PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

FEMILEVO 0,75 mg tablets

FEMILEVO 1,50 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

FEMILEVO 0,75 mg: Each tablet contains 0,75 mg levonorgestrel.

FEMILEVO 1,50 mg: Each tablet contains 1,50 mg levonorgestrel.

Excipients with known effect:

Contains sugar:

FEMILEVO 0,75 mg: Each tablet contains 44,0 mg lactose monohydrate.

FEMILEVO 1,50 mg: Each tablet contains 43,3 mg lactose monohydrate.

For the full list of excipients, see section 6 .1.

3. PHARMACEUTICAL FORM

Tablets.

FEMILEVO 0,75 mg: Round, white tablet, with a diameter 6.00 mm, engraved “C” on one side and “2” on the other side.

FEMILEVO 1,50 mg: Round, white tablet, with a diameter 6.00 mm, engraved “C” on one side and “1” on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Emergency contraception within 72 hours of unprotected sexual intercourse or failure of a contraceptive method.

FEMILEVO is intended for emergencies only and is completely unsuitable for regular contraception. Its reliability is not as high as that of the familiar “pill”, which is taken for at least 21 days of the menstrual cycle.

4.2 Posology and method of administration

Posology:

FEMILEVO 0,75 mg:

Take 2 tablets in a single administration as soon as possible, preferably within 12 hours, but not later than 72 hours after unprotected sexual intercourse.

FEMILEVO 1,5 mg:

Take 1 tablet as soon as possible in a single administration.

The tablet should be taken no later than 72 hours after unprotected sexual intercourse.

If the patient vomits within three to four hours of taking FEMILEVO, another dose should be taken immediately.

The earlier FEMILEVO is used, the more effective it is.

Even extremely high doses of hormone can no longer prevent pregnancy once a fertilised ovum has become implanted in the uterine mucosa.

FEMILEVO can be used at any time during the menstrual cycle unless menstrual bleeding is overdue. After using emergency contraception, it is recommended to use a local barrier method (e.g., condom, foam, pessary) until the next menstrual period starts. The use of FEMILEVO does not contraindicate the continuation of regular hormonal contraception.

Paediatric Population:

FEMILEVO is not recommended in children.

Very limited data is available in women under 16 years of age.

Method of administration

For oral administration.

4.3 Contraindications

- Hypersensitivity to levonorgestrel or to any of the excipients listed in section 6.1.
- Severe hepatic insufficiency.
- Pregnancy or suspected pregnancy (see section 4.6).

- Patients with undiagnosed vaginal bleeding, or those with a history of or current high risk of arterial disease.
- Depression, which is not well controlled with treatment.
- A history of depression with the use of oestrogen and/or progesterone/progestogen containing medicines irrespective of the indication, dosage formulation and route of administration.
- The repeated use of FEMILEVO within a monthly cycle is to be avoided, since it constitutes undesirable hormonal stress and may result in severe cycle disturbances.

4.4 Special warnings and precautions for use

Emergency contraception is an occasional method. It should in no instance replace a regular contraceptive method.

FEMILEVO does not prevent a pregnancy in every instance. If there is uncertainty about the timing of the unprotected intercourse or if the woman has had unprotected intercourse more than 72 hours earlier in the same menstrual cycle, conception may have occurred. Treatment with FEMILEVO following the second act of intercourse may therefore be ineffective in preventing pregnancy. If menstrual periods are delayed by more than 5 days or abnormal bleeding occurs at the expected date of menstrual periods or pregnancy is suspected for any other reason, pregnancy should be excluded.

If pregnancy occurs after treatment with FEMILEVO, the possibility of an ectopic pregnancy should be considered, especially in those women who present with abdominal/pelvic pain or collapse and those with a history of ectopic pregnancy, fallopian tube surgery or pelvic inflammatory disease. The absolute risk of ectopic pregnancy is likely to be low, as FEMILEVO prevents ovulation and fertilisation.

Ectopic pregnancy may continue, despite the occurrence of uterine bleeding.

Therefore, FEMILEVO is not recommended for patients who are at risk of ectopic pregnancy (previous history of salpingitis or of ectopic pregnancy).

FEMILEVO is not recommended in patients with severe hepatic dysfunction (see section 4.3).

Severe malabsorption syndromes, such as Crohn's disease, might impair the efficacy of FEMILEVO.

After FEMILEVO intake, menstrual periods are usually normal and occur at the expected date. They can sometimes occur earlier or later than expected by a few days. Women should be advised to make a medical appointment to initiate or adopt a method of regular contraception. If no withdrawal bleed occurs in the next pill-free period following the use of FEMILEVO after regular hormonal contraception, pregnancy should be ruled out.

Repeated administration within a menstrual cycle is not advisable because of the possibility of disturbance of the cycle.

A health care provider should be consulted 3 weeks after taking FEMILEVO regardless of whether bleeding has occurred or not.

Limited and inconclusive data suggest that there may be reduced efficacy of FEMILEVO with increasing body weight or body mass index (BMI) (see section 5.1). In all women, emergency contraception should be taken as soon as possible after unprotected intercourse, regardless of the woman's body weight or BMI.

FEMILEVO is not as effective as a conventional regular method of contraception and is suitable only as an emergency measure. FEMILEVO is intended for emergencies only and is completely unsuitable for regular contraception. Its reliability is not as high as that of the familiar “pill", which is taken for at least 21 days of the menstrual cycle.

Women who present for repeated courses of emergency contraception should be advised to consider long-term methods of contraception.

FEMILEVO should not be used diagnostically for pregnancy testing and should not be given in missed or incomplete abortion.

Use of emergency contraception does not replace the necessary precautions against sexually transmitted diseases.

Use of emergency contraception in patients with history of physical or sexual abuse.

FEMILEVO should be used with caution in patients with a history of mental depression.

Mood changes and depression are side effects reported with the use of hormonal contraceptives including FEMILEVO. 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.

Certain progesterone's may have an adverse effect on serum lipids.

Lactose monohydrate:

FEMILEVO contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take FEMILEVO. Contains lactose monohydrate which may have an effect on the glycaemic control of patients with diabetes mellitus.

4.5 Interaction with other medicines and other forms of interaction

The metabolism of levonorgestrel is enhanced by concomitant use of liver enzyme inducers, mainly CYP3A4 enzyme inducers. Concomitant administration of efavirenz has been found to reduce plasma levels of levonorgestrel (AUC) by around 50 %.

Medicines suspected of having similar capacity to reduce plasma levels of levonorgestrel include anticonvulsants (phenobarbitone, phenytoin, primidone and carbamazepine), herbal medicines containing *Hypericum perforatum* (St. John's wort), rifampicin, ritonavir, rifabutin, griseofulvin, ampicillin and other antibiotics, including medicines used to treat tuberculosis, ciclosporin.

For women who have used enzyme-inducing medicines in the past 4 weeks and need emergency contraception, the use of non-hormonal emergency contraception (i.e., a Cu-IUD) should be considered. Taking a double dose of FEMILEVO (i.e., 3 mg within 72 hours after the unprotected

intercourse) is an option for women who are unable or unwilling to use a Cu-IUD, although this specific combination (a double dose of FEMILEVO during concomitant use of an enzyme inducer) has not been studied.

The requirement for oral antidiabetics and insulin can change as a result of an effect on glucose tolerance.

Medicines containing levonorgestrel may increase the risk of ciclosporin toxicity due to possible inhibition of ciclosporin metabolism.

4.6 Fertility, pregnancy and lactation

Pregnancy:

FEMILEVO should not be given to pregnant women. There is no evidence stating that FEMILEVO will not interrupt a pregnancy. In the case of continued pregnancy, limited epidemiological data indicate no adverse effects on the foetus but there are no clinical data on the potential consequences if doses greater than 1,5 mg of levonorgestrel are taken.

In case of unprotected coitus more than 72 hours earlier, the patient may be pregnant. In these cases, pregnancy should be investigated.

Lactation:

About 0,1% of the maternal FEMILEVO dose can be transferred via breast milk to the nursed infant. Potential exposure of an infant to FEMILEVO can be reduced if the breastfeeding woman

takes the tablet immediately after feeding and avoids nursing at least 6 hours following FEMILEVO administration.

Fertility:

Levonorgestrel increases the possibility of cycle disturbances which can sometimes lead to earlier or later ovulation date resulting in modified fertility date. Although there are no fertility data in the long term, after treatment with FEMILEVO a rapid return to fertility is expected and therefore, regular contraception should be continued or initiated as soon as possible after FEMILEVO use.

4.7 Effects on ability to drive and use machines

FEMILEVO can cause side effects, such as dizziness and can affect the ability to drive a vehicle and use machines. Caution is advised when driving a vehicle or operating machinery until the effects of FEMILEVO are known.

4.8 Undesirable effects

Frequency	System Organ Class	Undesirable effects
Frequent	Nervous System disorders	Headache, dizziness
	Gastrointestinal disorders	Nausea, lower abdominal pain, diarrhoea, vomiting
	Reproductive system and breast disorders	Bleeding not related to menstruation*, delay of menstruation more than 7 days**, irregular menstruation or spotting, breast tenderness

	General disorders and administration site conditions	Fatigue, fever
Less Frequent	Immune system disorders	Anaphylaxis, Anaphylactoid reactions
	Reproductive system and breast disorders	Changes in libido
	Hepato-biliary disorders	Alterations in liver function tests, jaundice
Frequency unknown	Metabolism and Nutrition disorders	Changes in appetite or weight, fluid retention, oedema
	Psychiatric disorders	Mental depression
	Nervous System disorders	Drowsiness, insomnia
	Gastrointestinal disorders	Gastrointestinal disturbances
	Skin and subcutaneous tissue disorders	Acne, Melasma or Chloasma, Allergic skin reactions, hair loss or hirsutism
	Reproductive system and breast disorders	Breast changes, premenstrual syndrome-like symptoms

* Bleeding patterns may be temporarily disturbed, but most women will have their next menstrual cycle within 7 days of the expected time.

** If the next menstrual cycle is more than 5 days overdue, pregnancy should be excluded.

Post-marketing experience:

Psychiatric disorders:

Less frequent : severe depression with a higher risk of suicidal thoughts/behaviour and suicide

Gastrointestinal disorders:

Less frequent: abdominal pain

Skin and subcutaneous tissue disorders:

Less frequent: rash, urticaria, pruritus

Reproductive system and breast disorders:

Less frequent: pelvic pain, dysmenorrhoea

General disorders and administration site conditions:

Less frequent: face oedema.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of FEMILEVO is important. It allows continued monitoring of the benefit/risk balance of FEMILEVO. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Serious undesirable effects have not been reported following acute ingestion of large doses of oral contraceptives.

Overdose may cause nausea, and withdrawal bleeding may occur. There are no specific antidotes and treatment should be symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 21.8.2 Progesterones with or without oestrogens.

Pharmacotherapeutic group: Sex hormones and modulators of the genital system, emergency contraceptives.

ATC code: G03AD01.

Mechanism of action:

Levonorgestrel is thought to work mainly by preventing ovulation and fertilisation if intercourse has taken place in the preovulatory phase, when the likelihood of fertilisation is the highest. Levonorgestrel is not effective once the process of implantation has begun.

5.2 Pharmacokinetic properties

Absorption:

Orally administered levonorgestrel is rapidly and almost completely absorbed.

The absolute bioavailability of levonorgestrel was determined to be almost 100 % of the dose administered.

The results of a pharmacokinetic study carried out with 16 healthy women, showed that following ingestion of one tablet of Levonorgestrel 1,5 mg resulted in maximum medicine serum levels of levonorgestrel of 18,5 ng/mL which were found at 2 hours.

Distribution:

Levonorgestrel is bound to serum albumin and sex hormone binding globulin (SHBG). Only about 1,5 % of the total serum levels are present as free steroid, but 65 % are specifically bound to SHBG.

About 0,1 % of the maternal dose can be transferred via milk to the nursed infant.

Biotransformation:

The biotransformation follows the known pathways of steroid metabolism, the levonorgestrel is hydroxylated by liver enzymes mainly by CYP3A4 and its metabolites are excreted after glucuronidation by liver glucuronidase enzymes (see section 4.5).

No pharmacologically active metabolites are known.

Elimination:

After reaching maximum serum levels, the concentration of levonorgestrel decreased with a mean elimination half-life of about 26 hours.

Levonorgestrel is not excreted in unchanged form but as metabolites. Levonorgestrel metabolites are excreted in about equal proportions with urine and faeces.

Pharmacokinetics in obese women:

A pharmacokinetic study showed that levonorgestrel concentrations are decreased in obese women (BMI ≥ 30 kg/m²) (approximately 50 % decrease in C_{max} and AUC_{0-24}), compared to women with normal BMI (< 25 kg/m²).

Another study also reported a decrease of levonorgestrel C_{max} by approximately 50 % between obese and normal BMI women, while doubling the dose (3 mg) in obese women appeared to provide plasma concentration levels similar to those observed in normal women who received 1,5 mg of levonorgestrel. The clinical relevance of these data is unclear.

5.3 Preclinical safety data

No further information of relevance available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium (E468)

Lactose monohydrate

Magnesium stearate (E572)

Microcrystalline cellulose (E460(i))

Poloxamer 188

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C. Keep the blister strip in the outer carton until required for use.

6.5 Nature and contents of container

FEMILEVO 0,75 mg: Aluminium blister strip containing 2 tablets packed in an outer carton.

FEMILEVO 1,50 mg: Aluminium blister strip containing 1 tablet packed in an outer carton.

6.6 Special precautions for disposal and other handling

None.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

1 New Road,

Erand Gardens,

Midrand, 1685,

Customer Care: 0860 ADCOCK / 232625

8. REGISTRATION NUMBERS

FEMILEVO 0,75 mg: 51/21.8.2/0583

FEMILEVO 1,50 mg: 51/21.8.2/0584

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18 January 2022

10. DATE OF REVISION OF THE TEXT

To be updated