des-t-xxxxrxxx

Rx only

DETAILED PATIENT PACKAGE INSERT

DESOGEN® Tablets *28 Day Regimen*
(desogestrel and ethinyl estradiol tablets USP)

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

PLEASE NOTE: This labeling is revised from time to time as important new medical information becomes available. Therefore, please review this labeling carefully.

DESCRIPTION

DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP) contains a combination of a progestin and estrogen, the two kinds of female hormones.

Each white tablet contains 0.15 mg desogestrel and 0.03 mg ethinyl estradiol. Each green tablet contains inert ingredients.

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 doctor or healthcare 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 doctor's or healthcare provider's advice with regard to regular check-ups while you are on the pill.

EFFECTIVENESS OF ORAL CONTRACEPTIVES

Oral contraceptives or "birth control pills" or "the pill" are used to prevent pregnancy and are more effective than other non-surgical methods of birth control. When they are taken correctly, without missing any pills, the chance of becoming pregnant is about 1% (1 pregnancy per 100 women per year of use). Typical failure rates, including women who do not always take the pills exactly as directed, are actually 5% (5 pregnancies per 100 women per year of use). 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:

- No methods: 85%
- Spermicides alone: 26%
- Periodic abstinence: 25%
- Withdrawal: 19%
- Cervical Cap with spermicides: 20 to 40%
- Vaginal sponge: 20 to 40%
- Diaphragm with spermicides: 20%
- Condom alone (female): 21%
- Condom alone (male): 14%
- IUD: less than 1 to 2%
- Implants: less than 1%
- Injectable progestogen: less than 1%
- Male sterilization: less than 1%
- Female sterilization: less than 1%

WHO SHOULD NOT TAKE ORAL CONTRACEPTIVES

Cigarette smoking increases the risk of serious cardiovascular side effects from combination oral contraceptive (COC) use. This risk increases with age, particularly in women over 35 years of age, and with the number of cigarettes smoked. For this reason, do not use COCs if you are over 35 years of age and 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:

- A history of heart attack or stroke
- A history of blood clots in the legs (thrombophlebitis), lungs (pulmonary embolism), or eyes
- A history of blood clots in the deep veins of your legs
- Had a problem with your blood that makes it clot more than normal
- Chest pain (angina pectoris)
- Severe high blood pressure
- Diabetes with complications of the kidneys, eyes, nerves, or blood vessels
- Headaches with neurological symptoms
- Known or suspected breast cancer or cancer of the lining of the uterus, cervix, or vagina (now or in the past)
- Unexplained vaginal bleeding (until a diagnosis is reached by your healthcare provider)
- Yellowing of the whites of the eyes or of the skin (jaundice) during pregnancy or during previous use of hormonal birth control of any kind (the pill, patch, vaginal ring, injection, or implant)
- Liver tumor (benign or cancerous)
- Heart valve or heart rhythm disorders that may be associated with formation of blood clots
- Need for a long period of bed rest following major surgery
- Known or suspected pregnancy
- Active liver disease with abnormal liver function tests
- Take any Hepatitis C drug combination containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir. This may increase levels of the liver enzyme "alanine aminotransferase" (ALT) in the blood.
- An allergy or hypersensitivity to any of the components of DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP)

Tell your doctor or healthcare provider if you have ever had any of these conditions. Your doctor or healthcare provider can recommend another method of birth control.

OTHER CONSIDERATIONS BEFORE TAKING ORAL CONTRACEPTIVES

Tell your doctor or healthcare provider if you have:

- Breast nodules, fibrocystic disease of the breast, an abnormal breast x-ray or mammogram
- Diabetes
- Elevated cholesterol or triglycerides
- High blood pressure
- Migraine or other headaches or epilepsy
- Depression

- Gallbladder, liver, heart, or kidney disease
- Scanty or irregular menstrual periods

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

Talk to your healthcare provider about using DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP) if you:

- Smoke
- Recently had a baby
- Recently had a miscarriage or abortion
- Are breast-feeding
- Are taking any other medications

RISKS OF TAKING ORAL CONTRACEPTIVES

1. Risk of developing blood clots

Blood clots and blockage of blood vessels are one of the most serious side effects of taking oral contraceptives and can cause death or serious disability. In particular, a clot in the leg can cause thrombophlebitis and a clot that travels to the lungs can cause a sudden blockage of the vessel carrying blood to the lungs. The risks of these side effects may be greater with desogestrel-containing oral contraceptives, such as DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP), than with certain other low-dose pills. 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 or healthcare provider 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. 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 the section on Breast-Feeding in GENERAL PRECAUTIONS).

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. The risk of venous thromboembolic disease associated with oral contraceptives does not increase with length of use and disappears after pill use is stopped. The chance of getting a serious blood clot is highest when you first start taking birth control pills and after you restart the same or different birth control pills after not using them for a month or more. The risk of abnormal blood clotting increases with age in both users and non-users of oral contraceptives, but the increased risk from the oral contraceptive appears to be present at all ages.

2. Heart attacks and strokes

Oral contraceptives may increase the tendency to develop strokes (stoppage 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 with aura) who take oral contraceptives also may be at a higher risk of stroke.

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 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

Breast cancer has been diagnosed slightly more often in women who use the pill than in women of the same age who do not use the pill. This small increase in the number of breast cancer diagnoses gradually disappears during the 10 years after stopping use of the pill. It is not known whether the difference is caused by the pill. It may be that women taking the pill are examined more often, so that breast cancer is more likely to be detected. You should have regular breast examinations by a healthcare provider and examine your own breasts monthly. Tell your healthcare provider 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. There is insufficient evidence to rule out the possibility that pills may cause such cancers.

6. Lipid metabolism and inflammation of the pancreas

In patients with inherited defects of lipid metabolism, there have been reports of significant elevations of plasma triglycerides during estrogen therapy. This has led to pancreatitis in some cases.

WARNING SIGNALS

If any of these adverse effects occur while you are taking oral contraceptives, call your doctor or healthcare provider 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 doctor or healthcare provider 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

In addition to the risks and more serious side effects discussed above (see **RISKS OF TAKING ORAL CONTRACEPTIVES**, **ESTIMATED RISK OF DEATH FROM A BIRTH CONTROL METHOD OR PREGNANCY** and **WARNING SIGNALS** sections), the following may also occur:

1. Irregular vaginal bleeding

Irregular vaginal bleeding or spotting may occur while you are taking the pills. Irregular bleeding may vary from slight staining between menstrual periods to breakthrough bleeding, which is a flow much like a regular period. Irregular bleeding occurs most often during the first few months of oral contraceptive use, but may also occur after you have been taking the pill for some time. Such bleeding may be temporary and usually does not indicate any serious problems. It is important to continue taking your pills on schedule. If the bleeding occurs in more than one cycle or lasts for more than a few days, talk to your doctor or healthcare provider.

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 healthcare provider.

3. Fluid retention or raised blood pressure

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 doctor or healthcare provider.

4. Melasma

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

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 side effects bother you, call your doctor or healthcare provider.

GENERAL PRECAUTIONS

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

There may be times when you may not menstruate regularly after you have completed taking a cycle of pills. If you have taken your pills regularly and miss one menstrual

period, continue taking your pills for the next cycle but be sure to inform your doctor or healthcare provider before doing so. If you have not taken the pills daily as instructed and missed a menstrual period, or if you missed two consecutive menstrual periods, you may be pregnant. Check with your doctor or healthcare provider immediately to determine whether you are pregnant. Stop taking DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP) if you are pregnant.

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 or any other drugs should not be used during pregnancy unless clearly necessary and prescribed by your doctor or healthcare provider. You should check with your doctor or healthcare provider about risks to your unborn child of any medication taken during pregnancy.

2. While breast-feeding

If you are breast-feeding, consult your doctor or healthcare provider 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 or healthcare provider 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 potentially make them less effective in preventing pregnancy or cause an increase in breakthrough bleeding. Such drugs include rifampin, bosentan (used for high blood pressure in the blood vessels of the lungs), drugs used for epilepsy such as barbiturates (for example, phenobarbital), topiramate (Topamax®), carbamazepine (Tegretol® is one brand of this drug), phenytoin (Dilantin® is one brand of this drug), herbal products containing St. John's wort (hypericum perforatum), some HIV and/or HCV drugs such as ritonavir, nelfinavir, nevirapine, efavirenz, boceprevir and telaprevir and drugs used for other infectious diseases such as griseofulvin. You may need to use additional barrier contraception when you take drugs which may make oral contraceptives less effective. Because the effect of another medicine on Desogen may last up to 28 days after stopping the medicine, it is necessary to use the additional barrier contraceptive method for that long. Be sure to tell your doctor or healthcare provider if you are taking or start taking any medications while taking birth control pills.

Desogen may also interfere with how other medicines work, causing either an increase in their plasma concentrations (e.g., cyclosporine) or a decrease in their plasma concentrations (e.g., lamotrigine).

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.

HOW TO TAKE DESOGEN®

IMPORTANT POINTS TO REMEMBER

BEFORE YOU START TAKING YOUR PILLS:

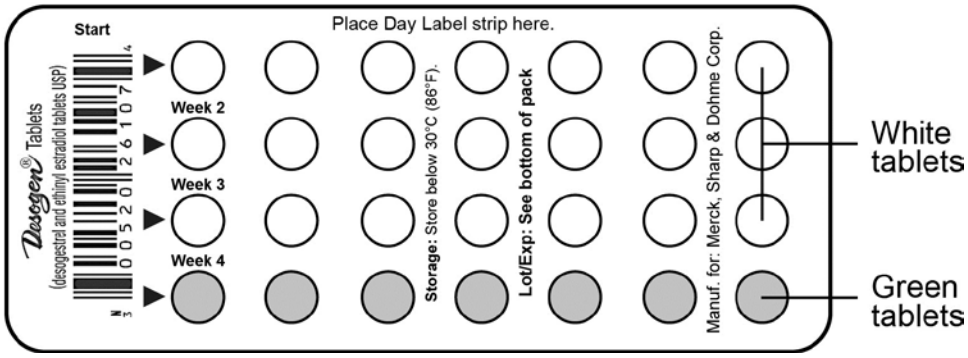
1. BE SURE TO READ THESE DIRECTIONS:
   - Before you start taking your pills
   - Anytime you are not sure what to do
2. THE RIGHT WAY TO TAKE THE PILL IS TO TAKE ONE PILL EVERY DAY AT THE SAME TIME.
   If you miss pills you could get pregnant. This includes starting the pack late.
   The more pills 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 have spotting or light bleeding or 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 healthcare provider.
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 CERTAIN MEDICINES, including some HIV drugs, some HCV drugs or the herbal supplement St. John's wort, your pills may not work as well.
   Use a back-up method (such as condoms, spermicides, or diaphragm) until you check with your doctor or healthcare provider.
6. IF YOU HAVE TROUBLE REMEMBERING TO TAKE THE PILL, talk to your doctor or healthcare provider 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 healthcare provider.

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: IT WILL HAVE 28 PILLS:
   This **28-pill pack** has 21 "active" [white] pills (with hormones) for Weeks 1, 2, and 3 and 7 "inactive" [green] pills (without hormones) for Week 4.
3. ALSO FIND:
   - where on the pack to start taking the pills,
   - in what order to take the pills (follow the arrows), and
   - the week numbers as shown in the picture below.

28 Pill Pack

Example Only:



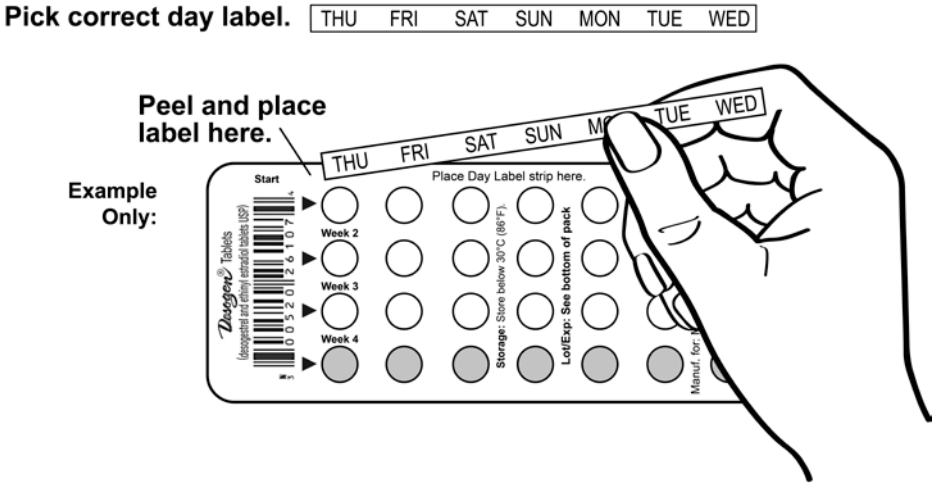
4. BE SURE YOU HAVE READY AT ALL TIMES:
   - ANOTHER KIND OF BIRTH CONTROL (such as condoms, spermicides, or diaphragm) to use as a back-up in case you miss pills.
   - AN EXTRA, FULL PILL PACK OF DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP).

WHEN TO START THE FIRST PACK OF PILLS

You have a choice of which day to start taking your first pack of pills. Decide with your doctor or healthcare provider 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 strip 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 strip on the blister card above the first row of tablets.



3. Take the first "active" [white] pill of the first pack during the first 24 hours of your period.
4. You will not need to use a back-up method of birth control, since you are starting the pill at the beginning of your period.

SUNDAY START:

1. Take the first "active" [white] pill of the first pack on the first 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 back-up method if you have sex anytime from the Sunday you start your first pack until the next Sunday (7 days). Condoms, spermicides, or a diaphragm are good back-up 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 PILLS:**
   Start the next pack on the day after your last pill. Do not wait any days between packs.

WHAT TO DO IF YOU MISS PILLS

If you **MISS 1** "active" [white] pill:

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 back-up birth control method if you have sex.

If you **MISS 2** "active" [white] pills 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 COULD BECOME PREGNANT if you have sex in the **7 days** after you restart your pills. You MUST use another birth control method (such as condoms, spermicides, or diaphragm) as a back-up method for those 7 days.

If you **MISS 2** "active" [white] pills in a row in **WEEK 3:**

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 healthcare provider because you might be pregnant.
3. You COULD BECOME PREGNANT if you have sex in the **7 days** after you restart your pills. You MUST use another birth control method (such as condoms, spermicides, or diaphragm) as a back-up method for those 7 days.

If you **MISS 3 OR MORE** "active" [white] pills 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 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 healthcare provider because you might be pregnant.
3. You COULD BECOME PREGNANT if you have sex on the days when you missed pills or during the first **7 days** after you restart your pills. You MUST use another

birth control method (such as condoms, spermicides, or diaphragm) as a back-up method the next time you have sex and for the first 7 days after restarting your pills.

IF YOU FORGET ANY OF THE 7 "INACTIVE" [GREEN] PILLS IN WEEK 4:

1. THROW AWAY the pills you missed.
2. Keep taking 1 pill each day until the pack is empty.
3. You do not need to use a back-up method of birth control.

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

1. Use a BACK-UP METHOD of birth control anytime you have sex.
2. KEEP TAKING ONE "ACTIVE" [WHITE] PILL EACH DAY until you can reach your doctor or healthcare provider.

ADDITIONAL INFORMATION

1. PREGNANCY DUE TO PILL FAILURE

The incidence of pill failure resulting in pregnancy is approximately one percent (i.e., one pregnancy per 100 women per year of use) if taken every day as directed, but more typical failure rates are about 5% (5 pregnancies per 100 women per year of use). If failure does occur, the risk to the fetus is minimal.

2. PREGNANCY AFTER STOPPING THE PILL

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

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

3. 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 doctor, healthcare provider, or pharmacist.

4. OTHER INFORMATION

Your doctor or healthcare provider will take a medical and family history and may examine you before prescribing an oral contraceptive. The physical examination may be delayed to another time if you request it and your doctor or the healthcare provider believes that it is a good medical practice to postpone it. You should be reexamined at least once a year. Be sure to inform your doctor or healthcare provider if there is a family history of any of the conditions listed previously in this leaflet. Be sure to keep all appointments with your doctor or healthcare 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.

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

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MERCK & CO., INC., Whitehouse Station, NJ 08889, USA

Active tablets manufactured by: N.V. Organon, Oss, The Netherlands
Inert tablets manufactured by: N.V. Organon, Oss, The Netherlands

For patent information: www.merck.com/product/patent/home.html

The entities above are all subsidiaries of **Merck & Co., Inc.**, Whitehouse Station, NJ 08889, USA.

Revised: XX/20XX

usppi-8276a-des-t-xxxxrxxx

Rx only

PATIENT PACKAGE INSERT BRIEF SUMMARY

DESOGEN® Tablets *28 Day Regimen*

(desogestrel and ethinyl estradiol tablets USP)

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

DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP) contain 21 round white tablets and 7 round green tablets in a blister card. Each white tablet contains 0.15 mg desogestrel and 0.03 mg ethinyl estradiol. Each green tablet contains inert ingredients.

Oral contraceptives, also known as "birth control pills" or "the pill", are taken to prevent pregnancy. When taken correctly, oral contraceptives have a failure rate of about 1% per year (1 pregnancy per 100 women per year of use) when used without missing any pills. The typical failure rate of large numbers of pill users is less than 5% per year (5 pregnancies per 100 women per year of use) when women who miss pills are included. Forgetting to take pills increases the chances of pregnancy.

For the majority of women, oral contraceptives can be taken safely. But, 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
- have high blood pressure, diabetes, high cholesterol
- have or have had clotting disorders, heart attack, stroke, angina pectoris, cancer of the breast or sex organs, jaundice, or malignant or benign liver tumors

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

You should not take DESOGEN® Tablets if you are taking any Hepatitis C drug combination containing ombitasvir/paritaprevir/ ritonavir, with or without dasabuvir. This may increase levels of the liver enzyme “alanine aminotransferase” (ALT) in the blood.

Although cardiovascular disease risks may increase with oral contraceptive use after age 40 in healthy, non-smoking women (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 cardiovascular side effects from combination oral contraceptive (COC) use. This risk increases with age particularly in women over 35 years of age, and with the number of cigarettes smoked. For this reason, do not use COCs if you are over 35 years of age and smoke.

Most side effects of the pill are not serious. The most common such effects are nausea, vomiting, bleeding or spotting 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.

The serious side effects of the pill occur very infrequently, especially if you are young and in good health. 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) or lungs (pulmonary embolism). The risks of these side effects may be greater with desogestrel-containing oral contraceptives, such as DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP), than with certain other low-dose pills.
2. Stoppage or rupture of a blood vessel in the brain (stroke), and blockage of blood vessels in the heart (heart attack or 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 headaches also may be at increased risk of stroke when taking the pill.
3. 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.
4. 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 **(DETAILED PATIENT PACKAGE INSERT)** given to you with your supply of pills. Notify your doctor or healthcare provider if you notice any unusual physical disturbances while taking the pill. In addition, drugs such as rifampin, as well as some anticonvulsants, some HIV and/or HCV drugs, and herbal preparations containing St. John's wort (hypericum perforatum) may decrease oral contraceptive effectiveness.

Breast cancer has been diagnosed slightly more often in women who use the pill than in women of the same age who do not use the pill. This very small increase in the number of breast cancer diagnoses gradually disappears during the 10 years after stopping use of the pill. It is not known whether the difference is caused by the pill. It may be that women taking the pill are examined more often, so that breast cancer is more likely to be detected. You should have regular breast examinations by a healthcare provider and examine your own breasts monthly. Tell your healthcare provider 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 hormonal contraceptives because breast cancer is usually a hormone-sensitive tumor.

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

Be sure to discuss any medical condition you may have with your doctor or healthcare provider. Your doctor or healthcare provider will take a medical and family history and may examine you before prescribing oral contraceptives. The physical examination may be delayed to another time if you request it and your doctor or healthcare provider believes that it is a good medical practice 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 doctor or healthcare provider.

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.

INSTRUCTIONS TO PATIENTS

HOW TO TAKE DESOGEN®

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 have spotting or light bleeding or 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 healthcare provider.
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 CERTAIN MEDICINES, including some HIV drugs, some HCV drugs or the herbal supplement St. John's wort, your pills may not work as well.

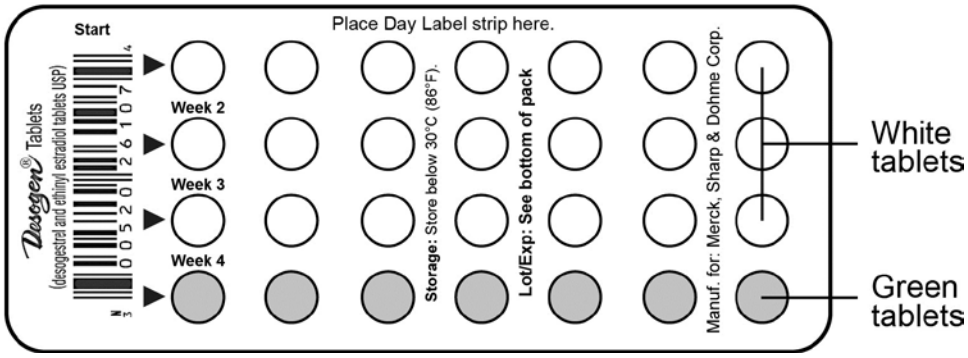
   Use a back-up method (such as condoms, spermicides, or diaphragm) until you check with your doctor or healthcare provider.
6. IF YOU HAVE TROUBLE REMEMBERING TO TAKE THE PILL, talk to your doctor or healthcare provider about how to make pill-taking easier or about using another method of birth control.
7. IF YOU HAVE ANY QUESTIONS OR ARE UNSURE ABOUT THE INFORMATION IN THIS LEAFLET, call your doctor or healthcare provider.

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: IT WILL HAVE 28 PILLS:
   This **28-pill pack** has 21 "active" [white] pills (with hormones) for Weeks 1, 2, and 3 and 7 "inactive" [green] pills (without hormones) for Week 4.
3. ALSO FIND:
   - where on the pack to start taking the pills,
   - in what order to take the pills (follow the arrows), and
   - the week numbers as shown in the picture below.

28 Pill Pack

Example Only:



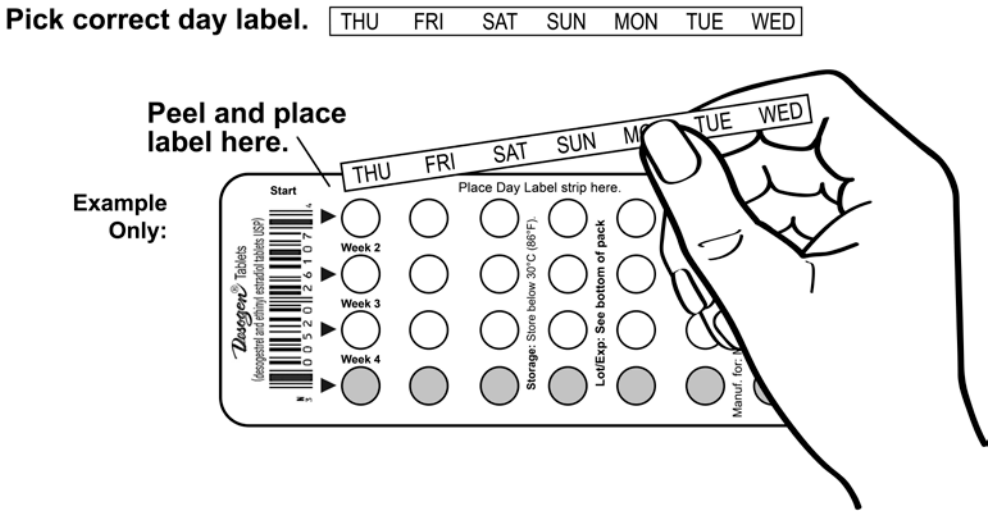
4. BE SURE YOU HAVE READY AT ALL TIMES:
   - ANOTHER KIND OF BIRTH CONTROL (such as condoms, spermicides, or diaphragm) to use as a back-up in case you miss pills.
   - AN EXTRA, FULL PILL PACK OF DESOGEN® Tablets (desogestrel and ethinyl estradiol tablets USP).

WHEN TO START THE FIRST PACK OF PILLS

You have a choice of which day to start taking your first pack of pills. Decide with your doctor or healthcare provider 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 strip 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 strip on the blister card above the first row of tablets.



3. Take the first "active" [white] pill of the first pack during the first 24 hours of your period.
4. You will not need to use a back-up method of birth control, since you are starting the pill at the beginning of your period.

SUNDAY START:

1. Take the first "active" [white] pill of the first pack on the first 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 back-up method if you have sex anytime from the Sunday you start your first pack until the next Sunday (7 days). Condoms, spermicides, or a diaphragm are good back-up 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 PILLS:**
   Start the next pack on the day after your last pill. Do not wait any days between packs.

WHAT TO DO IF YOU MISS PILLS

If you **MISS 1** "active" [white] pill:

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 back-up birth control method if you have sex.

If you **MISS 2** "active" [white] pills 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 COULD BECOME PREGNANT if you have sex in the **7 days** after you restart your pills. You MUST use another birth control method (such as condoms, spermicides, or diaphragm) as a back-up method for those 7 days.

If you **MISS 2** "active" [white] pills in a row in **WEEK 3:**

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 healthcare provider because you might be pregnant.
3. You COULD BECOME PREGNANT if you have sex in the **7 days** after you restart your pills. You MUST use another birth control method (such as condoms, spermicides, or diaphragm) as a back-up method for those 7 days.

If you **MISS 3 OR MORE** "active" [white] pills 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 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 healthcare provider because you might be pregnant.

3. You COULD BECOME PREGNANT if you have sex on the days when you missed pills or during the first **7 days** after restarting your pills. You MUST use another birth control method (such as condoms, spermicides, or diaphragm) as a back-up method the next time you have sex and for the first 7 days after you restart your pills.

IF YOU FORGET ANY OF THE 7 "INACTIVE" [GREEN] PILLS IN WEEK 4:

1. THROW AWAY the pills you missed.
2. Keep taking 1 pill each day until the pack is empty.
3. You do not need to use a back-up method of birth control.

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

1. Use a BACK-UP METHOD of birth control anytime you have sex.
2. KEEP TAKING ONE "ACTIVE" [WHITE] PILL EACH DAY until you can reach your doctor or healthcare provider.

Manufactured for: Merck Sharp & Dohme Corp., a subsidiary of
MERCK & CO., INC., Whitehouse Station, NJ 08889, USA

Active tablets manufactured by: N.V. Organon, Oss, The Netherlands
Inert tablets manufactured by: N.V. Organon, Oss, The Netherlands

For patent information: www.merck.com/product/patent/home.html

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Rx only