SCHEDULING STATUS **S3**

1 NAME OF THE MEDICINE

FAMYNOR 500 µg/50 µg (tablets)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each active white tablet of **FAMYNOR** contains:

Norgestrel 500 micrograms

Ethinyl estradiol 50 micrograms

Preservative: Methyl hydroxybenzoate 0,07 % *m/m*

Contains sugar:

Sucrose: ± 27,14 mg

Lactose monohydrate: 47,14 mg

The 7 red tablets are inert.

Each red inert tablet contains:

Preservative: Methyl hydroxybenzoate 0,1 % *m/m*

Contains sugar:

Sucrose: ± 24,5 mg

Lactose monohydrate: 71,38 mg

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets.

21 active white, circular, biconvex, sugar-coated tablets and 7 inert, red, circular, biconvex, sugar-coated tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

FAMYNOR is indicated for:

- Fertility control in women.
- Control of certain menstrual irregularities i.e. symptomatic treatment of primary dysmenorrhoea where contraception is also desired, and cases of dysfunctional uterine bleeding.

4.2 Posology and method of administration

Posology

FAMYNOR tablets must be taken as directed and at intervals not exceeding 24 hours to achieve maximum effectiveness. The tablets are to be taken at the same time every day, preferably after the evening meal or at bedtime. Withdrawal bleeding can be expected within 2 to 3 days after the last white tablet has been taken. If one has started the tablets after day 5 of a normal menstrual cycle, or the 3rd postpartum week, the possibility of pregnancy must be checked prior to commencement of administration as conception or ovulation might have occurred before starting.

1. **Beginning on day 1 of the menstrual cycle, i.e. the first day of bleeding**.
2. First 21 consecutive days: Take one white tablet daily following the arrows until all the white tablets are finished.
3. Next 7 consecutive days: Take one red, inert, tablet daily, following the arrows until all the red tablets are finished.
4. On the following day start a new package, taking the first white tablet of the next course as described under point 2.

NOTE: There must be no delay/interval between finishing one course and starting the next.

The changes the patient can expect:

The patient will probably have a menstrual period two or three days after taking the last white tablet in each

package. The blood now may be slightly less or more than the patient had before she started taking **FAMYNOR**.

The next and all subsequent courses will begin on the day after the last tablet in the package was completed, even if withdrawal bleeding has not occurred or is still in progress. Each course of **FAMYNOR** will start on the same day of the week and follows the same schedule (21 days of white tablets, 7 days of red, inert, tablets).

If for some reason, the tablets are not started on day 1 of the menstrual cycle, an additional method of contraception (mechanical) should be used until 14 tablets of the first course of **FAMYNOR** have been taken.

Patients changing from another oral contraceptive medicine:

When changing from another oral contraceptive to **FAMYNOR**, begin the first active tablet of **FAMYNOR** on the day after the last active tablet of the previous contraceptive's course has been taken. If a tablet-free interval is taken, then extra contraceptive precautions are advised for the first 7 days. If the inert tablets are inadvertently taken first, extra contraceptive precautions are necessary during the first 14 days. If transient spotting or breakthrough bleeding occurs, continue with the course. If the bleeding is persistent or prolonged, a medical practitioner should be consulted.

Missed tablets

If a tablet is missed, the risk of pregnancy is greatest when it happens at the beginning or end of a cycle. The missed white tablet should be taken as soon as possible. If tablets are missed for two consecutive days, both tablets should be taken as soon as possible. In either case, the next tablet should be taken at the usual time. Extra contraception methods (mechanical) are required for the next 7 days. If one or more tablets are missed during the last week of active (white) tablets, the inert (red) tablets must be discarded and the next cycle of **FAMYNOR** started immediately. A menstrual period should not be expected until the end of the next cycle.

If three consecutive white tablets are missed, **FAMYNOR** should be discontinued, and remaining tablets discarded. A new package should be started on the eighth day after the last tablet was taken. Extra contraception methods (mechanical) are required for the 7 days while no tablet is taken and for the 7 days after the new course has been started. If the patient does not have a period at the end of the second pack, she must return to her doctor to exclude the possibility of pregnancy.

Missing any of the inert tablets is not important, but the next course must be started at the right time.

Advice in case of gastrointestinal disturbances

If, while on **FAMYNOR** the patient develops severe vomiting and diarrhoea, the absorption of **FAMYNOR** may be diminished and women should be advised to use additional methods of contraception at a time of such disorders.

If vomiting or diarrhoea occurs within 3 to 4 hours after taking an active tablet of **FAMYNOR**, handle this as a missed tablet.

Method of administration

Take **FAMYNOR** tablets orally.

4.3 Contraindications

• Hypersensitivity to norgestrel, ethinyl estradiol or to any of the excipients listed (see section 6.1).

• Suspected pregnancy or pregnancy.

• Patients with previous or active thromboembolic disorders or those with a high risk of arterial or venous thrombotic diseases (see section 4.4). This includes:

- Patients who smoke and are over the age of 35 years.
- Patients who have a history of, or current deep vein thrombosis (DVT), pulmonary embolism or inherited thrombophilia.
- Patients who have inherited or acquired hypercoagulopathies.
- Patients who have cerebrovascular insufficiency or cerebrovascular disease.
- Patients with coronary artery disease. **FAMYNOR** should be discontinued immediately if there is an onset of unexplained chest pain.
- Patients with thrombogenic valvular or thrombogenic rhythm diseases of the heart (e.g. subacute bacterial endocarditis with valvular disease, or atrial fibrillation).
- Patients with uncontrolled hypertension.

- Patients with diabetes mellitus with vascular disease.
- Patients with headaches with focal neurological symptoms or patients who have migraine headaches with an aura. **FAMYNOR** should be discontinued immediately if migraine becomes focal, or if there is a loss of vision.
- Patients over the age of 35 with any migraine headaches.

• Previous myocardial infarction.

• Hyperlipidaemia.

• Patients with a history of or current hormone dependent (estrogen or progestin sensitive) neoplasms, or carcinoma of breast or endometrium.

• Hepatic adenoma.

• Abnormal, undiagnosed genital bleeding.

• History or presence of liver tumours (benign or malignant), liver disease, recurrent cholestatic jaundice, or markedly impaired liver function.

• Acute or chronic liver diseases, including Dubin-Johnson or Rotor syndromes. A history during pregnancy of pruritus or cholestatic jaundice.

• A history during pregnancy of chorea, pemphigoid gestationis (formerly herpes gestationis) or deteriorating otosclerosis.

• Concomitant administration of hepatitis C medicine combinations containing ombitasvir/paritaprevir/ritonavir with or without dasabuvir, due to the potential for ALT elevations.

• Depression not well controlled with treatment.

• A history of depression with the use of hormonal contraceptives.

• Patients known with inherited genetic mutations: BRCA 1 and BRCA 2 genes.

• Early menstrual periods (before the age of 12 years).

• History of non-cancerous breast diseases (atypical hyperplasia or lobular carcinoma *in situ*).

• Previous treatment using radiation therapy to the chest or breast.

• Previous exposure to diethylstilbestrol (DES).

4.4 Special warnings and precautions for use

CIGARETTE SMOKING INCREASES THE RISK OF SERIOUS CARDIOVASCULAR SIDE EFFECTS FROM THE USE OF FAMYNOR. THE RISK INCREASES WITH AGE AND WITH HEAVY SMOKING (15 OR MORE CIGARETTES PER DAY) AND IS MARKED IN WOMEN OVER 35 YEARS OF AGE. WOMEN WHO USE ORAL CONTRACEPTIVES SUCH AS FAMYNOR SHOULD BE STRONGLY ADVISED NOT TO SMOKE.

*Stopping **FAMYNOR***

Under no circumstances should **FAMYNOR** be stopped without having adopted a satisfactory alternative method of contraception.

Caution for use

FAMYNOR should be used with caution in patients with a history of epilepsy, asthma, or states in which fluid retention occur.

Antibiotic therapy

Oral contraceptive failure may occur with concomitant antibiotic therapy. For maximal protection, additional non-hormonal contraception is recommended for the duration of antibiotic therapy and for seven days thereafter. Those on long-term antibiotic therapy need only take extra precautions for the first two weeks of antibiotic therapy. Spotting and breakthrough bleeding are possible signs of diminished contraceptive effectiveness.

With liver enzyme inducing medicines, the barrier contraceptive method must be used during the whole time of the concomitant medicines therapy and for 28 days after its discontinuation (see to section 4.5).

Thrombotic disorders and other vascular problems

The incidence of diseases of the circulatory system in women using COCs (combined oral contraceptives), such as **FAMYNOR**, is significantly greater than those of controls and the mortality is slightly increased. **FAMYNOR** should be stopped if an arterial thrombotic event or venous thromboembolic (VTE) event occurs.

FAMYNOR should be stopped if there is unexplained loss of vision, proptosis, diplopia or papilledema. Evaluate for retinal vein thrombosis immediately (see section 4.8).

Surgery or prolonged periods of immobilisation are more likely to be associated with an increased incidence of thrombotic side effects. **FAMYNOR** should be discontinued 4 weeks prior to elective surgery or during periods of immobilisation and for 2 weeks after major surgery or other surgeries known to have an elevated risk of VTE.

FAMYNOR should not be started earlier than 4 weeks after delivery in women who are not breastfeeding. The risk of postpartum VTE decreases after the third postpartum week, whereas the risk of ovulation increases after the third postpartum week.

The use of COCs, such as **FAMYNOR**, increases the risk of VTE. However, pregnancy increases the risk of VTE as much or more than the use of COCs, such as **FAMYNOR**. The risk of VTE in women using COCs, such as **FAMYNOR**, is 3 to 9 cases per 10 000 woman-years. The risk of VTE is highest during the first year of use of **FAMYNOR** and when restarting oral contraception, such as **FAMYNOR**, after a break of 4 weeks or longer.

The risk of thromboembolic disease due to COCs, such as **FAMYNOR**, gradually disappears after **FAMYNOR** use is discontinued. Use of COCs, such as **FAMYNOR**, also increases the risk of arterial thromboses that result in strokes and myocardial infarctions, especially in women with other risk factors for these events. COCs, such as **FAMYNOR**, have been shown to increase both the relative and attributable risks of cerebrovascular events (thrombotic and haemorrhagic strokes).This risk increases with age, particularly in women over 35 years of age who smoke. COCs should be used with caution in women with cardiovascular disease risk factors.

Coronary thrombosis, cerebrovascular accidents, myocardial infarction and venous thrombosis are more likely to occur in smokers over the age of 35 years and non-smokers over the age of 40, particularly if they have used a contraceptive for longer than 5 years, if they are obese or if they are hypertensive (see section 4.3).

Additional risk factors are diabetes, hypercholesterolemia and familial hyperlipoprotelinaemia.

However, with the exception of women 35 years and older who smoke and non-smokers 40 years and older, the risk of mortality associated with all methods of birth control is less than that associated with childbirth. Since cigarette smoking increases the risk of serious side effects, women who use oral contraceptives should be strongly advised not to smoke (see section 4.3).

Impaired liver function

FAMYNOR should not be prescribed to women with liver disease, such as acute viral hepatitis or severe (decompensated) cirrhosis of liver (see section 4.3). Acute or chronic disturbances of liver function may necessitate the discontinuation of **FAMYNOR** use until markers of liver function return to normal and **FAMYNOR** causation has been excluded. Discontinue **FAMYNOR** if jaundice develops.

Hepatic tumours

FAMYNOR is contraindicated in women with benign and malignant liver tumours (see section 4.3).
Hepatic adenomas are associated with COC, such as **FAMYNOR**, use. Rupture of hepatic adenomas may cause death through intra-abdominal haemorrhage.
There is an increased risk of developing hepatocellular carcinoma in long-term (> 8 years) COC, such as **FAMYNOR**, users.
FAMYNOR should be discontinued if persistent upper abdominal pain develops.

Risk of liver enzyme elevations with concomitant hepatitis C treatment

It has been found that in patients on hepatitis C combination medicine regimen that contains ombitasvir/paritaprevir/ritonavir, with or without dasabuvir, ALT elevations greater than 5 times the upper limit of normal (ULN), including some cases greater than 20 times the ULN, were significantly more frequent in patients using ethinyl estradiol-containing medicines such as **FAMYNOR**. **FAMYNOR** should be discontinued prior to starting therapy with the combination medicine regimen ombitasvir/paritaprevir/ritonavir, with or without dasabuvir (see section 4.3). **FAMYNOR** can be restarted approximately 2 weeks following completion of treatment with the combination medicine regimen.

Hypertension

FAMYNOR is contraindicated in women with uncontrolled hypertension or hypertension with vascular disease (see section 4.3). Hypertension may occur in association with the use of **FAMYNOR**. Regular blood pressure checks, including a pre-treatment level, are advisable. For women with well-controlled hypertension, monitor blood pressure and stop **FAMYNOR** if blood pressure rises significantly.

An increase in blood pressure has been reported in women taking COCs, such as **FAMYNOR**, and this increase is more likely in older women with extended duration of use. The incidence of hypertension increases with increasing concentrations of progestin.

Gallbladder disease

There is a small increased risk of developing gallbladder disease among COC, such as **FAMYNOR**, users. Use of **FAMYNOR** may worsen existing gallbladder disease. A past history of cholestasis related to COC, such as **FAMYNOR**, use predicts an increased risk with subsequent COC, such as **FAMYNOR**, use. Women with a history of pregnancy-related cholestasis may be at an increased risk for COC, such as **FAMYNOR**, related cholestasis.

Carbohydrate and lipid metabolic effect

Decreased glucose tolerance and increase in triglycerides and total phospholipids have been observed in patients on COCs, such as **FAMYNOR**. Diabetic and prediabetic patients should be monitored closely. Consider alternative contraception for women with uncontrolled dyslipidaemias. A small proportion of women will have adverse lipid changes while on COCs, such as **FAMYNOR**. Women with hypertriglyceridemia, or a family history thereof, may be at an increased risk of pancreatitis when using **FAMYNOR**.

Headache

If a woman taking **FAMYNOR** develops new headaches that are recurrent, persistent, or severe, evaluate the cause and discontinue **FAMYNOR** if indicated.

Consider discontinuation of **FAMYNOR** in the case of increased frequency or severity of migraine during **FAMYNOR** use (which may be prodromal of a cerebrovascular event).

Unscheduled bleeding and spotting

Unscheduled (breakthrough or intra-cyclic) bleeding and spotting sometimes occur in patients on COCs, such as **FAMYNOR**, especially during the first three months of use. If bleeding persists or occurs after previously regular cycles, check for causes such as pregnancy or malignancy. If pathology and pregnancy are excluded,

bleeding irregularities may resolve over time or with a change to a different contraceptive medicine.

Amenorrhoea and oligomenorrhoea

Prolonged amenorrhoea following the use of oral contraceptives, such as **FAMYNOR**, may occur. Women who use **FAMYNOR** may experience amenorrhoea, absence of withdrawal bleeding, even if they are not pregnant. The incidence is in the order of 1 % of users. Caution is advised where oligomenorrhoea or amenorrhoea have occurred in the past. Some women may experience amenorrhea or oligomenorrhoea after discontinuation of **FAMYNOR**, especially when such a condition was pre-existent.

If scheduled (withdrawal) bleeding does not occur, consider the possibility of pregnancy. If the patient has not adhered to the prescribed dosing schedule (missed one or more active tablets or started taking them on a day later than she should have), consider the possibility of pregnancy at the time of the first missed period and take appropriate diagnostic measures. If the patient has adhered to the prescribed regimen and misses two consecutive periods, rule out pregnancy.

Note: **FAMYNOR** does not protect against sexually transmitted diseases or the virus that causes acquired immunodeficiency syndrome (AIDS).

Depression

Carefully observe women with a history of depression and discontinue **FAMYNOR** if depression recurs to a serious degree.

Mood changes and depression are side effects reported with the use of hormonal contraceptives including **FAMYNOR**. There is some evidence that hormonal contraceptive use may be associated with severe depression and a higher risk of suicidal thoughts/behaviour (e.g. talking about suicide, withdrawing from social contact, having mood swings, being preoccupied with death or violence, feeling hopeless about a situation, increasing use of alcohol/drugs, doing self-destructive things, personality changes) and suicide. Prescribers should inform their patients to contact their doctor for advice if they experience mood changes and depression whilst on treatment with **FAMYNOR**.

Depressed mood and depression are well-known undesirable effects of hormonal contraceptive use (see section 4.8). Depression can be serious and is a well-known risk factor for suicidal behaviour and suicide. Women should be advised to contact their medical practitioner in case of mood changes and depressive symptoms, including shortly after initiating the treatment.

Carcinoma of the breast

FAMYNOR contains estrogen and progestogen which, on prolonged use, may increase the risk of developing breast cancer. A meta-analysis of prospective epidemiological studies from 1992 to 2018 reported a significant increase in the risk of developing breast cancer in 55 575 women 40 to 59 years of age who used menopausal hormone therapy (MHT). The risk increased steadily with duration of use and was slightly greater for estrogen-progestogen than estrogen only medicines and the risk persisted for more than 10 years after stopping the treatment. The relative risk (RR) to develop breast cancer for estrogen-progestogen medicines was 1,60 at 1 to 4 years and RR = 2,08 at 5 to 14 years, while that for estrogen only medicines was 1,17 at 1 to 4 years and 1,33 at 5 to 14 years. There was no risk to develop breast cancer in women who started MHT at 60 years of age.

All women on **FAMYNOR** should receive yearly breast examinations by a healthcare provider and perform monthly breast self-examinations. Mammography evaluations should be done based on patient age, risk factors, and prior mammogram results.

Cervical cancer

Some data suggests that COCs, such as **FAMYNOR**, are associated with an increase in the risk of cervical cancer or intraepithelial neoplasia.

Effect on binding globulins

The estrogen component of COCs, such as **FAMYNOR**, may raise the serum concentrations of thyroxine-binding globulin, sex hormone-binding globulin, and cortisol-binding globulin. The dose of replacement thyroid hormone or cortisol therapy may need to be increased (see section 4.5).

Hereditary angioedema

In women with hereditary angioedema, exogenous estrogens as in **FAMYNOR** may induce or exacerbate symptoms of angioedema.

Chloasma

Chloasma may occasionally occur, 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 **FAMYNOR**.

Body mass index

The safety and efficacy of **FAMYNOR** in women with a body mass index (BMI) of more than 35 kg/m^2 has not been evaluated.

Oral contraceptive effectiveness may be reduced during vomiting and diarrhoea. Additional contraceptive measures may be necessary during and for 7 days after recovery from such episodes.

Geriatric use

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

Paediatric use

Not applicable.

Porphyria

FAMYNOR should be used with caution in patients with porphyria.

FAMYNOR is probably porphyrinogenic. **FAMYNOR** should be prescribed only for compelling reasons and precautions should be considered in all patients.

Excipients: Lactose and sucrose warning:

FAMYNOR contains lactose and sucrose which may have an effect on the glycaemic control of patients with diabetes mellitus.

Patients with rare hereditary problems of fructose intolerance, galactose intolerance, total lactase deficiency, sucrase-isomaltase insufficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

*Medicines decreasing the plasma concentrations of **FAMYNOR** and potentially diminishing the efficacy of **FAMYNOR***

Medicines and herbal medicines that induce certain enzymes, including cytochrome P450 3A4 (CYP3A4), may decrease the plasma concentrations of **FAMYNOR** and potentially diminish the effectiveness of **FAMYNOR** or increase breakthrough bleeding.

The efficacy of **FAMYNOR** may be decreased when it is administered concomitantly with other medicines such as phenytoin, barbiturates such as phenobarbitone, carbamazepine, bosentan, felbamate, griseofulvin, oxcarbazepine, topiramate, rufinamide, aprepitant, St. John's wort, rifabutin, rifampicin, phenylbutazone, ampicillin, primidone and modafinil.

Interactions between **FAMYNOR** and other medicines may lead to breakthrough bleeding and/or contraceptive failure. Counsel women to use an alternative non-hormonal method of contraception or a back-up method when enzyme inducers are used with **FAMYNOR**, and to continue back-up non-hormonal contraception for 28 days after discontinuing the enzyme inducer to ensure contraceptive reliability. Spotting and breakthrough bleeding are possible signs of diminished contraceptive effectiveness.

Colesevelam

Colesevelam, a bile acid sequestrant, given together with a COC, such as **FAMYNOR**, has been shown to significantly decrease the AUC of ethinyl estradiol (EE), as in **FAMYNOR**. The interaction can be decreased if the two medicines are given 4 hours apart.

*Medicines increasing the plasma concentrations of **FAMYNOR***

Co-administration of atorvastatin or rosuvastatin and certain COCs containing ethinyl estradiol (EE), such as **FAMYNOR**, increase AUC values for EE by approximately 20 % to 25 %.

Ascorbic acid and paracetamol may increase plasma EE concentrations, possibly by inhibition of conjugation.

Concomitant administration of CYP3A4 inhibitors such as itraconazole, voriconazole, fluconazole, grapefruit juice, or ketoconazole may increase plasma hormone concentrations.

Human immunodeficiency virus (HIV)/Hepatitis C virus (HCV) protease inhibitors and non-nucleoside reverse transcriptase inhibitors

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

Concomitant use with HCV combination therapy – Liver enzyme elevation

Co-administration of **FAMYNOR** with HCV medicine combinations containing ombitasvir/paritaprevir/ritonavir, with or without dasabuvir, is contraindicated due to potential for ALT elevations (see section 4.3 and section 4.4).

*Effects of **FAMYNOR** on other medicines*

FAMYNOR may inhibit the metabolism of other medicines (e.g. ciclosporin, prednisolone, theophylline, tizanidine, and voriconazole) and increase their plasma concentrations. COCs, such as **FAMYNOR**, have been shown to decrease plasma concentrations of paracetamol, clofibric acid, morphine, salicylic acid and temazepam. A significant decrease in plasma concentration of lamotrigine has been shown, likely due to

induction of lamotrigine glucuronidation. This may reduce seizure control; therefore, dosage adjustments of lamotrigine may be necessary.

Women on thyroid hormone replacement therapy may need increased doses of thyroid hormone because the serum concentration of thyroid-binding globulin increases with use of **FAMYNOR** (see section 4.4).

In addition to the above interactions, several medicines may be affected by concomitant use with **FAMYNOR.**

Anticoagulants – increased or decreased effects.

Antidepressants – both reduced effectiveness and increased toxicity reported with some antidepressants.

Antidiabetics such as sulfonylureas and insulin – antagonism of the effect.

Antihypertensives – antagonism of the effect.

Benzodiazepines – increased or decreased clearance.

Clofibrate – increased clearance and antagonism of the effect.

Corticosteroids – enhanced effect due to reduced clearance.

Lignocaine – increased free fraction.

Selegiline – decreased clearance.

Xanthines – decreased clearance.

Laboratory tests:

FAMYNOR may interfere with the result of some laboratory tests in particular hormones, glucose tolerance, thyroid function, binding proteins, blood coagulation factors, serum triglycerides and liver function tests.

4.6 Fertility, pregnancy and lactation

FAMYNOR is contraindicated in pregnancy (see section 4.3).

Pregnancy

Pregnancy should be ruled out before a course of **FAMYNOR** is initiated.

If the correct dosing schedule was followed and two consecutive menstrual cycles have been missed, the use of **FAMYNOR** should be discontinued, until the possibility of pregnancy has been ruled out.

If the correct dosing schedule was not followed, pregnancy should be ruled out after the first missed menstrual period.

It is recommended that conception be delayed for 3 months after discontinuation of **FAMYNOR** or until after the first regular menses.

There is little or no increased risk of birth defects in the children of females who inadvertently used COCs during early pregnancy. **FAMYNOR** should be discontinued if pregnancy is confirmed. **FAMYNOR** should not be administered to induce withdrawal bleeding as a test for pregnancy. Do not use **FAMYNOR** during pregnancy to treat threatened or habitual abortion.

Breastfeeding

Oral contraception is recommended to begin after the third postpartum month for mothers who are exclusively breastfeeding and in the third postpartum week for mothers who are only partially or not breastfeeding.

FAMYNOR and/or metabolites are present in human milk in small amounts. The effects of **FAMYNOR** on the breastfed child is unknown. **FAMYNOR** can reduce milk production in lactating women. Advise the nursing mother to use non-hormonal contraception, when possible, until she has weaned her child. This is less likely to occur once breastfeeding is well-established; however, it can occur at any time in some women. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for **FAMYNOR** and any potential adverse effects on the breastfed child from **FAMYNOR** or from the underlying maternal condition.

Fertility

Administration of norgestrel/ethinyl estradiol in mice and rats to suppress fertility was followed by a recovery of reproductive function and fertility.

4.7 Effects on ability to drive and use machines

Based on the side effect profile of **FAMYNOR**, no effect is expected on the ability to drive and use machines, however patients should not drive, use machinery or perform any tasks that require concentration until they are certain that **FAMYNOR** does not adversely affect their ability to do so safely (see section 4.8).

4.8 Undesirable effects

a) Summary of the safety profile

During the first few months of treatment, breakthrough bleeding, spotting and breast tenderness or enlargement can occur. These are usually temporary and normally disappear after continued treatment.

b) Tabulated list of adverse reactions

System Organ Class	**FAMYNOR Tablets Side Effects**
Neoplasms benign, malignant and unspecified (including cysts and polyps)	
Less frequent:	Carcinoma of the reproductive organs and breasts, hepatic neoplasia (including hepatic adenomas, or benign hepatic tumours)
Immune system disorders	
Frequency unknown:	Anaphylactic/anaphylactoid reactions including urticarial, angioedema and severe reactions with respiratory and circulatory symptoms
Endocrine disorders	
Frequency unknown:	Hirsutism
Metabolism and nutrition disorders	
Frequent:	Water/fluid retention, increased appetite
Less frequent:	Reduced/decreased glucose tolerance, carbohydrate and lipid effects, weight gain

Frequency unknown:	Decreased appetite, porphyria, exacerbation of porphyria, increase in triglycerides and total phospholipids
Psychiatric disorders	
Frequent:	Severe depression, nervousness and other mental changes
Frequency unknown:	Mood changes, mood swings
Nervous system disorders	
Frequent:	Headache
Less frequent:	Worsening or increasing frequency of headache or migraines, chorea
Frequency unknown:	Migraine, cerebral haemorrhage, cerebral thrombosis
Eye disorders	
Frequency unknown:	Intolerance to contact lenses has been reported and vision may deteriorate in myopic patients, ocular lesions, retinal vein/vascular thrombosis, change in corneal curvature (steepening), optic neuritis (which may lead to partial or complete loss of vision)
Cardiac disorders	
Frequency unknown:	Myocardial infarction
Vascular disorders	
Frequent:	Exacerbation of varicose veins

Less frequent:	Hypertension, arterial thromboembolism, venous thrombosis, stroke
Respiratory, thoracic and mediastinal disorders	
Frequency unknown:	Pulmonary embolism
Gastrointestinal disorders	
Frequent:	Nausea and/or vomiting, gastrointestinal symptoms, bloating, abdominal pain/cramps
Frequency unknown:	Gastrointestinal irritation, pancreatitis, mesenteric thrombosis, colitis
Hepato-biliary disorders	
Frequency unknown:	Impaired liver function, gall bladder disease, jaundice, cholestatic jaundice, Budd-Chiari syndrome
Skin and subcutaneous tissue disorders	
Frequent:	Acne, chloasma/melasma
Less frequent:	Skin rashes, gain or loss of body or facial hair
Frequency unknown:	Skin pigmentation, erythema multiforme, erythema nodosum, haemorrhagic skin eruption
Musculoskeletal, connective tissue and bone disorders	
Frequent:	Backache
Reproductive system and breast disorders	
Frequent:	Breast changes (tenderness, pain, discomfort enlargement and

	secretion), menstrual irregularities (spotting, breakthrough bleeding or amenorrhoea), vaginal infection, vaginal discharge, dysmenorrhoea, change in menstrual flow, cervical erosion
Less frequent:	Changes in libido, vaginal candidiasis
Frequency unknown:	Premenstrual syndrome, temporary infertility after discontinuation of treatment
General disorders and administration site conditions	
Frequent:	Fatigue
Investigations	
Frequency unknown:	Change in weight

c) Description of selected adverse reactions

The following side effects have been reported with the post marketing use of hormonal contraceptives: Severe depression with a higher risk of suicidal thoughts/behaviour and suicide.

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 providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Symptoms

Nausea may occur and withdrawal bleeding may occur in females.

Treatment

Treatment is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 18.8 Ovulation controlling agent

Pharmacotherapeutic group: Hormonal contraceptives for systemic use, progestogens and estrogens, fixed combinations

ATC code: G03AA06

Mechanism of action

Estrogen-progestogen combination oral contraceptives act primarily through the mechanism of gonadotrophin (luteinising hormone and follicle stimulating hormone) suppression, resulting in the prevention of ovulation. The viscosity of the cervical mucosa is increased, hindering penetration of the sperm. An endometrium which is less receptive for implantation is formed.

5.2 Pharmacokinetic properties

Norgestrel

Absorption

After oral administration, norgestrel is absorbed rapidly and completely. The active component of the racemate norgestrel is levonorgestrel which becomes completely bioavailable from the racemate and accounts for about half of the dose of norgestrel.

Distribution

On an average, maximum concentrations of levonorgestrel in serum of 7 to 8 ng/mL are already reached within

1 to 1,5 hours after a single administration of 500 µg of norgestrel. Subsequently, serum levels of levonorgestrel decline biphasically with a mean terminal half-life of 27 hours and reach minimum concentrations of about 1 ng/mL, 24 hours post dose. Levonorgestrel binds to albumin and SHBG. Only about 1 % to 1,5 % of the total levonorgestrel concentration in serum is not protein-bound. The relative fractions of free, albumin- and SHBG-bound levonorgestrel are strongly dependent on the concentration of SHBG in serum. After induction of the binding proteins, the fraction bound to SHBG increases whereas the unbound fraction and that bound to albumin decreases.

Biotransformation

Norgestrel is completely metabolised. Biotransformation of the active substance levonorgestrel follows the known pathways of steroid metabolism. Pharmacologically active metabolites are not known.

Elimination

The total clearance rate of levonorgestrel from serum is 1 mL/min/kg. With a half-life of about 1 day, approximately the same proportions of the metabolites of norgestrel are excreted with the urine and the bile.

Ethinyl estradiol

Absorption

Ethinyl estradiol is rapidly and completely absorbed from the gut but it undergoes some first pass metabolism in the gut wall.

Distribution

Ethinyl estradiol is rapidly distributed throughout most body tissues with the largest concentration found in adipose tissue. It distributes into breast milk in low concentrations. More than 80 % of ethinyl estradiol in serum is conjugated as the sulphate and almost all the conjugated form is bound to albumin.

Biotransformation

Ethinyl estradiol is metabolised in the liver. Hydroxylation appears to be the main metabolic pathway. 60 % of a dose is excreted in the urine and 40 % in the faeces. About 30 % is excreted in the urine and bile as the glucuronide or sulphate conjugate. The rate of metabolism of ethinyl estradiol is affected by several factors, including enzyme inducing medicines, antibiotics and cigarette smoking. After oral administration, an initial peak occurs in plasma at 2 to 3 hours, with a secondary peak at about 12 hours after dosing; the second peak is interpreted as evidence for extensive enterohepatic circulation of ethinyl estradiol.

Elimination

The elimination half-life of ethinyl estradiol ranges from 5 to 16 hours.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Active **FAMYNOR** tablets:

Acacia, disodium edetate, ethyl cellulose, lactose monohydrate, magnesium stearate, maize starch, methyl hydroxybenzoate, microcrystalline cellulose, polacrilin potassium, polyethylene glycol, purified talc, sucrose, titanium dioxide (CI no. 77891).

Inactive **FAMYNOR** tablets:

Carnauba wax, disodium edetate, ethyl cellulose, gum acacia, lactose monohydrate, magnesium stearate, maize starch, methyl hydroxybenzoate, polacrilin potassium, ponceau 4R lake (CI no. 16255), purified talc, sodium benzoate, sucrose, titanium dioxide (CI no. 77891).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 30 ºC. Protect from light.

KEEP THE BLISTERS IN THE CARTON UNTIL REQUIRED FOR USE.

6.5 Nature and contents of container

Alu/PVdC/PVC foil blister packs of 28 tablets (21 white and 7 red tablets), packed in a cardboard carton together with a leaflet.

6.6 Special precautions for disposal

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Viatris Healthcare (Pty) Ltd

4 Brewery Street,

Isando,

Gauteng,

1601

8 REGISTRATION NUMBER

A41/18.8/0036

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30 April 2010

10 DATE OF REVISION OF THE TEXT

30 January 2025