1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

ERMAFT 0,75 mg tablets

ERMAFT 1,5 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of ERMAFT 0,75 mg contains 0,75 mg of levonorgestrel (micronized).

Contains sugar: Lactose monohydrate 44,0 mg

Each tablet of ERMAFT 1,5 mg contains 1,5 mg of levonorgestrel (micronized).

Contains sugar: Lactose monohydrate 43,3 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

ERMAFT 0,75 mg is a round, biconvex, white tablet, engraved “C” on one side and “2” on the other side.

ERMAFT 1,5 mg is a round, biconvex, white tablet, 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.

ERMAFT 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

Adults

ERMAFT 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.

ERMAFT 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 ERMAFT, another dose should be taken immediately.

The earlier ERMAFT 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.

ERMAFT 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 ERMAFT does not contraindicate the continuation of regular hormonal contraception.

Paediatric population

ERMAFT is not recommended in children.

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

Method of administration

For oral administration.

4.3. Contraindications

ERMAFT is contraindicated in:

- 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 hormonal contraceptives.

The repeated use of ERMAFT 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.

ERMAFT 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 ERMAFT 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 ERMAFT, 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 ERMAFT prevents ovulation and fertilisation.

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

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

ERMAFT 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 ERMAFT.

After ERMAFT 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 ERMAFT 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 healthcare provider should be consulted 3 weeks after taking ERMAFT regardless of whether bleeding has occurred or not.

Limited and inconclusive data suggest that there may be reduced efficacy of ERMAFT 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.

ERMAFT is not as effective as a conventional regular method of contraception and is suitable only as an emergency measure. ERMAFT 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.

ERMAFT 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.

ERMAFT 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 ERMAFT. 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 ERMAFT.

Certain progesterones may have an adverse effect on serum lipids.

Lactose monohydrate
ERMAFT contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take ERMAFT.

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 ERMAFT (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 ERMAFT 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

ERMAFT should not be given to pregnant women. It 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.

Breastfeeding

About 0,1 % of the maternal ERMAFT dose can be transferred via breast milk to the nursed infant. Potential exposure of an infant to ERMAFT can be reduced if the breastfeeding woman takes the tablet immediately after feeding and avoids nursing at least 6 hours following ERMAFT 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 ERMAFT a rapid return to fertility is expected and therefore, regular contraception should be continued or initiated as soon as possible after ERMAFT use.

4.7 Effects on ability to drive and use machines

ERMAFT 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 ERMAFT are known.

4.8 Undesirable effects

a) *Tabulated list of adverse reactions*

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Metabolism and nutrition disorders			Changes in appetite or weight, fluid

			retention, oedema
Immune system disorders		Anaphylaxis, anaphylactoid reactions	
Psychiatric disorders			Mental depression
Nervous system disorders	Headache, dizziness		Drowsiness, insomnia
Gastrointestinal disorders	Nausea, lower abdominal pain, diarrhoea, vomiting		Gastrointestinal disturbances
Hepato-biliary disorders			Alterations in liver function tests, jaundice
Skin and subcutaneous tissue disorders			Acne, melasma or chloasma, allergic skin reactions, hair loss or hirsutism
Reproductive system and breast disorders	Bleeding not related to menses*, delay of menses more than 7 days **, irregular menstruation or spotting, breast tenderness	Gynaecomastia, changes in libido	Breast changes, premenstrual syndrome like symptoms
General disorders and administrative site conditions	Fatigue, fever		

*Bleeding patterns may be temporarily disturbed, but most women will have their next menstrual period within 7 days of the expected time (see section 4.4).

**If the next menstrual period is more than 5 days overdue, pregnancy should be excluded (see section 4.4).

Post-marketing

System organ class	Less frequent
Psychiatric disorders	Severe depression with a higher risk of suicidal thoughts/behaviour and suicide
Gastrointestinal disorders	Abdominal pain
Skin and subcutaneous tissue disorders	Rash, urticaria, pruritus
Reproductive system and breast disorders	Pelvic pain, dysmenorrhoea
General disorders and administrative site conditions	Face oedema

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: https://www.sahpra.org.za/health-products-vigilance/

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9 Overdose

Symptoms

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.

Treatment

There are no specific antidotes and treatment should be symptomatic and supportive.

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 maximum medicine serum levels of levonorgestrel of 18,5 ng/mL 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, lactose monohydrate, magnesium stearate, poloxamer 188, microcrystalline cellulose.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

ERMAFT 0,75 mg: A single PVC-PVDC/Aluminium blister containing 2 tablets, in a carton.

ERMAFT 1,5 mg: A single PVC-PVDC/Aluminium blister containing 1 tablet, in a carton.

6.6 Special precautions for disposal

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8 REGISTRATION NUMBER

ERMAFT 0,75 mg - 48/21.8.2/1033

ERMAFT 1,5 mg - 48/21.8.2/1034

9 DATE OF FIRST AUTHORISATION

26 October 2021

10 DATE OF REVISION OF TEXT

26 October 2021

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088.

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