NEW ZEALAND DATA SHEET

1. PRODUCT NAME

BREVINOR 21 Day Tablets

BREVINOR-1 21 Day Tablets

BREVINOR-1 28 Day Tablets

NORIMIN 28 Day Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

BREVINOR 21 Day

Each blue tablet contains norethisterone 0.5 mg and ethinylestradiol 35 µg.

NORIMIN 28 Day

Each blue tablet contains norethisterone 0.5 mg and ethinylestradiol 35 µg.

Each orange tablet contains inert lactose.

BREVINOR-1 21 Day

Each white tablet contains norethisterone 1.0 mg and ethinylestradiol 35 µg.

BREVINOR-1 28 Day

Each white tablet contains norethisterone 1.0 mg and ethinylestradiol 35 µg.

Each orange tablet contains inert lactose.

Excipients with known effects:

- Lactose
- Sunset yellow (Brevinor-1 28 Day and Norimin 28 Day)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

BREVINOR 21 Day

Tablets: 21 blue, round, flat bevel-edged tablets, 3/16" in diameter, engraved 'SEARLE' on one side and 'BX' on the reverse.

NORIMIN 28 Day

Tablets: 21 blue, round, flat bevel-edged tablets, 3/16" in diameter, engraved 'SEARLE' on one side and 'BX' on the other; 7 orange, round flat bevel-edged tablets, 3/16" in diameter, engraved 'SEARLE' on one side, and 'P' on the other.

BREVINOR-1 21 Day

Tablets: 21 white, round, flat bevel-edged tablets, 3/16" diameter, engraved 'SEARLE' on one side and 'BX' on the other.

BREVINOR-1 28 Day

Tablets: 21 white, round, flat bevel-edged tablets, 3/16" in diameter, engraved 'SEARLE' on one side and 'BX' on the other; 7 orange, round flat bevel-edged tablets, 3/16" in diameter, engraved 'SEARLE' on one side, and 'P' on the other.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Contraception.

4.2 Dose and method of administration

Brevinor 21 Day Pack

To achieve maximum contraceptive effectiveness, Brevinor 21 Day must be taken as directed and at daily intervals not exceeding 24 hours. Women should be instructed to take the tablets at the same time every day, preferably at bedtime.

First Cycle

On the first day of the menstrual cycle, i.e. the first day of bleeding, the woman is instructed to take a blue active tablet corresponding to the day of the week from the Brevinor 21 Day pack. Thereafter one blue active tablet is taken daily, following the arrows on the pack until all 21 blue tablets have been taken. The woman should then be instructed to take a seven day break during which withdrawal bleeding will usually occur. The next pack should be commenced after seven tablet free days. The woman should be advised that her first cycle after taking all Brevinor 21 Day tablets is likely to be shorter than usual, i.e. approximately 23 to 24 days. Thereafter, her cycles should return to normal, approximately 28 days. Brevinor 21 Day is effective from the first day if the tablets are taken as described above.

Changing from Another Pill

If a woman is switching to Brevinor 21 Day from another 21 Day oral contraceptive pack, then the woman should wait seven days from when the last active tablet was taken from the old pack and start the new Brevinor 21 Day pack on the eighth day by taking a blue active tablet which corresponds to the day of the week. A non-hormonal contraceptive method (other than the rhythm or temperature

method) should be used during the first Brevinor 21 Day cycle until seven consecutive blue active tablets have been taken.

If a woman is switching to Brevinor 21 Day from a 28 Day oral contraceptive pack, then all tablets in the current 28 day pack should be finished and Brevinor 21 Day started on the next day by taking a blue active tablet which corresponds to the day of the week. Once all 21 blue active tablets have been taken, the woman should have seven tablet free days during which withdrawal bleeding will usually occur. The next pack should be commenced on the eighth day. During the first Brevinor 21 Day cycle a non-hormonal contraceptive method (other than the rhythm or temperature method) should be used until seven consecutive blue active tablets have been taken. During the changeover, a period of shortened duration or no period may occur.

Brevinor-1 21 Day Pack

To achieve maximum contraceptive effectiveness, Brevinor-1 21 Day must be taken as directed and at daily intervals not exceeding 24 hours. Women should be instructed to take the tablets at the same time every day, preferably at bedtime.

First Cycle

On the first day of the menstrual cycle i.e. the first day of bleeding, the woman is instructed to take a white active tablet corresponding to the day of the week from the Brevinor-1 21 Day pack. Thereafter one white active tablet is taken daily, following the arrows on the pack until all 21 white tablets have been taken. The woman should then be instructed to take a seven day break during which withdrawal bleeding will usually occur. The next pack should be commenced after seven tablet free days. The woman should be advised that her first cycle after taking all Brevinor-1 21 Day tablets is likely to be shorter than usual, i.e. approximately 23 to 24 days. Thereafter, her cycles should return to normal, approximately 28 days. Brevinor-1 21 Day is effective from the first day if the tablets are taken as described above.

Changing from Another Pill

If a woman is switching to Brevinor-1 21 Day from another 21 day oral contraceptive pack, then the woman should wait seven days from when the last active tablet was taken from the old pack and start the new Brevinor-1 21 day pack on the eighth day by taking a white active tablet which corresponds to the day of the week. A non-hormonal contraceptive method (other than the rhythm or temperature method), should be used during the first Brevinor-1 21 Day cycle until seven consecutive white active tablets have been taken.

If a woman is switching to Brevinor-1 21 Day from a 28 day oral contraceptive pack, then all tablets in the current 28 day pack should be finished and Brevinor-1 21 Day started on the next day by taking a white active tablet which corresponds to the day of the week. Once all 21 white active tablets have been taken, the woman should have seven tablet free days during which withdrawal bleeding will usually occur. The next pack should be commenced on the eighth day. During the first Brevinor-1 21 Day cycle, a non-hormonal contraceptive method (other than the rhythm or temperature method) should be used until seven consecutive white active tablets have been taken. During the changeover, a period of shortened duration or no period may occur.

If transient spotting or breakthrough bleeding occurs with either Brevinor 21 Day or Brevinor-1 21 Day, the woman is instructed to continue the regimen since such bleeding is usually without significance. If the bleeding is persistent or prolonged, the woman is advised to consult her physician.

Brevinor 21 Day or Brevinor-1 21 Day can be prescribed postpartum for the nonlactating mother or postabortum as soon as the first normal menstrual period following a normal biphasic cycle occurs. If a further pregnancy is contraindicated for medical reasons, medication with Brevinor 21 Day or Brevinor-1 21 Day must be initiated by the 12th (but not before the 7th) day postpartum, or immediately postabortum or by the 5th day postabortum at the latest. When oral contraceptives are administered in the immediate postpartum/ postabortum period, the increased risk of thromboembolic disease must be considered.

Brevinor-1 28 Day Pack

First Cycle

On the first day of the menstrual cycle, i.e. the first day of bleeding, the woman is instructed to take a white active tablet corresponding to the day of the week from the green area of the Brevinor-1 28 Day pack. Thereafter one white active tablet is taken daily, following the arrows on the pack, until all 21 white tablets have been taken. The woman should then be instructed to take one orange inactive tablet daily for the next seven days. Withdrawal bleeding should usually occur within two to four days after the last white tablet has been taken. The woman should be advised that her first cycle after taking all Brevinor-1 28 Day tablets is likely to be shorter than usual, i.e. approximately 23 to 24 days. Thereafter, her cycles should return to normal, approximately 28 days.

The next and all subsequent courses of Brevinor-1 28 Day will begin on the day after the last package was completed, even if withdrawal bleeding is still in progress. Each course of Brevinor-1 28 Day is begun on the same day of the week as the first course, always beginning with a white active tablet from the green area.

Brevinor-1 28 Day is effective from the first day if taken as described above.

Changing from Another Pill

If a woman is switching to Brevinor-1 28 Day from another 28 day oral contraceptive pack, then all tablets in the current 28 day pack should be finished and Brevinor-1 28 Day started on the next day by taking a white active tablet which corresponds to the day of the week, from the green area of the pack. During the first Brevinor-1 28 Day cycle, a non-hormonal contraceptive method (other than the rhythm or temperature method), should be used until seven consecutive white active tablets have been taken. During this changeover, a period of shortened duration or no period may occur.

If a woman is switching to Brevinor-1 28 Day from a 21 day oral contraceptive pack, then the woman should wait seven days from when the last active tablet was taken from the old pack and start the new Brevinor-1 28 Day pack on the eighth day by taking a white active tablet which corresponds to the day of the week, from the green area of the pack. A non-hormonal contraceptive method (other than the rhythm or temperature method) should be used during the first Brevinor-1 28 Day cycle, until seven consecutive white active tablets have been taken.

If transient spotting or breakthrough bleeding occurs with Brevinor-1 28 Day, the woman is instructed to continue the regimen since such bleeding is usually without significance. If the bleeding is persistent or prolonged, the woman is advised to consult her physician.

Brevinor-1 28 Day can be prescribed postpartum for the nonlactating mother or postabortum as soon as the first normal menstrual period following a normal biphasic cycle occurs. If a further pregnancy is contraindicated for medical reasons, medication with Brevinor-1 28 Day must be initiated by the 12th (but not before the 7th) day postpartum, or immediately postabortum or by the 5th day postabortum at the latest. When oral contraceptives are administered in the immediate postpartum/postabortum period, the increased risk of thromboembolic disease must be considered.

Norimin 28 Day Pack

To achieve maximum contraceptive effectiveness, Norimin 28 Day must be taken as directed and at daily intervals not exceeding 24 hours. Women should be instructed to take the tablets at the same time every day, preferably at bedtime.

First Cycle

On the first day of the menstrual cycle, i.e. the first day of bleeding, the woman is instructed to take a blue active tablet corresponding to the day of the week from the silver area of the Norimin 28 Day pack. Thereafter one blue active tablet is taken daily, following the arrows on the pack, until all 21 blue tablets have been taken. The woman should then be instructed to take one orange inactive tablet daily for the next seven days. Withdrawal bleeding should usually occur within two to four days after the last blue active tablet has been taken. The woman should be advised that her first cycle after taking all Norimin 28 Day tablets is likely to be shorter than usual, i.e. approximately 23 to 24 days. Thereafter, her cycles should return to normal, approximately 28 days.

The next and all subsequent courses of Norimin 28 Day will begin on the day after the last pack was completed, even if withdrawal bleeding is still in progress. Each course of Norimin 28 Day is begun on the same day of the week as the first course, always beginning with a blue active tablet from the silver area.

Norimin 28 Day is effective from the first day if taken as described above.

Changing from Another Pill

If a woman is switching to Norimin 28 Day from another 28 day oral contraceptive pack, then all tablets in the current 28 day pack should be finished and Norimin 28 Day started on the next day by taking a blue active tablet which corresponds to the day of the week, from the silver area of the pack. During the first Norimin 28 Day cycle, a non-hormonal contraceptive method (other than the rhythm or temperature method), should be used until seven consecutive blue active tablets have been taken. During this changeover, a period of shortened duration or no period may occur.

If a woman is switching to Norimin 28 Day from a 21 day oral contraceptive pack, then the woman should wait seven days from when the last active tablet was taken from the old pack and start the new Norimin 28 Day pack on the eighth day by taking a blue active tablet which corresponds to the day of the week, from the silver area of the pack. A non-hormonal contraceptive method (other than

the rhythm or temperature method) should be used during the first Norimin 28 Day cycle, until seven consecutive blue active tablets have been taken.

If transient spotting or breakthrough bleeding occurs with Norimin 28 Day, the woman is instructed to continue the regimen since such bleeding is usually without significance. If the bleeding is persistent or prolonged, the woman is advised to consult her physician.

Norimin 28 Day can be prescribed postpartum for the nonlactating mother or postabortum as soon as the first normal menstrual period following a normal biphasic cycle occurs. If a further pregnancy is contraindicated for medical reasons, medication with Norimin 28 Day must be initiated by the 12th (but not before the 7th) day postpartum, or immediately postabortum or by the 5th day postabortum at the latest. When oral contraceptives are administered in the immediate postpartum period, the increased risk of thromboembolic disease must be considered.

Brevinor 21 Day, Brevinor-1 (21 Day and 28 Day), Norimin 28 Day Packs

Missed Tablets

If the woman is less than 12 hours late in taking one of her blue or white active tablets, she should take this tablet at once and then take the next one at her usual time. If the woman is more than 12 hours late in taking one of her blue or white active tablets, she should continue to take her tablets daily as usual, ignoring the missed tablet or tablets, but also take extra contraceptive precautions (other than the rhythm or temperature method) for the next seven days. If these seven days extend into the inactive orange tablet section (if using a 28 day pack) or the 7 tablet free days (if using a 21 day pack), she should start a new pack on the next day after having taken the last blue or white active tablet from the green (Brevinor 21 Day, Brevinor-1 (21 or 28 Day)) or silver (Norimin 28 Day) section of the current pack (i.e. skip the orange inactive tablets or the tablet free days). This will mean that the woman may not have a period until the end of two packs.

However, if the woman misses one or more orange inactive tablets, she will be protected against pregnancy provided she begins the active tablets on the appropriate day.

If the woman has not adhered to the prescribed regimen (missed one or more active tablets or started taking them on a day later than recommended), the probability of pregnancy should be considered at the time of the first missed period before Brevinor 21 Day, Brevinor-1 21 or 28 Day, or Norimin 28 Day is resumed. In the case of the continuous intake of active tablets from two packs of Brevinor 21Day, Brevinor-1 21 or 28 Day or Norimin 28 Day (see before), a period should occur at the end of the second pack. If it does not, pregnancy should be ruled out before medication is resumed.

Concurrent Medication

If the woman is taking other drugs that may interact with norethisterone or ethinylestradiol from her 21 day or 28 day pack, then she should continue to take her tablets as usual but also employ a non-hormonal method of contraception (other than the rhythm or temperature method) during the time she is taking the interacting medication and continue for seven days after the medication is stopped. If these seven days extend into the inactive orange tablet section (if using a 28 day pack) or the 7 tablet free days (if using a 21 day pack), the woman should start a new pack on the next day after having taken the last blue or white active tablet from the green (Brevinor 21 Day, Brevinor-1 (21 or

28 Day)) or silver (Norimin 28 Day) section of the current pack (i.e. skip the orange inactive tablets or the tablet free days). This will mean that the woman may not have a period until the end of two packs. If the woman is taking interacting medications on a chronic basis, another method of contraception should be considered.

Vomiting or Diarrhoea

Mild laxatives do not impair the effectiveness of Brevinor 21 Day, Brevinor-1 21 or 28 Day or Norimin 28 Day. If, however, vomiting or diarrhoea occurs during or shortly after the intake of Brevinor 21 Day, Brevinor-1 21 or 28 Day, or Norimin 28 Day contraceptive reliability may be jeopardised. Tablet taking should not be interrupted, to avoid premature withdrawal bleeding. A non-hormonal method of contraception (other than the rhythm or temperature method) should be employed during the period of vomiting or diarrhoea and continued for seven days following the gastrointestinal upset. If these seven days extend into the inactive orange tablet section (if using a 28 day pack) or the 7 tablet free days (if using a 21 day pack), the woman should start a new pack on the next day after having taken the last active tablet from the green (Brevinor 21 Day, Brevinor-1 (21 or 28 Day)) or silver (Norimin 28 Day) section of the current pack (i.e. skip the orange inactive tablets or the tablet free days). This will mean that the woman may not have a period until the end of two packs. If the circumstance reducing the effectiveness of Brevinor 21 Day, Brevinor-1 21 or 28 Day, or Norimin 28 Day is protracted, other methods of contraception should be considered.

Missed Period(s)

See section 4.4.

4.3 Contraindications

As with all combined progestogen/estrogen oral contraceptives, the following conditions should be regarded as contraindications:

- Hypersensitivity to any component of the medicine.
- A history of, or current deep vein thrombosis, thrombophlebitis, or thromboembolic disorders; thrombogenic valvulopathies or thrombogenic rhythm disorders.
- Hereditary or acquired thrombophilias.
- Cerebrovascular or coronary artery disease or history of such disorders.
- Known or suspected carcinoma of the breast.
- Known or suspected carcinoma of genital organs.
- Known or suspected estrogen dependent neoplasia.
- Undiagnosed vaginal bleeding.
- Known or suspected pregnancy.
- Hepatic adenomas or carcinomas or history of such tumours.
- Active liver disease as long as liver function has not returned to normal.

- A history of jaundice, cholestatic jaundice or pruritus of pregnancy.
- Dubin-Johnson or Rotor Syndrome.
- Herpes gestationis, a condition of the pemphigoid group of bulbous skin diseases, not to be confused with Herpes simplex or genitalis.
- A history of otosclerosis with deterioration during pregnancy.
- Sickle-cell anaemia.
- Abnormal lipid metabolism.
- Headaches with focal neurological symptoms (such as aura), including haemiplegic migraine.
- Diabetes with vascular involvement.
- Uncontrolled hypertension.
- Pancreatitis associated with severe hypertriglyceridemia (current or history).
- Use with the Hepatitis C combination drug regimen ombitasvir/paritaprevir/ritonavir and dasabuvir with or without ribavirin (see section 4.4).

4.4 Special warnings and precautions for use

Cigarette Smoking

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

Venous and Arterial Thrombosis and Thromboembolism

Use of combined oral contraceptives is associated with an increased risk of venous and arterial thrombotic and thromboembolic events.

The physician should be alert to the earliest manifestations of thrombotic disorders and medication should be discontinued immediately should any of these occur.

The risk of vascular disease is dose related. For any particular estrogen/progestin combination, the dosage regimen prescribed should be one which contains the least amount of estrogen and progestogen that is compatible with a low failure rate and the needs of the individual patient.

Thromboembolic disorders and other vascular problems including cerebrovascular disorders and myocardial infarction may persist following termination of oral contraceptives.

Venous Thrombosis and Thromboembolism

Use of COCs increases the risk of venous thrombotic and thromboembolic events. The use of any COC carries an increased risk of venous thrombotic and thromboembolic events compared with no use. The excess risk is highest during the first year a woman ever uses a combined oral contraceptive.

Epidemiological studies have shown that the incidence of venous thromboembolism in users of low-estrogen oral contraceptives (<50 mcg ethinylestradiol) ranges from about 20 to 40 cases per 100,000 women-years; this risk estimate varies according to the progestin.

The risk of venous thrombotic and thromboembolic events is further increased in women with conditions predisposing for venous thrombosis and thromboembolism.

Examples of predisposing conditions for venous thrombosis and thromboembolism are:

- obesity
- surgery or trauma with increased risk of thrombosis
- recent delivery or second-trimester abortion
- prolonged immobilisation
- increasing age

If feasible, COCs should be discontinued:

- for four weeks prior to and for two weeks after elective surgery with increased risk of thrombosis, and
- during prolonged immobilisation

Because the immediate postpartum period is associated with an increased risk of thromboembolism, COC use should begin no sooner than the 28th postpartum day following either delivery in a non-lactating woman or second-trimester abortion.

Arterial Thrombosis and Thromboembolism

The use of COCs increases the risk of arterial thrombotic and thromboembolic events. Reported events include myocardial infarction and cerebrovascular events (ischemic and haemorrhagic stroke, transient ischemic attack).

The risk of arterial thrombotic and thromboembolic events is further increased in women with underlying risk factors.

Caution must be exercised when prescribing COCs for women with risk factors for arterial thrombotic and thromboembolic events.

Examples of risk factors for arterial thrombotic and thromboembolic events:

- smoking
- hypertension
- hyperlipidaemias
- obesity

- increasing age

COC users with migraine (particularly migraine with aura) may be at increased risk of stroke.

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, the COC should be discontinued and the cause immediately evaluated.

Blood Pressure

Increases in blood pressure have been reported in women taking COCs.

In women with hypertension or a history of hypertension or hypertension-related diseases (including certain renal diseases), another method of birth control may be preferable. If COCs are used in such cases, close monitoring is recommended; if a significant increase in blood pressure occurs, COCs should be discontinued.

Malignant hypertension has been associated with the use of oral contraceptives.

COC use is contraindicated in women with uncontrolled hypertension (see section 4.3).

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.

However, there continues to be controversy about the extent to which such findings may be due to differences in sexual behaviour and other factors. In cases of undiagnosed abnormal genital bleeding, adequate diagnostic measures are indicated.

Breast Cancer

A meta-analysis from 54 epidemiological studies reported that there is a slightly increased relative risk (1.24) of having breast cancer diagnosed in women who are using COCs compared to never-users. The increased risk gradually disappears during the course of the 10 years after cessation of COC use. These studies do not provide evidence for causation. The observed pattern of increased risk of breast cancer diagnosis may be due to earlier detection of breast cancer in COC users (due to more regular clinical monitoring), the biological effects of COCs, or a combination of both. Because breast cancer is rare in women under 40 years of age, the excess number of breast cancer diagnoses in current and recent COC users is small in relation to the lifetime risk of breast cancer. Breast cancers diagnosed in ever-users tend to be less advanced clinically than the cancers diagnosed in never-users.

Hepatic Neoplasia/Liver Disease/Hepatitis C

In very rare cases, hepatic adenomas, and in extremely rare cases, hepatocellular carcinoma may be associated with COC use. The risk appears to increase with duration of COC use. Rupture of hepatic adenomas may cause death through intra-abdominal haemorrhage.

Women with a history of COC-related cholestasis and women who develop cholestasis during pregnancy are more likely to develop cholestasis with COC use. Such patients who use COCs should be carefully monitored, and COC use should be discontinued if cholestasis recurs.

Hepatocellular injury has been reported with COC use. Early identification of drug-related hepatocellular injury can decrease the severity of hepatotoxicity when the drug is discontinued. If hepatocellular injury is diagnosed, patients should stop their COC, use a non-hormonal form of birth control, and consult their doctor.

Acute or chronic disturbances of liver function may necessitate the discontinuation of COC use until liver function has returned to normal.

Hepatitis C

During clinical trials with the combination drug regimen ombitasvir/paritaprevir/ritonavir and dasabuvir with and without ribavirin, transient, asymptomatic elevations of alanine transaminase (ALT) greater than 5 times the upper limit of normal (ULN) were significantly more frequent in women using ethinylestradiol-containing medications such as combined oral contraceptives.

Brevinor 21 Day, Brevinor-1 (21 or 28 Day) and Norimin 28 Day must be discontinued 2 weeks prior to starting therapy with the combination drug regimen ombitasvir/paritaprevir/ritonavir and dasabuvir with or without ribavirin. Brevinor 21 Day, Brevinor-1 (21 or 28 Day) and Norimin 28 Day can be restarted approximately 2 weeks following completion of treatment with the combination drug regimen (see section 4.3).

Migraine/Headache

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

Women with migraine (particularly migraine with aura) who take COCs may be at increased risk of stroke (see section 4.3).

Angioedema

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

Medical Examinations

Before COC use is initiated, a thorough individual history, family history, and physical examination, including a blood pressure determination, should be performed. An examination of the breasts, liver,

extremities, and pelvic organs should also be conducted. A Papanicolaou (Pap) smear should be performed if the patient has been sexually active or if it is otherwise indicated.

Such medical examinations should be repeated at least annually during the use of COCs.

Carbohydrate and Lipid Effects

Glucose intolerance has been reported in COC users. Women with impaired glucose tolerance or diabetes mellitus who use COCs should be carefully monitored (see section 4.3).

A small proportion of women will have adverse lipid changes while taking OCs. Non-hormonal birth control should be considered in women with uncontrolled dyslipidemias. Persistent hypertriglyceridemia may occur in a small proportion of COC users. Elevations of plasma triglycerides in COC users may lead to pancreatitis and other complications.

Estrogens increase serum high-density lipoproteins (HDL cholesterol), whereas a decline in serum HDL cholesterol has been reported with many progestational agents. Some progestins may elevate low-density lipoprotein (LDL) levels and may render the control of hyperlipidaemias more difficult. The net effect of a COC depends on the balance achieved between doses of estrogen and progestin and the nature and absolute amount of progestins used in the contraceptive. The amount of both hormones should be considered in the choice of a COC.

Women who are being treated for hyperlipidaemias should be followed closely if they elect to use COCs.

Genital Bleeding

In some women withdrawal bleeding may not occur during the "tablet-free" or "inactive-tablet" interval. If the COC has not been taken according to directions prior to the first missed withdrawal bleed, or if two consecutive withdrawal bleeds are missed, tablet taking should be discontinued and a non-hormonal back-up method of birth control should be used until the possibility of pregnancy is excluded.

Breakthrough bleeding/spotting may occur in women taking COCs, especially during the first three months of use. If this bleeding persists or recurs, non-hormonal causes should be considered and adequate diagnostic measures may be indicated. If pathology has been excluded, continued use of the COC or a change to another formulation may solve the problem.

Some women may encounter post-pill amenorrhea (possibly with anovulation) or oligomenorrhea, especially when such a condition was pre-existent.

Depression

Women with a history of depression who use COCs should be carefully observed and the drug discontinued if depression recurs to a serious degree. Patients becoming significantly depressed while taking COCs should stop the medication and use an alternative method of birth control in an attempt to determine whether the symptom is drug-related.

Vomiting and/or Diarrhoea

Diarrhoea and/or vomiting may reduce hormone absorption resulting in decreased serum concentrations (see section 4.2).

Missed Period(s)

Since the safety of oral contraceptives in pregnancy has not been established it is recommended that for any patient who has missed a period, pregnancy should be ruled out before continuing medication (see section 4.6).

Other

Under the influence of oral contraceptives pre-existing uterine fibroids may increase in size.

The use of oral contraceptives has also been associated with a possible increased incidence of gall bladder disease.

Acute renal failure and haemolytic uraemic syndrome have been associated with the use of oral contraceptives.

Discontinue oral contraceptives during prolonged periods of bed rest.

The use of oral contraceptive may cause fluid retention. Patients with conditions such as diabetes, hypertension, epilepsy, migraine, asthma and cardiac or renal dysfunction require careful observation whilst on oral contraceptive therapy.

Patients with diseases affecting calcium or phosphorus metabolism should be carefully observed.

Because estrogens may hasten epiphyseal closure oral contraceptives should be used judiciously in young patients in whom bone growth is not complete.

The pathologist should be advised of oral contraceptive therapy when relevant specimens are submitted (for further information see section 4.4, Effects on Laboratory Tests).

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

Paediatric Use

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

Use in the Elderly

Combined oral contraceptives are not indicated for use in postmenopausal women.

Effects on Laboratory Tests

Oral contraceptives may cause alterations in certain laboratory estimations. A medicine free period of two months may be required before some of these parameters return to normal.

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

1. Increased norepinephrine-induced platelet aggregatility.

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

3. Other binding proteins may be elevated in serum.

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

5. Triglycerides may be increased.

6. Glucose tolerance may be decreased.

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

8. Metyrapone test - decrease in urinary 17 ketosteroids and 17 ketogenic steroids.

9. Pregnanediol determinations - decrease in urinary pregnanediol levels.

10. False positive rheumatoid factors and antinuclear factor.

11. Lipid metabolism may be affected with increased serum levels of HDL cholesterol, triglycerides and phospholipids being observed.

12. Serum albumin levels are usually decreased (along with the associated calcium levels).

With the following tests abnormal results may indicate impairment of organ function:

13. Liver - increase in serum transaminases, alkaline phosphatase, gamma glutamyl transpeptidase, bilirubin, binding proteins and bromsulphalein retention.

14. Increased prothrombin and factors VII, VIII, IX and X; Decreased antithrombin 3.

4.5 Interaction with other medicines and other forms of interaction

Interactions between ethinylestradiol and other substances may lead to decreased or increased serum ethinylestradiol concentrations, respectively.

Concomitant use with the medicinal products containing ombitasvir/paritaprevir/ritonavir and dasabuvir, with or without ribavirin may increase the risk of ALT elevations (see section 4.3 and section 4.4, Hepatic Neoplasia/Liver Disease/Hepatitis C).

Therefore, COC users must switch to an alternative method of contraception (e.g. progestogen-only contraception or non-hormonal methods) prior to starting therapy with anti-viral HCV medicinal products such as ombitasvir, paritaprevir, ritonavir, dasabuvir. COCs can be restarted 2 weeks

following completion of treatment with an anti-viral HCV medicinal product.

Decreased ethinylestradiol serum concentrations may cause an increased incidence of breakthrough bleeding and menstrual irregularities and may possibly reduce efficacy of the COC.

During concomitant use of ethinylestradiol-containing products and substances that may lead to decreased ethinylestradiol serum concentrations, it is recommended that a non-hormonal back-up method of birth control (such as condoms and spermicide) be used in addition to the regular intake of Brevinor 21 Day, Brevinor-1 21 or 28 Day or Norimin 28 Day. In the case of prolonged use of such substances COCs should not be considered the primary contraceptive.

After discontinuation of substances that may lead to decreased ethinylestradiol serum concentrations, use of a non-hormonal back-up method is recommended for at least 7 days. Longer use of a back-up method is advisable after discontinuation of substances that have led to induction of hepatic microsomal enzymes, resulting in decreased ethinylestradiol serum concentrations. It may sometimes take several weeks until enzyme induction has completely subsided, depending on dosage, duration of use and rate of elimination of the inducing substance.

Examples of substances that may decrease serum ethinylestradiol concentrations:

- Any substance that reduces gastrointestinal transit time and, therefore, ethinylestradiol absorption
- Substances that induce hepatic microsomal enzymes, such as rifampicin, rifabutin, barbiturates, primidone, phenytoin, dexamethasone, griseofulvin, topiramate, some protease inhibitors, modafinil
- *Hypericum perforatum*, also known as St. John's wort, and ritonavir (possibly by induction of hepatic microsomal enzymes)

Other drugs that may decrease effectiveness of COCs include analgesics, antihistamines, antimigraine preparations, chloramphenicol, isoniazid, neomycin, nitrofurantoin, and tranquilizers.

Examples of substances that may increase serum ethinylestradiol concentrations:

- Atorvastatin
- Competitive inhibitors for sulfation in the gastrointestinal wall, such as ascorbic acid (vitamin C) and paracetamol (acetaminophen)
- Substances that inhibit cytochrome P450 3A4 isoenzymes such as indinavir and fluconazole.

Ethinylestradiol may interfere with the metabolism of other drugs by inhibiting hepatic microsomal enzymes, or by inducing hepatic drug conjugation, particularly glucuronidation. Accordingly, plasma and tissue concentrations may either be increased (e.g., cyclosporine, theophylline, corticosteroids) or decreased (e.g., lamotrigine).

Oral contraceptives may alter the effectiveness of other types of medicines, such as anticonvulsants, antihypertensive agents (for example, guanethidine), beta-blockers, hypnotics, hypoglycaemic agents, oral anticoagulants, theophylline, tranquillizers, tricyclic antidepressants and vitamins.

There have been reports of pregnancy when COCs were co-administered with certain antibiotics (e.g. ampicillin and other penicillins, tetracyclines).

The prescribing information of concomitant medications should be consulted to identify potential interactions.

4.6 Fertility, pregnancy and lactation

Fertility

Recovery of fertility may be delayed following use.

Pregnancy - Category B3

If pregnancy occurs during treatment with COCs, further intake should be discontinued. There is no conclusive evidence that the estrogen and progestin contained in the COC will damage the developing child if conception accidentally occurs during COC use (see section 4.3).

Breast-feeding

Small amounts of contraceptive steroids and/or metabolites have been identified in the milk of nursing mothers, and a few adverse effects on the child have been reported, including jaundice and breast enlargement. Lactation may be affected by COCs, as COCs may reduce the quantity and change the composition of breast milk.

The use of COCs is generally not recommended until the nursing mother has completely weaned her child.

4.7 Effects on ability to drive and use machines

None stated.

4.8 Undesirable effects

Adverse reactions are listed in the Table per CIOMS frequency categories:

Very common:	≥10%
Common:	≥1% and <10%
Uncommon:	≥0.1% and <1%
Rare:	≥0.01% and <0.1%
Very rare:	<0.01%

Use of combined oral contraceptives has been associated with an increased risk of the following:

- Arterial and venous thrombotic and thromboembolic events, including myocardial infarction, stroke, transient ischaemic attack, venous thrombosis and pulmonary embolism.
- Cervical intraepithelial neoplasia and cervical cancer.
- Breast cancer diagnosis.
- Benign hepatic tumours (e.g. focal nodular hyperplasia, hepatic adenomas).

System Organ Class	Adverse Reaction
Cardiac disorders	
Not known	Myocardial infarction
Infections and infestations	
Common:	Vaginitis, including candidiasis
Musculoskeletal and connective tissue disorders	
Not known	Muscle spasms, back pain
Neoplasms benign, malignant, and unspecified	
Very rare	Hepatic adenomas, carcinomas, or benign liver tumours
Immune system disorders	
Rare	Anaphylactic/anaphylactoid reactions, including very rare cases of urticaria, angioedema, and severe reactions with respiratory and circulatory symptoms
Very rare	Exacerbation of systemic lupus erythematosus
Metabolism and nutrition disorders	
Uncommon	Changes in appetite (increase or decrease)
Rare	Glucose intolerance
Very rare	Exacerbation of porphyria
Not known	Vitamin B6 deficiency
Psychiatric disorders	
Common	Mood changes, including depression, changes in libido
Nervous system disorders	
Very common	Headache, including migraines
Common	Nervousness, dizziness
Very rare	Exacerbation of chorea
Not known	Somnolence
Eye disorders	
Rare	Intolerance to contact lenses
Very rare	Optic neuritis*, retinal vascular thrombosis
Not known	Change in corneal curvature (steepening), cataract

Vascular disorders

Very rare	Aggravation of varicose veins
Not known	Arterial thromboembolism, cerebral haemorrhage, cerebral thrombosis, mesenteric vessel thrombosis, pulmonary embolism, thrombophlebitis, hypertension

Gastrointestinal disorders

Common	Nausea, vomiting, abdominal pain
Uncommon	Abdominal cramps, bloating
Very rare	Pancreatitis, ischaemic colitis
Not known	Inflammatory bowel disease (Crohn's Disease, ulcerative colitis), dypspepsia

Hepatobiliary disorder

Rare	Cholestatic jaundice
Very rare	Gallbladder disease, including gallstones**
Not known	Hepatocellular injury (e.g. hepatitis, hepatic function abnormal), Budd-Chiari syndrome

Skin and subcutaneous tissue disorders

Common	Acne
Uncommon	Rash, chloasma (melasma), which may persist, hirsutism, alopecia
Rare	Erythema nodosum
Very rare	Erythema multiforme
Not known	Purpura, pruritus, photosensitivity

Renal and urinary disorders

Very rare	Haemolytic uraemic syndrome
Not known	Renal impairment, cystitis-like syndrome

Reproductive system and breast disorders

Very common	Breakthrough bleeding/spotting
Common	Breast pain, tenderness, enlargement, secretion, dysmenorrhea, change in menstrual flow, change in cervical ectropion and secretion, amenorrhoea
Not known	Diminution in lactation when given immediately postpartum, temporary infertility after discontinuation of treatment, anovulation post treatment

General disorders and administration site conditions

Common	Fluid retention/oedema
Not known	Fatigue

Investigations

Common	Changes in weight (increase or decrease)
Uncommon	Increase in blood pressure, changes in serum lipid levels, including hypertriglyceridemia
Rare	Decrease in serum folate levels***
Not known	Carbohydrate tolerance decreased

* Optic neuritis may lead to partial or complete loss of vision.
** COCs may worsen existing gallbladder disease and may accelerate the development of this disease in previously asymptomatic women.
*** Serum folate levels may be depressed by COC therapy.

Reporting of Suspected Adverse Reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose

Symptoms

Symptoms of oral contraceptive overdosage in adults and children may include nausea, vomiting, breast tenderness, dizziness, abdominal pain, drowsiness/fatigue and withdrawal bleeding may occur in females.

Serious ill effects have not been reported following acute ingestions of large doses of oral contraceptives by young children.

Treatment

There is no specific antidote and further treatment of overdose, if necessary, is directed to the symptoms. If a patient is seen within 3 hours of swallowing a significant number of tablets, emesis may be induced with syrup of ipecacuanha (15 mL for a child one year and older, followed by a large glass of fluid; this may be repeated once only if vomiting does not occur).

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Synthetic steroidal combination oral contraceptives. The triphasic preparation offers a constant low dose of ethinylestradiol with a variable dose of norethisterone. Estrogenic, progestational and antigonadotrophic characteristics are revealed by the endocrine profile of these combinations.

Like other combination type pills, (estrogen and progestogen combinations), Brevinor 21 Day, Brevinor-1 21 or 28 Day, and Norimin 28 Day suppress gonadotropins in a manner that inhibits ovulation, which leads to contraception.

Clinical Trials

Different pregnancy and adverse reaction rates have been reported with the use of each oral contraceptive. In as much as these rates are usually derived from separate studies conducted by different investigators in several population groups, they cannot be compared with precision. Furthermore, pregnancy and adverse reaction rates tend to be lower as clinical experience is expanded, possibly due to retention in the clinical study of those patients who accept the treatment regimen and did not discontinue due to adverse reactions or pregnancy.

In clinical trials with Brevinor tablets, 1,168 patients completed 16,345 cycles of use, and a total of 3 pregnancies were reported. In each case, the tablets were not taken as directed. This represents a pregnancy rate of 0.22/100 women years. In clinical trials with Brevinor-1 tablets, 940 patients completed 14,366 cycles of use and a total of 2 pregnancies were reported. In each case, the tablets were not taken as directed. This represents a pregnancy rate of 0.17/100 women years.

5.2 Pharmacokinetic properties

Studies using ^{14}C labelled compounds have shown that both norethisterone and ethinylestradiol are rapidly absorbed from the gastrointestinal tract. Following oral administration, metabolites of both compounds appear in the urine as conjugated glucuronides and sulphates, with unconjugated metabolites appearing in the faeces.

5.3 Preclinical safety data

None stated.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

BREVINOR 21 Day

Indigo carmine
Lactose monohydrate
Magnesium stearate
Maize starch

Povidone

NORIMIN 28 Day

Each blue tablet contains:
Indigo carmine
Lactose monohydrate
Magnesium stearate
Maize Starch
Povidone

Each orange tablet contains:
Lactose
Lactose monohydrate
Magnesium stearate
Microcrystalline cellulose
Sunset yellow FCF as FD&C Yellow Lake

BREVINOR-1 21 Day

Lactose monohydrate
Magnesium stearate
Maize starch
Povidone

BREVINOR-1 28 Day

Each white tablet contains:
Lactose monohydrate
Magnesium stearate
Maize starch
Povidone

Each orange tablet contains:
Lactose
Lactose monohydrate
Magnesium stearate
Microcrystalline cellulose
Sunset yellow FCF as FD&C Yellow #6 Lake

6.2 Incompatibilities

None stated.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

BREVINOR 21 Day calendar packs: 3 x 21

BREVINOR-1 21 Day calendar packs: 3 x 21

BREVINOR-1 28 Day calendar packs: 3 x 28

NORIMIN 28 Day calendar packs: 3 x 28

6.6 Special precautions for disposal and other handling

None stated.

7. MEDICINE SCHEDULE

Prescription Medicine.

8. SPONSOR

Pfizer New Zealand Limited
PO Box 3998
Auckland
NEW ZEALAND

Toll Free Number: 0800 736 363

9. DATE OF FIRST APPROVAL

BREVINOR 21 Day

26 August 1976

NORIMIN 28 Day

16 January 1997

BREVINOR-1 21 Day

30 August 1979

BREVINOR-1 28 Day

30 August 1979

10. DATE OF REVISION OF THE TEXT

13 May 2022

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
1, 2, 3, 4.2, 4.5, 6.1, 6.5, 9	Remove provisional registration details for Brevinor 28 Day (4 x 28 tablets).