Product Monograph

Including Patient Medication Information

[Pr]BREVICON ® 0.5/35

Norethindrone and Ethinyl Estradiol

Tablet

For Oral use

0.5 mg / 35 mcg

[Pr]BREVICON ® 1/35

Norethindrone and Ethinyl Estradiol

Tablet

For Oral use

1 mg / 35 mcg

Ph.Eur. and Ph.Eur./ Ph.Japan (J.P)

Oral Contraceptive

Pfizer Canada ULC
17300 Trans-Canada Highway
Kirkland, Quebec H9J 2M5

Date of Authorization:
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Table of Contents

Certain sections or subsections that are not applicable at the time of the preparation of the most recent authorized product monograph are not listed.

Part 1: Healthcare Professional Information

1. Indications

BREVICON 0.5/35 and BREVICON 1/35 (norethindrone and ethinyl estradiol) are indicated for:

- the prevention of pregnancy.

1.1. Pediatrics

The safety and efficacy of BREVICON has been established in women of reproductive age. Use of these products before menarche is not indicated.

1.2. Geriatrics

BREVICON is not indicated for use in postmenopausal women.

2. Contraindications

BREVICON is contraindicated in women with:

- a history of or actual thrombophlebitis or thromboembolic disorders (such as deep vein thrombosis or pulmonary embolism);
- a history of or actual cerebrovascular disorders;
- a history of or actual myocardial infarction or coronary artery disease;
- valvular heart disease with complications;
- history of or actual prodromi of a thrombosis (e.g., transient ischemic attack, angina pectoris);
- active liver disease, or history of or actual benign or malignant liver tumours;
- known or suspected carcinoma of the breast;
- carcinoma of the endometrium or other known or suspected estrogen-dependent neoplasia;
- undiagnosed abnormal vaginal bleeding;
- steroid-dependent jaundice, cholestatic jaundice, history of jaundice of pregnancy;
- any ocular lesion arising from ophthalmic vascular disease, such as partial or complete loss of vision or defect in visual fields;
- known or suspected pregnancy;
- current or history of migraine with focal aura;
- history of or actual pancreatitis if associated with severe hypertriglyceridaemia;
- presence of severe or multiple risk factor(s) for arterial or venous or thrombosis such as:
    - severe hypertension (persistent values of ≥160/100 mmHg)
    - uncontrolled hypertension

- hereditary or acquired predisposition for venous or arterial thrombosis such as Factor V Leiden mutation and activated protein C (APC-) resistance, antithrombin-III-deficiency, protein C deficiency, protein S deficiency, hyperhomocysteinemia (e.g., due to MTHFR C677T, A1298 mutations), prothrombin mutation G20210A, and antiphospholipid-antibodies (anticardiolipin antibodies, lupus anticoagulant)
- severe dyslipoproteinemia
- over age 35 and smoke
- diabetes mellitus with vascular involvement
- major surgery associated with an increased risk of postoperative thromboembolism
- prolonged immobilization

- hypersensitivity to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, See 6 Dosage Forms, Strengths, Composition and Packaging.
- Hepatitis C virus (HCV) combination drug regimen ombitasvir, paritaprevir, ritonavir and dasabuvir with or without ribavirin. See 7 Warnings and Precautions: Hepatic/Biliary/Pancreatic and 9 Drug Interactions.

3. Serious Warnings and Precautions Box

- Cigarette smoking increases the risk of serious adverse effects on the heart and blood vessels. This risk increases with age and becomes significant in Oral Contraception (OC) users over 35 years of age. Women should be counselled not to smoke. See 2 Contraindications.
- Oral contraceptives do not protect against sexually transmitted diseases including HIV/AIDS. For protection against Sexually Transmitted Diseases (STDs), it is advisable to use latex condoms in combination with oral contraceptives.

4. Dosage and Administration

4.1. Dosing Considerations

- Pregnant women: BREVICON should not be used in women with known or suspected pregnancy.
- Hepatic impairment: BREVICON is contraindicated in women with active liver disease, or history of or actual benign or malignant liver tumours, and women with steroid-dependent jaundice, cholestatic jaundice, history of jaundice of pregnancy. No studies were conducted to evaluate the effect of liver diseases on the pharmacokinetics of BREVICON.
- Concomitant medications: Please See 9.4 Drug-Drug Interactions.

4.2. Recommended Dose and Dosage Adjustment

21-DAY PACK:

- With this type of birth control pill, the patient is 21 days on pills with seven days off pills. The patient must not be off the pills for more than seven days in a row.
- The first day of the patient's menstrual period (bleeding) is day 1 of a cycle. The doctor may advise the patient to start taking the pills on Day 1, on Day 5, or on the first Sunday after a period begins. If a period starts on Sunday, the patient starts that same day.

- The pack must be labelled correctly before starting. The pack is pre-printed with a Sunday starting day. If the patient is starting on a day other than a Sunday, she should use the Flexi-start™ sticker labels provided. The patient peels off the label with the chosen starting day and applies it over the pre-printed days on top of the card.
- The patient takes one pill at approximately the same time every day for 21 days; then she takes no pills for seven days. She starts a new pack on the eighth day. She will probably have a period during the seven days off the pill. (This bleeding may be lighter and shorter than a usual period.)

28-DAY PACK:

- With this type of birth control pill, the patient takes 21 pills which contain hormones and seven pills which contain no hormones.
- The first day of the patient's menstrual period (bleeding) is day 1 of a cycle. The doctor may advise the patient to start taking the pills on Day 1, on Day 5, or on the first Sunday after a period begins. If a period starts on Sunday, the patient starts that same day.
- The pack must be labelled correctly before starting. The pack is pre-printed with a Sunday starting day. If the patient is starting on a day other than a Sunday, she should use the Flexi-start™ sticker labels provided. The patient peels off the label with the chosen starting day and applies it over the pre-printed days on top of the card.
- The patient takes one pill at approximately the same time every day for 28 days. She begins a new pack the next day, not missing any days on the pills. The patient's period should occur during the last seven days of using that pill pack.

When a pack is finished:

- 21 Pills:
  - The patient must wait seven days to start the next pack. A period will begin during that week.
- 28 Pills:
  - The patient starts the next pack on the next day. She takes one pill every day. She does not wait any days between packs.

The safety and efficacy of BREVICON has been established in women of reproductive age. The use of BREVICON before menarche is not indicated.

4.4. Administration

What to do during the month:

- The patient takes a pill at approximately the same time every day until the pack is empty.
- The patient should try to associate taking the pill with some regular activity like eating a meal or going to bed.
- The patient must not skip pills even if she has bleeding between monthly periods or feels sick to her stomach (nausea).

- The patient must not skip pills even if she does not have sex very often.

It is recommended that the patient uses a second method of birth control (e.g. latex condoms and spermicidal foam or gel) for the first seven days of the first cycle of pill use. This will provide a back-up in case pills are forgotten while the patient is getting used to taking them.

4.5. Missed Dose

The following outlines the actions you should take if you miss one or more of your birth control pills. Match the number of pills missed with the appropriate starting time for your type of pill pack.

SUNDAY START	OTHER THAN SUNDAY START
MISS ONE PILL Take it as soon as you remember, and take the next pill at the usual time. This means that you might take two pills in one day.	**MISS ONE PILL** Take it as soon as you remember, and take the next pill at the usual time. This means that you might take two pills in one day.
MISS TWO PILLS IN A ROW **First two Weeks:** 1. Take two pills the day you remember and two pills the next day. 2. Then take one pill a day until you finish the pack. 3. Use a back-up method of birth control if you have sex in the seven days after you miss the pills. **Third Week:** 1. Keep taking one pill a day until Sunday. 2. On Sunday, safely discard the rest of the pack and start a new pack that day. 3. Use a back-up method of birth control if you have sex in the seven days after you miss the pills. 4. You may not have a period this month. **IF YOU MISS TWO PERIODS IN A ROW, CALL YOUR DOCTOR OR CLINIC.**	**MISS TWO PILLS IN A ROW** **First two Weeks:** 1. Take two pills the day you remember and two pills the next day. 2. Then take one pill a day until you finish the pack. 3. Use a back-up method of birth control if you have sex in the seven days after you miss the pills. **Third Week:** 1. Safely dispose of the rest of the pill pack and start a new pack that same day. 2. Use a back-up method of birth control if you have sex in the seven days after you miss the pills. 3. You may not have a period this month. **IF YOU MISS TWO PERIODS IN A ROW, CALL YOUR DOCTOR OR CLINIC.**
MISS THREE OR MORE PILLS IN A ROW **Anytime in the Cycle:** 1. Keep taking one pill a day until Sunday. 2. On Sunday, safely discard the rest of the pack and start a new pack that day. 3. Use a back-up method of birth control if you have sex in the seven days after you miss the pills.	**MISS THREE OR MORE PILLS IN A ROW** **Anytime in the Cycle:** 1. Safely dispose of the rest of the pill pack and start a new pack that same day. 2. Use a back-up method of birth control if you have sex in the seven days after you miss the pills. 3. You may not have a period this month.

4. You may not have a period this month. **IF YOU MISS TWO PERIODS IN A ROW, CALL YOUR DOCTOR OR CLINIC.**	**IF YOU MISS TWO PERIODS IN A ROW, CALL YOUR DOCTOR OR CLINIC.**

NOTE: 28-DAY PACK: If you forget any of the seven "reminder" pills (without hormones) in Week 4, just safely dispose of the pills you missed. Then keep taking one pill each day until the pack is empty. You do not need to use a back-up method.

Always be sure you have on hand:

- A back-up method of birth control (such as latex condoms and spermicidal foam or gel) in case you miss pills, and
- An extra, full pack of pills.

If you forget more than one pill two months in a row, talk to your doctor or clinic. Talk about ways to make pill-taking easier or about using another method of birth control.

5. Overdose

Numerous cases of the ingestion, by children, of estrogen progestogen combinations have been reported. Although mild nausea may occur, there appears to be no other reaction. Treatment should be limited to a laxative such as citrate of magnesia with the aim of removing unabsorbed material as rapidly as possible.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6. Dosage Forms, Strengths, Composition, and Packaging

Table 1 – Dosage Forms, Strengths, and Composition

Route of Administration	Dosage Form/ Strength/Composition	Non-Medicinal Ingredients
Oral	tablet 0.5 mg norethindrone and 0.035 mg (35 mcg) ethinyl estradiol	Active tablets: corn starch, FD&C Blue No. 2, lactose monohydrate, magnesium stearate, povidone Inactive tablets: FD&C Yellow No. 6 Lake, lactose CDL21, lactose monohydrate, magnesium stearate, microcrystalline cellulose.
	tablet 1 mg norethindrone and 0.035 mg (35 mcg) ethinyl estradiol	Active tablets: Corn starch, lactose monohydrate, magnesium stearate, povidone. Inactive tablets: FD&C Yellow No. 6 Lake,

		lactose CDL21, lactose monohydrate, magnesium stearate, microcrystalline cellulose.

Description

BREVICON 0.5/35

Available in 21 day dispensers, each containing 21 active tablets.

Also available in 28 day dispensers, each containing 21 active and 7 inactive tablets.

Active tablets
Pale Blue circular tablets, impressed "SEARLE" on one side and "BX" on the other.

Inactive tablets
Orange tablets impressed "SEARLE" on one side and "P" on the other.

BREVICON 1/35

Available in 21 day dispensers, each containing 21 active tablets.

Also available in 28 day dispensers, each containing 21 active and 7 inactive tablets.

Active Tablets
White circular tablets impressed "SEARLE" on one side and "BX" on the other.

Inactive tablets
Orange tablets impressed "SEARLE" on one side and "P" on the other.

7. Warnings and Precautions

See 3 Serious Warnings and Precautions Box.

General

The following information is provided from studies of combination oral contraceptives (COCs).

The use of combination hormonal contraceptives is associated with increased risks of several serious conditions including myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gallbladder disease, although the risk of serious morbidity and mortality is small in healthy women without underlying risk factors. The risk of morbidity and mortality increases significantly if associated with the presence of other risk factors such as hypertension, hyperlipidemias, obesity, and diabetes. Other medical conditions which have been associated with adverse circulatory events include systemic lupus erythematosus, hemolytic uremic syndrome, chronic inflammatory bowel disease (Crohn's disease or ulcerative colitis), sickle cell disease, valvular heart disease and atrial fibrillation.

The following conditions have been reported to occur or deteriorate with both pregnancy and COC use, although a direct association with COCs has not been firmly established: porphyria, systemic lupus erythematosus, hemolytic uremic syndrome, Sydenham's chorea, herpes gestationis, and otosclerosis-related hearing loss.

The information contained in this section is principally from studies carried out in women who used combination oral contraceptives with higher formulations of estrogens and progestogens than those in common use today. The effect of long-term use of combination hormonal contraceptives with lower doses of both estrogen and progestogen administered orally remains to be determined.

Carcinogenesis and Genotoxicity

Breast Cancer:

Increasing age and a strong family history are the most significant risk factors for the development of breast cancer. Other established risk factors include obesity, nulliparity and late age at first full-term pregnancy. The identified groups of women that may be at increased risk of developing breast cancer before menopause are long-term users of oral contraceptives (more than eight years) and starters at early age. In a few women, the use of oral contraceptives may accelerate the growth of an existing but undiagnosed breast cancer. Since any potential increased risk related to oral contraceptive use is small, there is no reason to change prescribing habits at present.

Women receiving oral contraceptives should be instructed in self-examination of their breasts. Their health professionals should be notified whenever any masses are detected. A yearly clinical breast examination is also recommended because, if a breast cancer should develop, drugs that contain estrogen may cause a rapid progression.

Cervical Cancer:

The most important risk factor for cervical cancer is persistent human papillomavirus infection. Some studies suggest that COC use may be associated with an increase in the risk of cervical intraepithelial neoplasia or invasive cervical cancer in some populations of women. For example, the results of one meta-analysis of 24 epidemiological studies indicated that among current users of oral contraceptives, the relative risk of invasive cervical cancer increased with increasing duration of use. The relative risk for 5 or more years' use versus never-use was 1.90 (95% confidence interval 1.69-2.13). The relative risk declined after use ceased and by 10 or more years was not significantly different from that in never-users. 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 cases of undiagnosed abnormal genital bleeding, adequate diagnostic measures are indicated.

Cardiovascular

At the earliest manifestation of thromboembolic and cardiovascular disorders (Thrombophlebitis, pulmonary embolism, cerebrovascular disorders, myocardial ischemia, mesenteric thrombosis, and retinal thrombosis) discontinue the medication. Conditions such as immobilization after accidents or confinement to bed during long-term illness predispose venous stasis and vascular thrombosis; discontinue medication at the earliest manifestation of such conditions.

Predisposing Factors for Coronary Artery Disease:

Cigarette smoking increases the risk of serious cardiovascular side effects and mortality. Birth control pills increase this risk, especially with increasing age. Convincing data are available to support an upper age limit of 35 years for oral contraceptive use by women who smoke.

Other women who are independently at high risk for cardiovascular disease include those with diabetes, hypertension, abnormal lipid profile, or a family history of these. Whether OCs accentuate this risk is unclear.

In low risk, non-smoking women of any age, the benefits of oral contraceptive use outweigh the possible cardiovascular risks associated with low dose formulations. Consequently, oral contraceptives may be prescribed for these women up to the age of menopause.

Hypertension:

Patients with essential hypertension whose blood pressure is well-controlled may be given oral contraceptives but only under close supervision. If a significant elevation of blood pressure in previously normotensive or hypertensive subjects occurs at any time during the administration of the drug, cessation of medication is necessary.

Connective Tissue Disease

The use of oral contraceptives in some women has been associated with positive lupus erythematous cell tests and with clinical lupus erythematous. In some instances exacerbation of rheumatoid arthritis and synovitis have been observed.

Endocrine and Metabolism

In metabolic or endocrine diseases and when metabolism of calcium and phosphorus is abnormal, careful clinical evaluation should precede medication and a regular follow-up is recommended.

Diabetes:

Current low dose OCs exert minimal impact on glucose metabolism. Diabetic patients, or those with a family history of diabetes, should be observed closely to detect any worsening of carbohydrate metabolism. Patients predisposed to diabetes who can be kept under close supervision may be given oral contraceptives. Young diabetic patients whose disease is of recent origin, well-controlled, and not associated with hypertension or other signs of vascular disease such as ocular fundal changes, should be monitored more frequently while using oral contraceptives.

Gastrointestinal

Abdominal cramps and bloating. Published epidemiological studies indicate a possible association of COC use and the development of Crohn's disease and ulcerative colitis, although this has not been firmly established.

Genitourinary

Vaginal Bleeding:

Persistent irregular vaginal bleeding requires assessment to exclude underlying pathology.

Fibroids:

Patients with fibroids (leiomyomata) should be carefully observed. Sudden enlargement, pain, or tenderness require discontinuation of the use of OCs.

Hematologic

Epidemiological studies have suggested an association between the use of COCs and an increased risk of arterial and venous thrombotic and thromboembolic diseases such as myocardial infarction, deep venous thrombosis, pulmonary embolism, and of cerebrovascular accidents.

Venous Thromboembolism:

The use of any combined oral contraceptive carries an increased risk of venous thromboembolism (VTE) compared with no use. The excess risk of VTE is highest during the first year a woman ever uses a combined oral contraceptive or restarts (following a 4-week or greater pill-free interval) the same or a different COC. Data from a large, prospective 3-armed cohort study suggest that this increased risk is mainly present during the first 3 months. VTE is fatal in 1% to 2% of cases.

A large, prospective 3-armed cohort study has shown that the frequency of VTE diagnosis ranges from about 8 to 10 per 10,000 woman-years in users of oral contraceptives with low estrogen content (<50 µg ethinyl estradiol). The most recent data suggest that the frequency of VTE diagnosis is approximately 4.4 per 10,000 woman-years in nonpregnant, non-COC users and ranges from 20 to 30 per 10,000 women-years in pregnant women or postpartum.

Overall the risk for VTE in users of COCs with low estrogen content (<50 µg ethinyl estradiol) is 2- to 3-fold higher than for nonusers of COCs who are not pregnant and remains lower than the risk associated with pregnancy and delivery.

The risk of VTE with COCs has been shown to be related to the estrogen dose, as risk has decreased as doses have decreased from 100 µg to 50 µg to 30 µg. Whether doses as low as 10 µg are further protective is unknown. BREVICON provides a daily dose of ethinyl estradiol of 35 µg, for 21 of 28 days each cycle.

Extremely rarely, thrombosis has been reported to occur in other blood vessels (eg, hepatic, mesenteric, renal, cerebral, or retinal veins and arteries) in COC users. There is no consensus as to whether the occurrence of these events is associated with the use of COCs.

Arterial Thromboembolism:

The risk for arterial thromboembolism (ATE) in users of oral contraceptives with <50 µg ethinyl estradiol ranges from about 1 to 3 cases per 10,000 woman-years. An ATE can include cerebrovascular

accident, vascular occlusion, or myocardial infarction (MI). Arterial thromboembolic events may be fatal.

Other Risk Factors for Venous or Arterial Thromboembolism or of a Cerebrovascular Accident:

Other generalized risk factors for venous or arterial thromboembolism include but are not limited to age, severe obesity (body mass index >30 kg/m^2), a personal history, a positive family history (the occurrence of VTE/ATE in a direct relative at a relatively early age may indicate genetic predisposition) and systemic lupus erythematosus. If a hereditary or acquired predisposition for venous or arterial thromboembolism is suspected, the woman should be referred to a specialist for advice before deciding on any COC use. The risk of VTE/ATE may be temporarily increased with prolonged immobilization, major surgery, or trauma. In these situations, it is advisable to discontinue COC use (in the case of elective surgery at least four weeks in advance) and not to resume COC use until two weeks after complete remobilization. Also, patients with varicose veins and leg cast should be closely supervised. Other risk factors may include smoking (with heavier smoking and increasing age, the risk further increases, especially in women over 35 years of age), dyslipoproteinemia, hypertension, migraine, valvular heart disease, and atrial fibrillation.

Biochemical factors that may be indicative of hereditary or acquired predisposition for venous or arterial thrombosis include Factor V Leiden mutation and activated protein C (APC-) resistance, antithrombin-III-deficiency, protein C deficiency, protein S deficiency, hyperhomocysteinemia (eg, due to MTHFR C677T, A1298 mutations), prothrombin mutation G20210A, and antiphospholipid-antibodies (anticardiolipin antibodies, lupus anticoagulant).

When considering risk/benefit, the health professional should take into account that adequate treatment of a condition may reduce the associated risk of thrombosis and that the risk associated with pregnancy is higher than that associated with COCs containing <0.05 mg ethinyl estradiol).

Hepatic/Biliary/Pancreatic

Hepatitis C:

During clinical trials with patients treated for HCV infections with the combination of ombitasvir, paritaprevir, ritonavir and dasabuvir with or without ribavirin, it was found that transaminase (ALT) elevations > 5 times the upper limit of normal (ULN) were significantly more frequent in women using ethinyl estradiol-containing medications such as COCs. Therefore BREVICON 1/35 and BREVICON 0.5/35 are contraindicated in hepatitis C patients during treatment with these drugs (see 2 Contraindications and 9 Drug Interactions).

Jaundice:

Patients who have had jaundice including a history of cholestatic jaundice during pregnancy should be given oral contraceptives with great care and under close observation.
The development of severe generalized pruritus or icterus requires that the medication be withdrawn until the problem is resolved.

If a patient develops jaundice that proves to be cholestatic in type, the use of oral contraceptives should not be resumed. In patients taking oral contraceptives, changes in the composition of the bile may occur and an increased incidence of gallstones has been reported.

Gallbladder Disease:

Patients taking oral contraceptives have a greater risk of developing gallbladder disease requiring surgery within the first year of use. The risk may double after four or five years.

Hepatic Nodules**:**

Hepatic nodules have been reported to be associated with use of oral contraceptives, particularly in long-term users of oral contraceptives. These nodules include benign hepatic adenomas, focal nodular hyperplasia and other hepatic lesions. In addition, hepatocellular carcinoma has been reported.

Although these lesions are extremely rare, they have caused fatal intra-abdominal hemorrhage and should be considered in women presenting with an abdominal mass, acute abdominal pain, or evidence of intra-abdominal bleeding.

Immune

Angioedema:

COC may induce or exacerbate symptoms of angioedema, particularly in women with hereditary angioedema.

Monitoring and Laboratory Tests

Physical Examination and Follow-up:

Before oral contraceptives are used, a thorough history and physical examination should be performed, including a blood pressure determination. Breasts, liver, extremities and pelvic organs should be examined and a Papanicolaou smear should be taken if the patient has been sexually active.

The first follow-up visit should be done three months after oral contraceptives are prescribed. Thereafter, examinations should be performed at least once a year or more frequently if indicated. At each annual visit, examination should include those procedures that were done at the initial visit as outlined above or per recommendations of the Canadian Workshop on Screening for Cancer of the Cervix. Their suggestion was that, for women who had two consecutive negative Pap smears, screening could be continued every three years up to the age of 69.

Tissue Specimens:

Pathologists should be advised of oral contraceptive therapy when specimens obtained from surgical procedures and Pap smears are submitted for examination.

Neurologic

At the earliest manifestation of severe headache of unknown etiology, worsening of pre existing migraine headache or increase in epileptic seizures discontinue medication.

Migraine and Headache:

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

Women with migraine headaches who take oral contraceptives may be at increased risk of stroke. See 2 Contraindications.

Ophthalmologic

At the earliest manifestation of partial or complete visual defects, papilledema or ophthalmic vascular lesions discontinue medication

Ocular Disease:

Patients who are pregnant or are taking oral contraceptives, may experience corneal edema that may cause visual disturbances and changes in tolerance to contact lenses, especially of the rigid type. Soft contact lenses usually do not cause disturbances. If visual changes or alterations in tolerance to contact lenses occur, temporary or permanent cessation of wear may be advised.

Ocular Lesions:

With use of COCs, there have been reports of retinal vascular thrombosis which may lead to partial or complete loss of vision. If there are signs or symptoms such as visual changes, onset of proptosis or diplopia, papilledema, or retinal vascular lesions, BREVICON should be discontinued and the cause immediately evaluated.

Perioperative Considerations

There is an increased risk of post-surgery thromboembolic complications in oral contraceptive users, after major surgery. If feasible, oral contraceptives should be discontinued and an alternative method substituted at least one month prior to **MAJOR** elective surgery. Oral contraceptives should not be resumed until the first menstrual period after hospital discharge following surgery.

Psychiatric

Emotional Disorders:

Patients with a history of emotional disturbances, especially the depressive type, may be more prone to have a recurrence of depression while taking oral contraceptives. In cases of a serious recurrence, a trial of an alternate method of contraception should be made which may help to clarify the possible relationship. Women with premenstrual syndrome (PMS) may have a varied response to oral contraceptives, ranging from symptomatic improvement to worsening of the condition.

Reduced Efficacy

The efficacy of COCs may be reduced in the event of missed tablets (see 4.5 Missed Dose), gastrointestinal disturbances or concomitant medication (see 9 Drug Interactions).

Renal

Fluid Retention:

Hormonal 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.

Reproductive Health

BREVICON is contraindicated in pregnancy (See 2 Contraindications, 7.1.1 Pregnancy).

- **Fertility**

  After discontinuing oral contraceptive therapy, the patient should delay pregnancy until at least one normal spontaneous cycle has occurred in order to date the pregnancy. An alternate contraceptive method should be used during this time.

- **Amenorrhea**

  Women having a history of oligomenorrhea, secondary amenorrhea, or irregular cycles may remain anovulatory or become amenorrheic following discontinuation of estrogen-progestin combination therapy.

  Amenorrhea, especially if associated with breast secretion, that continues for six months or more after withdrawal, warrants a careful assessment of hypothalamic-pituitary function.

- **Vaginal Bleeding**

  Breakthrough bleeding/spotting may occur in women taking COCs, especially during the first three months of use. The type and dose of progestin may be important. If this bleeding persists or recurs, nonhormonal causes should be considered and adequate diagnostic measures may be indicated to rule out pregnancy, infection, malignancy, or other conditions. If pathology has been excluded, continued use of the COC or a change to another formulation may solve the problem.

Sensitivity/Resistance

BREVICON is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 Dosage Forms, Strengths, Composition and Packaging. Brevicon contains lactose therefore caution should be exercised in patients with a known or suspected hypersensitivity to cow's milk or its components or other dairy products.

Skin

Chloasma may occasionally occur with use of COCs, especially in women with a history of chloasma gravidarum. Women with a tendency to chloasma should avoid exposure to the sun or ultraviolet radiation while taking COCs. Chloasma is often not fully reversible.

7.1. Special Populations

7.1.1. Pregnancy

Fetal abnormalities have been reported to occur in the offspring of women who have taken estrogen-progestogen combinations in early pregnancy. Rule out pregnancy as soon as it is suspected. See 2 Contraindications.

7.1.2. Breastfeeding

In breast-feeding women, the use of oral contraceptives results in the hormonal components being excreted in breast milk and may reduce its quantity and quality. The long-term effects on the developing child are not known. However, cases of breast enlargement have been reported in breast-fed infants. 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.

7.1.3. Pediatrics

Safety and efficacy of COCs have been established in women of reproductive age. Use of these products before menarche is not indicated.

7.1.4. Geriatrics

COCs are not indicated for use in postmenopausal women.

8. Adverse Reactions

8.1. Adverse Reaction Overview

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

- being diagnosed with breast cancer (See 7 Warnings and Precautions)
- hypertension (See 7 Warnings and Precautions)

The following adverse reactions also have been reported in patients receiving oral contraceptives:

Nausea and vomiting, usually the most common adverse reaction, occurs in approximately 10% or fewer of patients during the first cycle.

The following other reactions, as a general rule, are seen less frequently or only occasionally:

Ear and labyrinth: auditory disturbances
Gastrointestinal: abdominal pain, gastrointestinal symptoms (such as abdominal cramps and bloating)
General: edema
Investigations: change in weight (increase or decrease)
Nervous system: dizziness, headache
Psychiatric: mental depression, nervousness
Renal and urinary: cystitis-like syndrome

Reproductive system and breast: amenorrhea during and after treatment, breakthrough bleeding change in menstrual flow, dysmenorrhea, premenstrual-like syndrome, spotting. See 7 Warnings and Precautions.
Skin and subcutaneous tissue: loss of scalp hair, rash (allergic)
Vascular: hypertension*
* Occurrence or deterioration of conditions for which association with COC use is not conclusive.

8.5. Post-Market Adverse Reactions

During post-marketing experience, an increased risk of the following serious adverse reactions has been associated with the use of oral contraceptives:

- arterial and venous thromboembolism
- benign and malignant hepatic tumours
- cerebral hemorrhage
- cerebral thrombosis
- congenital anomalies
- gallbladder disease
- mesenteric thrombosis
- myocardial infarction
- neuro-ocular lesions (e.g., retinal thrombosis)
- pulmonary embolism
- thrombophlebitis

The following other reactions, as a general rule, are seen less frequently or only occasionally:

Blood and lymphatic system: hemolytic uremic syndrome
Ear and labyrinth: otosclerosis-related hearing loss*
Eye: cataracts, change in corneal curvature (steepening), intolerance to contact lenses, retinal thrombosis
Gastrointestinal: Crohn's disease*, diarrhea, pancreatitis, ulcerative colitis*
Hepatobiliary: cholestatic jaundice, gallstone formation*, liver function disturbances*
Immune system: hypersensitivity
Infections and infestations: rhinitis, vaginal candidiasis, vaginitis
Investigations: reduced tolerance to carbohydrates
Metabolism and nutrition: changes in appetite, hypertriglyceridemia (increased risk of pancreatitis when using COCs) *, porphyria
Musculoskeletal and connective tissue: systemic lupus erythematosus*
Neoplasms benign, malignant and unspecified (incl cyst and polyps): increase in size of uterine leiomyomata
Nervous system: chorea, migraine, optic neuritis, Sydenham's chorea*
Psychiatric: changes in libido
Renal and urinary: impaired renal function
Reproductive system and breast: breast changes including tenderness, enlargement, and secretion, endocervical hyperplasias, possible diminution in lactation when given immediately post-partum, temporary infertility after discontinuance of treatment, vaginal discharge

Skin and subcutaneous tissue: chloasma or melasma which may persist, hirsutism, erythema multiforme, erythema nodosum, hemorrhagic eruption, herpes gestationis*, pruritis related to cholestasis*, urticaria
Vascular: Raynaud's phenomenon
* Occurrence or deterioration of conditions for which association with COC use is not conclusive.

9. Drug Interactions

9.2. Drug Interactions Overview

Since the introduction of oral contraceptives more than 30 years ago, there have been many reports of drug interactions with these agents. Some are well documented and of clinical significance but others are less so and are of questionable or unknown clinical relevance. There are two major types of interactions between OCs and concomitant drugs. First, the efficacy of OCs may be altered usually decreased by interacting agents. Second, OCs may alter the efficacy, or alter the adverse effects, of other drugs.

The potential for drug interactions with OCs seems more likely today, and the occurrence perhaps more frequent, due to the expanding use of low-dose estrogen OCs. Confounding factors make the actual incidence and therapeutic significance of these interactions difficult to determine. It is well accepted that approximately one per cent of women will experience contraceptive failure while taking OCs. Failure may occur because of improper use of the OC (i.e. not taking OCs at the same time each day, missing pills, etc.). The efficacy of OCs also may be diminished in women with certain diseases (e.g. persistent diarrhea). Contraceptive failure also could be due to concomitant drug therapy. Most of the information concerning drug interactions with OCs comes from case reports and data reported retrospectively.

Clinical trials have not been done because of the large numbers of patients that would need to be recruited and the ethical considerations of conducting such trials. Therefore, clinicians must rely on the information available and interpret it carefully.

Several mechanisms are thought to be responsible for altering the efficacy of OCs:

- interference with absorption of the OCs from the GI tract;
- increased levels of plasma sex hormone binding globulin (SHBG) leading to decreased levels of active steroid;
- competition between the OCs and interacting drug for the same metabolizing enzyme;
- microsomal enzyme induction (or inhibition) in the liver, which may increase or decrease the metabolism of the OC; and
- interference with the enterohepatic recirculation of steroid metabolites.

Unexpected spotting or breakthrough bleeding may suggest reduced contraceptive efficacy. If the efficacy of the OC is reduced sufficiently, pregnancy may result.

The proposed mechanisms of known and suspected drug interactions that have been reported with OCs are reviewed in Tables 1 and 2 at the end of this section. Table 2 lists those drugs that interfere with the efficacy of OCs. Most anticonvulsant agents, including phenobarbital, phenytoin, primidone, carbamazepine, and ethosuximide, have been implicated in contraceptive failure with OCs. These

agents induce hepatic microsomal enzymes responsible for the metabolism of OCs, leading to increased metabolism and lower effective levels of steroids. It also has been reported that an increase in SHBG leads to lower free progesterone levels. As these anticonvulsants are often prescribed to women of childbearing age, it is generally recommended that an alternative method of contraception be used. Some experts suggest using an OC with 50 µg or more of ethinyl estradiol. The benefits of this approach must be weighed against the increased risk of adverse effects such as thromboembolic disorders. No reports of an interaction between valproic acid and OCs could be found.

Anti-infective agents also have been implicated in the failure of OCs. Rifampin was the first drug reported to interfere with OCs. Like the anticonvulsants, rifampin is a hepatic microsomal enzyme inducer, and can effectively reduce steroid levels. Griseofulvin, an antifungal agent, may also interact with OCs in a similar way. Women receiving OCs and rifampin or griseofulvin should be counselled about the possible interaction and be advised about alternative methods of birth control.

Perhaps more controversial is the proposed interaction between OCs and broad-spectrum antibiotics. This interaction may be mediated through some of the mechanisms mentioned above. Some anti-infectives may cause hepatic microsomal enzyme induction (as seen with rifampin and griseofulvin). Adverse effects of antibiotics, such as diarrhea, may speed transit time through the gastrointestinal tract and decrease absorption of the OC. In addition, antibiotics may alter gut bacterial flora. It is known that approximately 60 per cent of ethinyl estradiol is metabolized on its first pass through the liver, and the conjugates are excreted in the bile. Bacteria in the gut hydrolyse the conjugates back to active ethinyl estradiol, which is then reabsorbed. Antibiotic-induced alterations in gut bacteria could reduce this enteroheptic recirculation of ethinyl estradiol.

There have been several well-documented case reports of pregnancy occurring while women, correctly using OCs, were taking antibiotics, especially ampicillin, other penicillins and tetracycline. Contraceptive failures have also been reported with chloramphenicol, isoniazid, neomycin, nitrofurantoin, penicillin V, sulfonamides, erythromycin and cotrimoxazole. The number of case reports is small compared to the number of women receiving OCs. However, that fact does not diminish the clinical implications of the interaction, even if it occurs only in a few women. As many women on OCs are likely to be prescribed antibiotics sometime, the controversy expands to how to counsel these patients. Some experts believe that an alternative form of birth control should not be recommended during a short course of antibiotic therapy. Others believe that because of the potential risk of interaction, and the inability to predict those who are likely to experience interaction, all women should be advised of the risk, and additional methods of contraception should be recommended. Women to be placed on long-term antibiotic therapy, such as tetracycline for acne, should also be advised of the interaction.

There are a few drugs and classes of drugs in Table 2 for which the evidence of reduced OC efficacy is questionable. The most recent evidence concerning the interaction between OCs and clofibrate indicates that OCs probably have more of an effect on reducing the efficacy of clofibrate than the opposite (see Table 3 under Cholesterol Lowering Agents). The same is probably true for analgesics in that OCs actually reduce the efficacy of ASA (acetylsalicylic acid) and acetaminophen (see Table 3 under Antipyretics). It has been reported that long-term use of OCs and phenylbutazone may result in an increased incidence of breakthrough bleeding. Although it has been reported that antihistamines may reduce OC efficacy, this was not supported by the results of a pharmacokinetic study with OCs, doxylamine and diphenhydramine. The antimigraine preparations in Table 3 refer primarily to

ergotamine preparations that also contain barbiturates. As mentioned previously with the anticonvulsants, barbiturates can increase the metabolism of OCs, leading to reduced efficacy.

It should be mentioned that there are a few drugs that may actually increase the action and/or plasma concentration of OCs. There is little information in the literature on these types of interactions, possibly because the interaction is likely to increase the efficacy of the OC. However, there is also the possibility of increased risk of toxicity with the OCs. There are two potential interactions worth noting. When vitamin C and OCs are given concurrently, there is an increase in plasma ethinyl estradiol levels. This should not be of concern unless a person stops intake of regular vitamin C which may cause a drop in steroid plasma levels. Acetaminophen can also increase ethinyl estradiol levels by decreasing its metabolism during absorption.

Again, this should not be clinically significant unless a person stops taking regular high doses of acetaminophen abruptly. If patients are on OCs and either vitamin C or acetaminophen, it is recommended that they be slowly tapered off these agents if they are to be stopped.

As shown in Table 3, OCs can interfere with the efficacy of other drugs. OCs may increase the levels of some clotting factors and reduce antithrombin III levels, diminishing the effect of anticoagulants. Paradoxically, OCs also may enhance the effects of anticoagulants. It is probably best to avoid concomitant use of these drugs. OCs also can affect the blood levels of theophylline. When these drugs are used together, the clearance of theophylline is decreased by up to 30 to 40 per cent, due to decreased oxidation via cytochrome P-450 and P-448 systems. This effect is greater in smokers because of the induction of theophylline metabolism. Smoking itself can lead to an increased risk of cardiovascular effects due to OCs. Alcohol too, is affected by OC use. Ethanol is eliminated at a slower rate in OC users because up to 25 per cent of ethanol undergoes metabolism via hepatic microsomal enzymes. It is recommended that women using OCs should not increase their consumption of alcohol.

In conclusion, OCs are among the most commonly used drugs in the world, with approximately 60 to 70 million women using them. Although they are extremely safe compounds, OCs have potential interactions with many drugs, which could possibly lead to contraceptive failure. When one considers the possibility of multiple drug regimens, the perplexing pharmacologic nature of OCs and their failure rate of about 1 per cent, the situation only becomes more complex.

Health professionals clearly have a role to play in providing accurate information to the patient, discussing the potential ramifications with her and listening to her concerns. Drug and disease histories of the patient should be gathered and blood levels of the interacting drugs may have to be monitored. With the uncertainty of many of these drug interactions, individualized patient therapy is very important.

9.4. Drug-Drug Interactions

The concurrent administration of oral contraceptives with other drugs may result in an altered response to either agent. Reduced effectiveness of the oral contraceptive, should it occur, is more likely with the low dose formulations. It is important to ascertain all drugs that a patient is taking, both prescription and non-prescription, before oral contraceptives are prescribed.

During concomitant use of BREVICON and substances that may lead to decreased ethinyl estradiol serum concentrations, it is recommended that a nonhormonal back-up method of birth control (such as

condoms and spermicide) be used in addition to the regular intake of BREVICON. In the case of prolonged use of such substances COCs should not be considered the primary contraceptive.

In addition, the following drugs may also interact with BREVICON: ritonavir, indinavir, flunarizine, topiramate, lamotrigine, rifabutin, fluconazole, atorvastatin, dexamethasone, and modafinil.

Concomitant use with the drug combination regimen ombitasvir, paritaprevir, ritonavir and dasabuvir, with or without ribavirin may increase the risk of ALT elevations (see 2 Contraindications and 7 Warnings and Precautions: Hepatic/Biliary/Pancreatic). Therefore, COC users must switch to an alternative method of contraception (e.g., progestagen-only contraception or non-hormonal methods) prior to starting therapy with anti-viral HCV combination drug regimen ombitasvir, paritaprevir, ritonavir and dasabuvir. COCs can be restarted 2 weeks following completion of treatment with an anti-viral HCV medicinal product.

The drugs listed in table 2 and 3 are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table 2 – Drugs that May Decrease the Efficacy of Oral Contraceptives

Class of Compound	Drug	Proposed Mechanism	Suggested Management
Antacids		Decreased intestinal absorption of progestins.	Dose two hours apart.
Antibiotics	Ampicillin Penicillin	Intestinal hurry.	For short course, use additional method or use another drug. For long course, use another method.
	Cotrimoxazole	Enterohepatic circulation disturbance, intestinal hurry.	For short course, use additional method or use another drug. For long course, use another method
	Rifabutin Rifampin	Increased metabolic of progestins. Suspected acceleration of estrogen metabolism.	Use another method.
	Chloramphenicol Metronidazole Neomycin Nitrofurantoin Sulfonamides Tetracyclines	Induction of hepatic microsomal enzymes. Also disturbance of enterohepatic circulation, except for tetracyclines.	For short course, use additional method or use another drug. For long course, use another method.

Class of Compound	Drug	Proposed Mechanism	Suggested Management
	Troleandomycin	May retard metabolism of OCs, increasing the risk of cholestatic jaundice.	
Anticonvulsants	Carbamazepine Ethosuximide Felbamate Lamotrigine Oxcarbazepine Phenobarbital Phenytoin Primidone Topiramate	Induction of hepatic microsomal enzymes. Rapid metabolism of estrogen and increased binding of progestin and ethinyl estradiol to SHBG.	Use higher dose OCs (50 ug ethinyl estradiol), another drug, or another method.
Antifungals	Griseofulvin	Stimulation of hepatic metabolism of contraceptive steroids may occur.	Use another method.
Cholesterol Lowering Agents	Clofibrate	Reduces elevated serum triglycerides and cholesterol; this reduces OC efficacy.	Use another method.
HCV Protease Inhibitors	Boceprevir Telaprevir	Uncertain, but may be due to an effect on GI transporters, leading to a decrease in the AUC of ethinyl estradiol.	Exposure to ethinyl estradiol was decreased when co-administered with telaprevir or boceprevir. Additional methods of non-hormonal contraception should be used when hormonal contraceptives are co-administered with telaprevir or boceprevir.
HIV Protease Inhibitors	Ritonavir	Induction of hepatic microsomal enzymes.	Use another drug or another method.
Non-nucleoside reverse transcriptase inhibitors	Nevirapine	Induction of hepatic microsomal enzymes.	Use another drug or another method.
Sedatives and Hypnotics	Benzodiazepines Barbiturates Chloral Hydrate Glutethimide Meprobamate	Induction of hepatic microsomal enzymes.	For short course, use additional method or another drug. For long course, use another method or higher dose OCs.

Class of Compound	Drug	Proposed Mechanism	Suggested Management
Other Drugs	Antihistamines Analgesics Antimigraine preparations Phenylbutazone preparations Vitamin E	Reduced OC efficacy has been reported. Remains to be confirmed.	
Other Drugs	Bosentan	Induction of hepatic microsomal enzymes.	Consider switching to a non-hormonal contraceptive method or adding a barrier method to oral contraceptive therapy

Table 3 – Modification of Other Drug Action by Oral Contraceptives

Class of Compound	Drug	Modification of Other Drug Action	Suggested Management
Alcohol		Possible increased levels of ethanol or acetaldehyde.	Use with caution.
Alpha-II Adrenoreceptor Agents	Clonidine	Sedation effect increased.	Use with caution.
Anticoagulants	All	OCs increase clotting factors, decrease efficacy. However, OCs may potentiate action in some patients.	Use another method.
Anticonvulsants	All	Estrogens may increase risk of seizures.	Use another method.
	Lamotrigine	Decreased lamotrigine levels, may lead to breakthrough seizures.	Use another method.
Antidiabetic Drugs	Oral Hypoglycemics and Insulin	OCs may impair glucose tolerance and increase blood glucose.	Use low-dose estrogen and progestin OC or another method. Monitor blood glucose.
Antihypertensive Agents	Guanethidine and Methyldopa	Estrogen component causes sodium retention, progestin has no effect.	Use low estrogen OC or use another method.
	Beta Blockers	Increased drug effect (decreased metabolism).	Adjust dose of drug if necessary. Monitor

Class of Compound	Drug	Modification of Other Drug Action	Suggested Management
			cardiovascular status.
Antipyretics	Acetaminophen	Increased metabolism and renal clearance.	Dose of drug may have to be increased.
	Antipyrine	Impaired metabolism.	Decrease dose of drug.
	ASA	Effects of ASA may be decreased by the short-term use of OCs.	Patients on chronic ASA therapy may require an increase in ASA dosage.
Anti-viral hepatitis C virus	Ombitasvir Paritaprevir Ritonavir Dasabuvir	May increase the risk of ALT elevations	Concomitant use is contraindicated (see 2 Contraindications).
Aminocaproic Acid		Theoretically, a hypercoagulable state may occur because OCs augment clotting factors.	Avoid concomitant use.
Betamimetic Agents	Isoproterenol	Estrogen causes decreased response to these drugs.	Adjust dose of drug as necessary. Discontinuing OCs can result in excessive drug activity.
Caffeine		The actions of caffeine may be enhanced as OCs may impair the hepatic metabolism of caffeine.	Use with caution.
Cholesterol Lowering Agents	Clofibrate	Their action may be antagonized by OCs. OCs may also increase metabolism of clofibrate.	May need to increase dose of clofibrate.
Corticosteroids	Prednisone	Markedly increased serum levels.	Possible need for decrease in dose.
Cyclosporine		May lead to an increase in cyclosporine levels and hepatotoxicity.	Monitor hepatic function. The cyclosporine dose may have to be decreased.
Folic Acid		OCs have been reported to impair folate metabolism.	May need to increase dietary intake; or supplement.
Meperidine		Possible increased analgesia and CNS depression due to decreased metabolism of meperidine.	Use combination with caution.

Class of Compound	Drug	Modification of Other Drug Action	Suggested Management
Phenothiazine Tranquilizers	All Phenothiazines, Reserpine, and similar drugs	Estrogen potentiates the hyperprolactinemia effect of these drugs.	Use other drugs or lower dose OCs. If galactorrhea or hyperprolactinemia occurs, use other method.
Sedatives and Hypnotics	Chlordiazepoxide Lorazepam Oxazepam Diazepam	Increased effect (increased metabolism).	Use with caution.
Theophylline	All	Decreased oxidation, leading to possible toxicity.	Use with caution. Monitor theophylline levels.
Tricyclic Antidepressants	Clomipramine (possibly others)	Increased side effects: i.e., depression.	Use with caution.
Vitamin B_{12}		OCs have been reported to reduce serum levels of Vitamin B_{12}.	May need to increase dietary intake; or supplement.

9.5. Drug-Food Interactions

Interactions with food have not been established.

9.6. Drug-Herb Interactions

Herbal products containing St. John's wort (*hypericum perforatum*) may induce hepatic enzymes (cytochrome P450) and p-glycoprotein transporter and may reduce the effectiveness of contraceptive steroids. This may also result in breakthrough bleeding.

9.7. Drug-Laboratory Test Interactions

Results of laboratory tests should be interpreted in the light of the fact that the patient is on OCs. The laboratory tests listed below are modified.

- **Liver function tests**
  Aspartate serum transaminase (AST) - variously reported elevations. Alkaline phosphatase and gamma glutamine transaminase (GGT) - slightly elevated.
- **Coagulation tests**
  Minimal elevation of test values reported for such parameters as Factors VII, VIII, IX and X. Increased platelet aggregation, decreased antithrombin III.
- **Thyroid function tests**
  Protein binding of thyroxine is increased as indicated by increased total serum thyroxine concentrations and decreased T_3 resin uptake.

- **Lipoproteins**
  Small changes of unproven clinical significance may occur in lipoprotein cholesterol fractions.
- **Gonadotropins**
  LH and FSH levels are suppressed by the use of oral contraceptives. Wait two weeks after discontinuing the use of oral contraceptives before measurements are made.
- **Glucose Tolerance**
  Oral glucose tolerance remained unchanged or was slightly decreased.
- **Tissue Specimens**
  Pathologists should be advised of oral contraceptive therapy when specimens obtained from surgical procedures and PAP smears are submitted for examination.

10. Clinical Pharmacology

10.1. Mechanism of Action

Estrogen-progestogen combinations act primarily through the mechanism of gonadotropin suppression due to the estrogenic and progestational activity of their components, in a manner that inhibits ovulation, which leads to contraception. Some studies have demonstrated changes in the endometrium and cervical mucus with the use of hormonal contraceptives. However, further research is required to determine, quantitatively, whether or not the contribution of changes in endometrium and cervical mucus, observed with combination oral contraceptives, have a role in the prevention of pregnancy.

10.3. Pharmacokinetics

Following oral administration, the absolute bioavailability of norethindrone is about 65%. The time to peak plasma concentration ranges from 0.5 to 4 hours, being more delayed as the dose increases. There is extensive first-pass metabolism. In the plasma, about 80% is bound to sex hormone binding globulin and albumin. The elimination half-life is about 5-14 hours. Norethindrone is partially eliminated, mainly as metabolites, in the feces via biliary excretion.

After oral administration, the absolute bioavailability of ethinyl estradiol is about 40%. Peak plasma concentration is reached in 1 to 2 hours. Protein binding, primarily to albumin, is about 98%. There is extensive first-pass metabolism, and extensive enterohepatic circulation. The elimination half-life is 6 to 20 hours.

Special Populations and Conditions:

Ethnic origin
The effect of ethnic origin on the disposition of BREVICON has not been evaluated.

Renal Insufficiency
The effect of renal disease on the disposition of BREVICON has not been evaluated.

Hepatic Insufficiency
The effect of hepatic disease on the disposition of BREVICON has not been evaluated. However, ethinyl estradiol and norethindrone may be poorly metabolized in patients with impaired liver function.

11. Storage, Stability, and Disposal

Store BREVICON between 15°C and 25°C.

Keep BREVICON and all medication out of reach of children.

Any unused medicinal product should be disposed of in accordance with local requirements.

Part 2: Scientific Information

13. Pharmaceutical Information

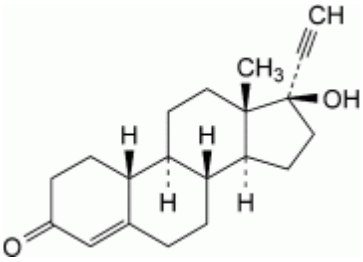
Drug Substance

Non-proprietary name of the drug substance(s): Norethindrone

Chemical name: 19-Norpregn-4-en-20-yn-3-one, 17-hydroxy-, (17 α)-.17-hydroxy-19-nor-17α-pregn-4-en-20-yn-3-one17α-ethinyl-17β-hydroxyestra-4-en-3-one

Molecular formula and molecular mass: $C_{20}H_{26}O_2$, 298; 43 g/mol

Structural formula:



Physicochemical properties: Norethindrone is a white or creamy-white, crystalline powder. Norethindrone is soluble in chloroform and dioxane, sparingly soluble in alcohol slightly soluble in ether and practically insoluble in water. The melting range for norethindrone was determined by capillary melting point technique to be 202-208 °C.

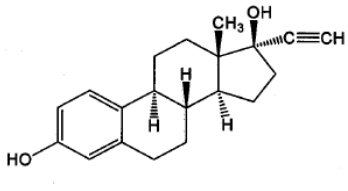
Pharmaceutical standard: Ph.Eur.

Non-proprietary name of the drug substance(s): Ethinyl Estradiol

Chemical name: 19-Nor-17α-pregna-1,3,5(10)-trien-20-yne-3,17 diol

Molecular formula and molecular mass: $C_{20}H_{24}O_2$ 296; 40 g/mol

Structural formula:



Physicochemical properties: Ethinyl Estradiol is a white to creamy white, odorless, crystalline powder with a melting range between 180°C and 186°C. Ethinyl Estradiol is insoluble in water and soluble in alcohol, chloroform, ether, vegetable oils, and solutions of fixed alkali hydroxides.

Pharmaceutical standard: Ph.Eur./USP

14. Clinical Trials

The authorized indication was based on safety and efficacy clinical trials which were conducted with BREVICON.

15. Microbiology

No microbiological information is required for this drug product.

16. Non-Clinical Toxicology

The toxicity of norethisterone is very low. Reports of teratogenic effects in animals are uncommon. No carcinogenic effects have been found even in long-term studies.

Long-term continuous administration of estrogens in some animals increases the frequency of carcinoma of the breast, cervix, vagina and liver.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr] BREVICON ® 0.5/35 and [Pr] BREVICON ® 1/35

ethinyl estradiol and norethindrone tablets

This patient medication information is written for the person who will be taking **BREVICON**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This patient medication information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **BREVICON**, talk to a healthcare professional.

Serious warnings and precautions box

- Cigarette smoking increases the risk of serious adverse effects on the heart and blood vessels. This risk increases with age and becomes significant in oral contraception (OC) users over 35 years of age. You should not use birth control pills while smoking.

- Oral contraceptives **do not protect** against sexually transmitted infections (STIs) including HIV/AIDS. For protection against STIs, it is advisable to use latex condoms **together with** oral contraceptives.

What BREVICON is used for:

BREVICON is used for the prevention of pregnancy.

How BREVICON works:

BREVICON is a birth control pill (oral contraceptive) that contains two female sex hormones (ethinyl estradiol and norethindrone).
Combination hormonal contraceptives, like BREVICON work in two ways:

- To stop the monthly release of an egg by the ovaries.
- To change the mucus produced by your cervix. This slows the movement of the sperm through the mucus and through the uterus.

BREVICON has been shown to be highly effective in preventing pregnancy when taken as directed by your healthcare professional. The chance of becoming pregnant increases with incorrect use.

Effectiveness of Birth Control Pills
Combination birth control pills (like BREVICON) are more than 99 percent effective in preventing pregnancy when:

- The pill is **TAKEN AS DIRECTED**, and
- The amount of estrogen is 20 micrograms or more.

A 99 percent effectiveness rate means that if 100 women used birth control pills for one year, one woman in the group would get pregnant.

Birth control pills (like BREVICON) may become less effective when:

- You miss taking tablets.
- You have vomiting or diarrhea.
- You take other medications that may interact with BREVICON.

Other Ways to Prevent Pregnancy

Other methods of birth control are available. They are usually less effective than birth control pills. If used properly, the other methods of birth control are effective enough for many women.

The following table lists pregnancy rates for different types of birth control, including no birth control. A pregnancy rate is the number of women out of 100 who would become pregnant in one year.

Reported Pregnancies per 100 Women per Year

Combination pill	less than 1 to 3
Intrauterine device (IUD)	less than 1 to 6
Condom with spermicidal foam or gel	1 to 6
Mini-pill (progesterone-only pill)	3 to 6
Condom	2 to 12
Diaphragm with spermicidal foam or gel	3 to 18
Spermicide	3 to 21
Sponge with spermicide	3 to 28
Cervical cap with spermicide	5 to 18
Periodic abstinence (rhythm), all types	2 to 20
No birth control	60 to 85

There are differences in these pregnancy rates. This is because not all people use birth control as carefully or as regularly as they should. This does not apply to IUDs since they are implanted in the uterus. If you are careful and use your birth control regularly, pregnancy rates should be lower. Regular users may achieve pregnancy rates in the lower ranges.

The effective use of birth control methods other than birth control pills and IUDs requires more effort than taking a single pill every day. It is an effort that many couples undertake successfully.

The ingredients in BREVICON are:

Medicinal ingredients: ethinyl estradiol and norethindrone.

Non-medicinal ingredients:

BREVICON 0.5/35 active tablets (pale blue): corn starch, FD&C Blue No. 2, lactose monohydrate, magnesium stearate, povidone.

BREVICON 1/35 active tablets (white): Corn starch, lactose monohydrate, magnesium stearate, povidone.

Inactive tablets (orange): FD&C Yellow No. 6 Lake, lactose CDL21, lactose monohydrate, magnesium stearate, microcrystalline cellulose.

BREVICON comes in the following dosage form(s):

BREVICON is available in 21-day or 28-day packs.

The BREVICON 0.5/35 21-day pack contains 21 pale blue active tablets (containing the 2 hormones norethindrone 0.5 mg and ethinyl estradiol 0.035 mg).

The BREVICON 0.5/35 28-day pack contains 21 pale blue active tablets (containing the 2 hormones norethindrone 0.5 mg and ethinyl estradiol 0.035 mg) and 7 orange inactive tablets (no hormones).

The BREVICON 1/35 21-day pack contains 21 white active tablets (containing the 2 hormones norethindrone 1 mg and ethinyl estradiol 0.035 mg).

The BREVICON 1/35 28-day pack contains 21 white active tablets (containing the 2 hormones norethindrone 1 mg and ethinyl estradiol 0.035 mg) and 7 orange inactive tablets (no hormones).

Do not use BREVICON if:

- You have or have had a blood clot in the legs (deep vein thrombosis), lung (pulmonary embolism), eyes or somewhere else in your body.
- You have or have had inflammation of a vein. This is called thrombophlebitis.
- You have or have had a stroke or a condition that may be a first sign of stroke (for example, mini-stroke).
- You have disease of the heart valves with complications.
- You have or have had an irregular heartbeat.
- You have or have had a heart disease, heart attack or chest pain.
- You have or have had jaundice, or liver problems, including tumors/cancer.
- You have or have had breast cancer, cancer of the endometrium (lining of the uterus), cancer of a sex organ, or a family history of it.
- You have or have had a tumour associated with use of estrogen containing products.
- You have or have had unusual bleeding from your vagina.
- You have or have had loss of vision due to a blood vessel disease of the eye.
- You are pregnant or think you may be pregnant.
- You have or have had migraines with visual and/or sensory disturbances. You may be at increased risk of having a stroke.

- You have diabetes or have high blood sugar levels.
- You have severe or uncontrolled high blood pressure.
- You have or have had an inflamed pancreas.
- You are allergic reaction to norethindrone, ethinyl estradiol or to any other ingredients in BREVICON or its container.
- You have or have had a condition that increases your risk for developing blood clots.
- You have a blood clotting problem such as:
    - Factor V Leiden mutation,
    - Activated protein C (APC) resistance,
    - Protein C deficiency,
    - Protein S deficiency,
    - Hyperhomocysteinemia,
    - Prothrombin mutation G20210A,
    - Antiphospholipid-antibodies.
- You have very high blood cholesterol or triglyceride levels.
- You are a smoker and over age 35.
- You had an injury or trauma, or are scheduled for major surgery.
- You have severe obesity (body mass index of 30 or more).
- You had prolonged bed rest, or immobility (for example long air travel).
- You have enlarged and twisted veins (varicose).
- You need a leg cast.
- You have not yet started to menstruate.
- You are in menopause.
- You are using medicines to treat Hepatitis C Virus (HCV) which contain combination of ombitasvir, paritaprevir, ritonavir and dasabuvir with or without ribavirin. Using these drugs at the same time as BREVICON can cause problems with your liver, such as an increase in the ALT liver enzyme. You must finish your hepatitis C treatment first before starting BREVICON. Your healthcare professional will tell you when to start, stop or restart BREVICON if you need to take these hepatitis C drugs.

The birth control pill is not suitable for every woman. In a small number of women, serious side effects may occur. Your healthcare professional can advise you if you have any conditions that would pose a risk to you. The use of the birth control pill always should be supervised by your healthcare professional.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take BREVICON. Talk about any health conditions or problems you may have, including if you:

- Are pregnant or breastfeeding.
- Have a history of jaundice or other liver problems.
- Have cholestasis. This is a condition where the bile flow from the liver is decreased.
- Have high blood pressure.
- Have migraines and headaches.
- Have diabetes or family history of diabetes.
- Wear contact lenses.
- Have or have had a family history of breast disease (e.g. breast lumps) or a family history of breast cancer.

- Have or have had fibroid tumours on the uterus.
- Have porphyria. This is a disease of blood pigment that is passed down in families (inherited).
- Have or have had Sydenham chorea (a condition that causes random, involuntary body movements).
- Have or have had herpes gestationis (a skin condition that may happen during pregnancy and shortly after childbirth).
- Have otosclerosis (a condition that causes loss of hearing).
- Have or have had a history of emotional disorders, especially depression.
- Have or have had metabolic or endocrine diseases and abnormal metabolism of calcium and phosphorus.
- Have or have had rheumatoid arthritis or synovitis.
- Have or have had hereditary or history of angioedema (episodes of swelling in body parts such as hands, feet, face, or airway passage).
- Have an abnormal level of fat in the blood stream (high cholesterol or triglycerides).
- Smoke cigarettes.
- Have or have had heart or kidney disease.
- Have or have had epilepsy/seizures.
- Have or have had gallbladder or pancreatic disease.
- Have or have had a family history of blood clots, heart attacks or strokes.
- Have or have had persistent irregular vaginal bleeding.
- Are overweight.
- Have or have had systemic lupus erythematosus (a condition where your body's immune system attacks your tissues and organs).
- Have or have had inflammatory bowel disease such as Crohn's disease or ulcerative colitis.
- Have or have had hemolytic uremic syndrome (a condition where blood vessels in your kidneys become damaged).
- Have sickle cell disease. This is a disease that affects hemoglobin, a molecule in red blood cells that delivers oxygen throughout the body.
- Have problems with the valves in your heart.
- Have an irregular heartbeat.
- Have hepatitis C.
- Have an allergy or intolerance to dairy products.

Other warnings you should know about:

Surgery
Be sure to tell your healthcare professional if you are scheduled for surgery or other medical treatment. You may need to stop using BREVICON four weeks before surgery. You may need to wait until after your first period following surgery before restarting BREVICON.

Check-ups and tests
BREVICON should be used only under the supervision of a healthcare professional, with regular check-ups to identify side effects related to its use. Your healthcare
professional will conduct a physical exam. He or she will examine your breasts, abdomen, liver, arms and legs. They will conduct a pelvic exam, which includes a PAP smear. Your healthcare professional will also ask you some questions about your personal health history and that of your close relatives. He or she will also measure your blood pressure and do blood tests.

While you are taking BREVICON, you will need to have regular check-ups with your healthcare professional. Visit your healthcare professional about three months after starting BREVICON. Afterward, visit your healthcare professional about once a year. At these visits, your healthcare professional will conduct physical and internal exams. He or she will also measure your blood pressure and do blood tests. Use BREVICON only on the advice of your healthcare professional and carefully follow all directions given to you. You must use the birth control pill exactly as directed. If not you may become pregnant.

If you are scheduled for any laboratory tests, be sure to tell your healthcare professional that you are taking BREVICON. This is because birth control pills can affect some blood tests.

Vaginal Bleeding
Abnormal bleeding (breakthrough bleeding or spotting) may occur while you are taking birth control pills like BREVICON. This blood is coming from the vagina in between periods. This is most likely to happen in the first 3 months of starting a birth control pill. If this bleeding does not stop or begins again, you should tell your healthcare professional.

Missing periods
You may miss periods when taking hormonal birth control, even if you are not pregnant. However, if you are having regular periods and then do not have one, it is possible that you may be pregnant. If you were not taking BREVICON as directed by your healthcare professional, you should have a pregnancy test. This will rule out if the missed period is because you are pregnant.

Women with history of missing periods (amenorrhea) or have irregular or infrequent periods (oligomenorrhea) may continue to miss periods even after stopping the use of birth control pills like BREVICON.

Blood Clots in legs, lungs, heart, eyes or brain
Women who use birth control pills, like BREVICON, have a higher risk of developing blood clots. Blood clots are the most common serious side effect of birth control pills. Clots can occur in many areas of the body.

- In the brain, a clot can result in a stroke.
- In a blood vessel of the heart, a clot can result in a heart attack.
- In the legs and pelvis, a clot can break off and travel to the lung resulting in a condition called pulmonary embolus.
- In a blood vessel leading to an arm or leg, a clot can result in damage to or loss of a limb.

Any of these conditions can cause death or disability. Clots can also occur in the blood vessels of the eye, resulting in blindness or impaired vision.

Women who use birth control pills have a higher incidence of blood clots. While the risk of blood clots is greater with age, the increased risk from the pill appears to be present at all ages.

The risk of developing a blood clot seems to increase with higher estrogen doses. **It is important, therefore, to use the lowest dose of estrogen as possible.**

While you are taking BREVICON, if you have any of the below symptoms, contact your healthcare professional right away. These are signs of blood clots.

- Sharp pain in your chest.
- Coughing up blood.
- Sudden shortness of breath.
- Pain and / or swelling in your calf.
- Crushing chest pain or chest heaviness.
- Sudden severe or worsening headache.
- Vomiting.
- Dizziness.
- Fainting.
- Changes in vision.
- Changes in speech.
- Weakness or numbness in an arm or leg.
- Sudden pain, swelling and slight blue discoloration of an arm or leg.

Cancer
Using birth control pills may increases the risk of certain cancers including cancer of the breast, cervix and liver.

Breast Cancer
The risk of breast cancer in women increases as you get older. It also increases if there is family history of breast cancer, meaning if your mother or sister have or had breast cancer.
Other factors that increase your risk for breast cancer are being obese, never having children, or having your first full-term pregnancy at a late age.

If you have breast cancer now, or had it in the past, do not use birth control pills. The hormones in these pills can affect some cancers.

Some women who use birth control pills may have a higher risk of developing breast cancer before menopause. These women may have used birth control pills for a long time (more than eight years) or may have started using birth control pills at an early age.

In a few women, using of birth control pills can speed up the growth of a breast cancer that has not yet been found. The risks for breast cancer related to using birth control pills seem to be small. You should have a healthcare professional check your breasts at least once per year, especially if:

- A history of breast cancer in the family.
- Breast nodules or thickenings.
- Discharge from the nipple.

While you are taking BREVICON, check your breasts often. See your healthcare professional if you notice any changes such as:

- Dimpling or sinking of the skin,
- Changes in the nipple, or
- Any lumps you can see or feel.

Talk to your healthcare professional for advice and instructions on how to self-examine your breasts. If you detect any new masses on your breasts while taking BREVICON you should talk to your healthcare professional.

Cervical cancer
Women who use birth control pills may have a higher chance of getting cervical cancer. However, this may be due to other reasons including infection with the Human Papilloma Virus (HPV). HPV is an important risk factor for cervical cancer. However, it is possible that oral birth control pills may also cause such cancers.

Liver cancer
Liver cancer (hepatocellular carcinoma) and liver tumours may be linked to oral birth control pills. The risk for liver cancer increases the longer these pills are used. However, liver tumours are extremely rare. If you feel severe abdominal pain or find a lump in your abdomen, contact your healthcare professional right away.

Pregnancy
Birth control pills should not be taken by pregnant women. This is because there may be risks of damaging the developing child. Tell your healthcare professional if you have symptoms of pregnancy such as morning sickness or unusual breast tenderness. Stop taking BREVICON if you get pregnant. You should check with your healthcare professional about risks to your unborn child from any medicines taken during pregnancy.

If you want to get pregnant talk to your healthcare professional before stopping BREVICON.

Pregnancy after stopping BREVICON
You will have a period when you stop taking birth control pills like BREVICON. You should delay pregnancy until another period occurs within four to six weeks. This will help to better date the pregnancy. Contact your healthcare professional for advice on other methods of birth control during this time.

Use after pregnancy, miscarriage or an abortion
Your healthcare professional will tell you when to start using BREVICON after childbirth, miscarriage or an abortion.

Breastfeeding
If you are breast-feeding, talk to your healthcare professional before starting BREVICON. The hormones in birth control pills like BREVICON are known to appear in breast milk. These hormones may reduce the flow of breast milk. The long-term effects on the developing child are not known. However, cases of breast enlargement have been reported in breast-fed infants. You should use another method of birth

control and only consider starting BREVICON once you have stopped breastfeeding your child.

Gallbladder disease
Women who use birth control pills, like BREVICON, have a higher chance of developing gallbladder disease within the first year of use. This risk may double after four or five years of use.

Increase in epileptic seizures
If you are having seizures, stop taking BREVICON and talk to your healthcare professional.

There are also conditions that your healthcare professional will want to watch closely or that might cause your healthcare professional to recommend a method of birth control other than birth controls pills.

If you see a different healthcare professional, inform them that you are taking BREVICON.

Skin conditions

Chloasma may develop while you are using BREVICON. This appears as yellowish-brown patches on the skin, particularly of the face. It is more likely to happen if you have previously had chloasma gravidarum. This is when these patches appear on the skin of the face during pregnancy. This is commonly known as "the mask of pregnancy."

If you have or had chloasma, avoid too much exposure to the sun while using BREVICON. Sunlight contains invisible rays (ultraviolet light) that can burn the skin.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with BREVICON:

- Medicines used to treat epilepsy (anticonvulsants) such as carbamazepine, ethosuximide, felbamate, oxcarbazepine, phenobarbital, phenytoin, primidone, topiramate, lamotrigine, barbiturates).
- Antibiotics such as ampicillin, cotrimoxazole, penicillin, rifampin, chloramphenicol, metronidazole, neomycin, nitrofurantoin, sulfonamides, tetracyclines, troleandomycin, rifabutin.
- Medicines used to treat fungal infections (antifungals) such as griseofulvin, fluconazole.
- Medicines used to lower cholesterol such as clofibrate, atorvastatin.
- Medicines used to treat anxiety and sleeping disorders (sedatives and hypnotics such as benzodiazepines, barbiturates, chloral hydrate, glutethimide, meprobamate, chlordiazepoxide, lorazepam, oxazepam, diazepam.
- Medicines used to treat heartburn, indigestion or upset stomach (antacids).
- Medicines used to treat high blood pressure and attention deficit hyperactivity disorder (ADHD). (Alpha-II Adrenoreceptor Agents) such as clonidine.
- Medicines used to treat diabetes such as oral hypoglycemics and insulin.
- Medicines used to lower blood pressure (antihypertensive Agents) such as guanethidine, methyldopa and beta blockers.
- Medicines used to treat fevers (antipyretics) such as acetaminophen, antipyrine, acetylsalicylic acid (ASA).
- Medicines used to inhibit contractions of the uterus (betamimetic agents) such as isoproterenol.

- Medicines used to treat inflammation (corticosteroids) such as prednisone, dexamethasone.
- Medicines used to treat mental and emotional disorders (phenothiazine tranquilizers) including all phenothiazines, reserpine and similar drugs.
- Medicines used to treat human immunodeficiency virus (HIV) infection such as ritonavir, indinavir, nevirapine.
- Medicines used to treat Hepatitis C virus (HCV) infection such asboceprevir, telaprevir, ombitasvir, paritaprevir, ritonavir and dasabuvir, with or without ribavirin.
- Medicines used to relax the muscles in longs and widen airways (bronchodilator) such as theophylline.
- Stimulants such as modafinil.
- Medicines used to treat depression (tricyclic antidepressants) such as clomipramine.
- Medicine used to treat high blood pressure in the lungs called bosentan.
- Phenylbutazone, a medicine used to relieve pain and reduce inflammation.
- Medicines used to treat allergies (antihistamines).
- Medicines used to relieve pain (analgesics).
- Medicines used to treat migraines (antimigraine preparations).
- Medicines used to help prevent blood clots (anticoagulants).
- Aminocaproic acid, a medicine used to manage and treat bleeding disorders.
- Vitamin E, vitamin B12, and vitamin C.
- Cyclosporine, a medicine used to prevent organ rejection in patients who have received an organ transplant.
- Folic acid, a herbal product used for healthy cell growth and function.
- Meperidine, a medicine used to relieve pain.
- St. John's Wort, an herbal product used to treat depression and other conditions.
- Flunarizine, a medicine used to treat migraines.

The effects of caffeine and alcohol may also be increased. This is because birth control pills affect how these are metabolized.

When using BREVICON with products that may affect its effectiveness, it is recommended that you use a non-hormonal back-up method of birth control in addition to BREVICON. In the case of prolonged use of such products, birth control pills, like BREVICON, should not be considered the main contraceptive. Talk to your healthcare professional for guidance if you are taking medicines that interact with BREVICON.

This is not a complete list of possible drug interactions with BREVICON. Talk to your healthcare professional for more information about drug interactions.

How to take BREVICON:

Be sure to read these instructions;

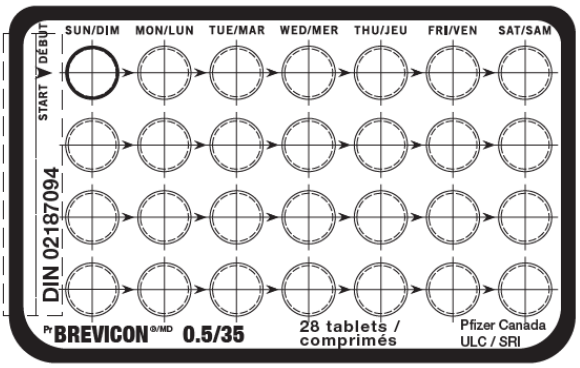
- Before you start taking BREVICON, and
- Any time you are not sure what to do.

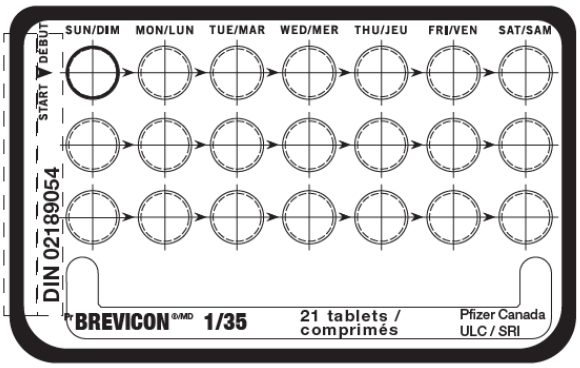
1. **Look at your pill pack** to see if it has 21 or 28 pills:
   - 21-PILL PACK: 21 active pills (with hormones) taken daily for 3 weeks, and then no pills for 1 week.

OR

- 28-PILL PACK: 21 active pills (with hormones) taken daily for 3 weeks, and then 7 inactive "reminder" pills (no hormones) taken daily for 1 week.

Note: Pictures below apply to both BREVICON 0.5/35 and BREVICON 1/35.





2. Use a second method of birth control (e.g. latex condoms and spermicidale) for the first 7 days of the first cycle of pill use. This will provide a back-up in case pills are forgotten while you are getting used to taking them.
3. Decide with your healthcare professional what is the best day and time for you to start taking your pill. Pick a time of day that will be easy to remember. It is important to take it at the same time every day and in the order as directed on pack. Your pills may be either a 21-day or a 28-day type.

   Note:

   - The pack is pre-printed with Sunday as the starting day. If starting on a day other than Sunday, you should use the provided Flexi-start sticker labels provided to correctly mark the starting date.

     Choose the label for the appropriate starting day and apply it over the pre-printed days on top of the card.

When to start the first pack of BREVICON pills:

- **21-day combination:**

With this type of birth control pill, you are on pills for 21 days and off pills for 7 days. You must not be off the pills for more than 7 days in a row.

- **The first day of your period (bleeding) is Day 1 of your cycle.** Your healthcare professional may advise you to start taking the pills on Day 1, on Day 5, or on the first Sunday after your period begins. If your period starts on Sunday, start that same day.

- Take 1 pill at approximately the same time every day for 21 days. **Then take no pills for 7 days.** Start a new pack on the 8th day. You will probably have a period during the 7 days off the pill. (This bleeding may be lighter and shorter than your usual period).

- **28-day combination**

With this type of birth control pill, you take 21 pills that contain hormones and 7 pills that contain no hormones.

- **The first day of your period (bleeding) is Day 1 of your cycle.** Your healthcare professional may advise you to start taking the pills on Day 1, on Day 5, or on the first Sunday after your period begins. If your period starts on Sunday, start that same day.

- Take 1 pill at approximately the same time every day for 28 days. Begin a new pack the next day, **not missing any days.** Your period should occur during the last 7 days of using the pills

What to do during the month

- **Take a pill at approximately the same time every day until the pack is empty.**
  - Try to associate taking your pill with some regular activity such as eating a meal or going to bed.
  - Do not skip pills or days even if you feel sick to your stomach or bleeding between monthly periods. Tell your healthcare professional if this feeling does not go away.
  - Do not skip pills even if you do not have sex very often.
  - There is no need to stop taking birth control pills for a rest period.
  - When you first start taking BREVICON, spotting or light bleeding in between your periods may occur. Talk to your healthcare professional if this does not go away after a few months.
  - When receiving any medical treatment, be sure to tell your healthcare professional that you are using birth control pills.
  - Keep a calendar to track your period.

- **When you finish a pack**
  - **21 Pills: Wait 7 days** to start the next pack. You will have your period during that week.
  - **28 Pills:** Start the next pack **on the next day.** Take 1 pill every day. Do not wait any days between packs.

If your questions are not answered here, talk to your healthcare professional

Usual dose:

Take 1 tablet per day.

Overdose:

Numerous cases of the ingestion, by children, of estrogen progestogen combinations have been reported. Although mild nausea may occur in case of overdosage, there appears to be no other reaction.

If you think you, or a person you are caring for, have taken too much BREVICON, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed dose:

If you miss pills at any time, **you could get pregnant.** The greatest risks for pregnancy are when you start a pack late, or when you miss pills at the beginning or at the very end of the pack.

Missing pills also can cause some spotting or light bleeding, even if you make up the missed pills. You also could feel a little sick to your stomach on the days you take two pills to make up for missed pills.

The following outlines the actions you should take if you miss one or more of your birth control pills. Match the number of pills missed with the appropriate starting time for your type of pill pack.

SUNDAY START	
If you miss 1 pill	▪ Take it as soon as you remember and take the next pill at the usual time. This means that you might take 2 pills in 1 day.
If you miss 2 pills in a row	**First two Weeks:** ▪ Take 2 pills the day you remember and 2 pills the next day. ▪ Then take 1 pill a day until you finish the pack. ▪ Use a back-up method of birth control if you have sex in the 7 days after you miss the pills. **Third Week:** ▪ Keep taking 1 pill a day until Sunday. ▪ On Sunday, safely discard the rest of the pack and start a new pack that day. ▪ Use a back-up method of birth control if you have sex in the 7 days after you miss the pills. ▪ You may not have a period this month.

	IF YOU MISS 2 PERIODS IN A ROW, talk to your healthcare professional.
If you miss 3 or more pills in a row	**Anytime in the Cycle:** ▪ Keep taking 1 pill a day until Sunday. ▪ On Sunday, safely discard the rest of the pack and start a new pack that day. ▪ Use a back-up method of birth control if you have sex in the 7 days after you miss the pills. ▪ You may not have a period this month. **IF YOU MISS 2 PERIODS IN A ROW, talk to your healthcare professional.**

OTHER THAN SUNDAY START	
If you miss 1 pill	▪ Take it as soon as you remember and take the next pill at the usual time. This means that you might take 2 pills in 1 day.
If you miss 2 pills in a row	**First two Weeks:** ▪ Take 2 pills the day you remember and 2 pills the next day. ▪ Then take 1 pill a day until you finish the pack. ▪ Use a back-up method of birth control if you have sex in the 7 days after you miss the pills. **Third Week:** ▪ Safely dispose of the rest of the pill pack and start a new pack that same day. ▪ Use a back-up method of birth control if you have sex in the 7 days after you miss the pills. ▪ You may not have a period this month. **IF YOU MISS 2 PERIODS IN A ROW, talk to your healthcare professional.**
If you miss 3 or more pills in a row	**Anytime in the Cycle:** ▪ Safely dispose of the rest of the pill pack and start a new pack that same day. ▪ Use a back-up method of birth control if you have sex in the 7 days after you miss the pills. ▪ You may not have a period this month.

	IF YOU MISS 2 PERIODS IN A ROW, talk to your healthcare professional.

NOTE: 28-DAY PACK: If you forget any of the seven inactive "reminder" pills (without hormones) in Week 4, just safely dispose of the pills you missed. Then keep taking one pill each day until the pack is empty. You do not need to use a back-up method.

Always be sure you have on hand:

- A back-up method of birth control (such as latex condoms and spermicidale) in case you miss pills, and
- An extra, full pack of pills.

If you forget more than 1 pill 2 months in a row, talk to your healthcare professional. They will suggest ways to make pill-taking easier or about using another method of birth control.

If you experience vomiting or diarrhea, or if you take certain medicines, such as antibiotics, you pills may not work as well. Use a back-up method, such as latex condoms and spermicide, until you can talk to your healthcare professional.

Possible side effects from using BREVICON:

These are not all the possible side effects you may have when taking BREVICON. If you experience any side effects not listed here, tell your healthcare professional.

- Abdominal pain.
- Nausea and vomiting.
- Weight change.
- Change in appetite.
- High or low blood pressure.
- Growth of pre-existing fibroid tumours of the uterus.
- Increased blood sugar levels.
- Hirsutism.
- Changes in libido (increase or decrease).
- Abnormal cervical (Pap) smear.
- Painful period cramps.
- Vaginal infection.
- Difficult or painful urination, blood in the urine.
- Flu-like symptoms.
- Acne.
- Breast tenderness, pain, swelling.
- Anxiety.
- Headache, dizziness, irritability.
- Migraines.
- Skin pigmentation.
- Changes or loss of hearing.
- Cloudy vision, sore eyes.

- Rash.
- Feeling bloated and gassy.

Serious side effects and what to do about them

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Uncommon			
Hypersensitivity (Allergic Reaction): difficulty swallowing or breathing, wheezing; drop in blood pressure; feeling sick to your stomach and throwing up; hives or rash; swelling of the face, lips, tongue or throat			√
Pulmonary embolism (Blood clot in the lung): Sharp pain in the chest, coughing blood, or sudden shortness of breath			√
Deep vein thrombosis (blood clot in the legs) or **Thrombophlebitis** (inflammation of a vein often in the leg): sudden leg swelling or pain; redness, warmth, tenderness and pain in affected area			√
Arterial thromboembolism, Myocardial infarction (blood clot in the artery, heart attack): sudden pain, discomfort, pressure, heaviness, sensation of squeezing or fullness in the shoulder, chest, arm, or below the breastbone; discomfort radiating to the back, jaw, throat, arm, stomach, feeling of being full, having indigestion or choking; sweating, nausea, vomiting or dizziness; extreme weakness, anxiety, or shortness of breath; rapid or irregular heartbeats			√
Stroke: Sudden severe or worsening headache or vomiting, dizziness or fainting, disturbance of vision or speech, or weakness or			√

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
numbness in an arm or leg, or numbness in the face			
Blood clot in the eye: Sudden partial or complete loss of vision, double vision			√
Tumour in the liver: Severe pain or lump in the abdomen			√
Depression: persistent sad mood accompanied by difficulty in sleeping, weakness, lack of energy, fatigue			√
Jaundice: Yellowing of the skin or eyeballs, accompanied frequently by fever, fatigue, loss of appetite, dark-coloured urine, or light-coloured bowel movements			√
Neuro-ocular lesions (damaged eye nerves): blurred vision, sudden complete or partial loss of vision in eye, eye pain			√
Unexpected (abnormal) vaginal bleeding		√	
Unusual swelling of the arms and legs		√	
Breast lumps		√	
Crohn's Disease or Ulcerative Colitis: Cramps and bloating, diarrhea		√	
Inflammation of the Pancreas: Abdominal pain that lasts and gets worse when you lie down, nausea, vomiting		√	
Lupus: A combination of fever, muscle or joint pain, and general fatigue and feeling unwell and memory changes.		√	
Raynaud's phenomenon: Pain, numbness change in colour, and feeling cold in the hands and feet.		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting side effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store BREVICON between 15°C and 25°C.

Keep out of reach and sight of children.

If you want more information about BREVICON:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada Drug Product Database website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website http://www.pfizer.ca, or by calling 1-800-463-6001.

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