Professional Information for LEVONORGESTREL 1,5 UNICORN

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

LEVONORGESTREL 1,5 UNICORN tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each LEVONORGESTREL 1,5 UNICORN contains 1,5 mg levonorgestrel (micronized).

Contains sugar: lactose monohydrate 43,3 mg per tablet.

For the full list of excipients, **see section 6.1**

3. PHARMACEUTICAL FORM

Tablet.

Round, biconvex, with a diameter of 6,0 mm approximately and white in colour. The tablet is engraved with ‘C’ on one side and ‘1’ on the other.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

LEVONORGESTREL 1,5 UNICORN is indicated for the emergency prevention of pregnancy (emergency contraception) within 72 hours of unprotected sexual intercourse or the failure of contraceptive method.

4.2 Posology and method of administration

Posology

Adults (female):

One tablet must be taken as soon as possible, no later than 72 hours after, following unprotected sexual intercourse.

Another tablet of LEVONORGESTREL 1,5 UNICORN should be taken immediately if vomiting occurs within 3 - 4 hours of taking the tablet.

LEVONORGESTREL 1,5 UNICORN can be used at any time during the menstrual cycle except if menstrual bleeding is overdue.

Following the use of **LEVONORGESTREL 1,5 UNICORN**, it is recommended to avoid unprotected sexual intercourse and to use a mechanical method of contraception (for example, a condom, diaphragm, cervical cap) until the next menstrual period starts.

The use of **LEVONORGESTREL 1,5 UNICORN** does not contra-indicate the continuation of regular hormonal contraception.

Paediatric population:

The use of **LEVONORGESTREL 1,5 UNICORN** is not recommended in children. There is very limited data available on the use of levonorgestrel in females under the age of 16 years.

Method of administration

Oral administration.

4.3 Contraindications

- Hypersensitivity to levonorgestrel or any of the excipients of **LEVONORGESTREL 1,5 UNICORN** (see **Section 6.1**).
- Severe hepatic impairment.
- Pregnancy or suspected pregnancy (see **Section 4.6**)

- Depression not well controlled with treatment.
- A history of depression with the use of hormonal contraceptives.

4.4 Special warnings and precautions for use

Emergency contraception is an occasional method to be used in an “emergency situation” only. It should in no instance replace a regular contraceptive method.

LEVONORGESTREL 1,5 UNICORN 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 **LEVONORGESTREL 1,5 UNICORN** 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 LEVONORGESTREL 1,5 UNICORN, the possibility of an ectopic pregnancy should be considered, especially in women presenting with abdominal/pelvic pain or collapse and in women 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 levonorgestrel prevents ovulation and fertilisation. Ectopic pregnancy may continue, despite the occurrence of uterine bleeding.

Therefore, **LEVONORGESTREL 1,5 UNICORN** is not recommended for patients who are at risk of ectopic pregnancy (previous history of salpingitis or of ectopic pregnancy).

LEVONORGESTREL 1,5 UNICORN is not recommended in patients with severe hepatic dysfunction.

Severe malabsorption syndromes, such as Crohn's disease, might impair the efficacy of levonorgestrel as in **LEVONORGESTREL 1,5 UNICORN**.

After **LEVONORGESTREL 1,5 UNICORN** 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 levonorgestrel 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.

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

Levonorgestrel as in **LEVONORGESTREL 1,5 UNICORN** is not as effective as a conventional regular method of contraception and is suitable only as an emergency measure. Women who present for repeated courses of emergency contraception should be advised to consider long-term methods of contraception.

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

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

including **LEVONORGESTREL 1,5 UNICORN**. 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 **LEVONORGESTREL 1,5 UNICORN**.

LEVONORGESTREL 1,5 UNICORN contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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 barbiturates (including primidone), phenytoin, carbamazepine, herbal medicines containing *Hypericum perforatum* (St. John's Wort), rifampicin, ritonavir, rifabutin, and griseofulvin, ampicillin and other antibiotics, including medicines used to treat tuberculosis, ciclosporin.

The requirement for oral anti-diabetic medicines and insulin can change as a result of an effect on glucose tolerance.

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 CuIUD)

should be considered. Taking a double dose of levonorgestrel (i.e. 3000 mcg within 72 hours after the unprotected intercourse) is an option for women who are unable or unwilling to use a CuIUD, although this specific combination (a double dose of levonorgestrel during concomitant use of an enzyme inducer) has not been studied.

LEVONORGESTREL 1,5 UNICORN may increase the risk of ciclosporin toxicity due to possible inhibition of ciclosporin metabolism.

4.6 Fertility, pregnancy and lactation

Pregnancy

Levonorgestrel as in **LEVONORGESTREL 1,5 UNICORN** should not be given to pregnant women. It will not interrupt a pregnancy.

In case of failure of this emergency contraception with developing pregnancy, epidemiological studies indicate no adverse effects of progestogens on the foetus.

If unprotected sex has occurred more than 72 hours earlier, pregnancy should be investigated.

Breastfeeding

Levonorgestrel is secreted into breast milk. Approximately 0,1 % of the maternal dose may be transferred via milk to the nursed infant. Potential exposure of an infant to levonorgestrel can be reduced if the breastfeeding woman takes the tablet immediately after feeding and avoids nursing at least 8 hours following administration of **LEVONORGESTREL 1,5 UNICORN**.

Fertility

Levonorgestrel increases the possibility of cycle disturbances which can sometimes lead to earlier or later ovulation

date. These changes can result in modified fertility date, however, there are no fertility data in the long term.

4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

4.8 Undesirable effects

The most frequently reported undesirable effect was nausea.

System Organ Class	**Frequency**	**Adverse reaction**
Nervous system disorders	*Frequent*	Headache Dizziness
Gastrointestinal disorders	*Frequent*	Nausea Lower abdominal pain Diarrhoea Vomiting
	Less frequent	Abdominal pain
Skin and subcutaneous tissue disorders	*Less frequent*	Rash Urticaria Pruritus
Reproductive system and breast disorders	*Frequent*	Bleeding not related to menses* Delay of menses more than 7 days** Menstruation irregular Breast tenderness
	Less frequent	Pelvic pain

		Dysmenorrhoea
General disorders and administration site conditions	*Frequent*	Fatigue
	Less frequent	Face oedema

*Bleeding patterns may be temporarily disturbed. 78 % of women will have their next menstrual period within 5 days of expected time.

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

Post-marketing data:

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. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Medicine Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

Adverse reactions can also be reported directly to Unicorn Pharmaceuticals (Pty) Ltd at vigiiance@unicornpharma.co.za.

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 and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A. 21.8.2 Progesterones with or without estrogens.

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

ATC code: G03AD01

Mechanism of action

The precise mode of action of levonorgestrel as an emergency contraceptive is not known.

At the recommended regimen, levonorgestrel is thought to work mainly by preventing ovulation and fertilisation by altering tubal transport of sperm and/or ova, if intercourse has taken place in the pre-ovulatory phase, when the likelihood of fertilisation is the highest. It may also cause endometrial changes that discourage implantation. Levonorgestrel is not effective once the process of implantation has begun.

Efficacy:

A clinical study has demonstrated that 84 % of expected pregnancies were prevented by levonorgestrel when administered within 72 hours of unprotected sex. At the recommended dosage, levonorgestrel is not expected to induce significant modification of blood clotting factors, and lipid and carbohydrate metabolism.

5.2 Pharmacokinetic properties

Orally administered levonorgestrel is rapidly and almost completely absorbed.

The results of a pharmacokinetic study carried out with 16 healthy women showed that following ingestion of single dose of 1,5 mg levonorgestrel maximum medicine serum levels of 18,5 ng/ml were found at 2 hours.

Pharmacokinetic studies have shown that within 2 hours of a single dose of 1,5 mg levonorgestrel, a maximum plasma level of 18,5 ng/ml was attained. The mean value of area under the concentration-time curve (0 – infinity) was calculated as 310,2 ng.hr/ml. 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. The biotransformation follows the known pathways of steroid metabolism, the levonorgestrel is hydroxylated in the liver and the metabolites are excreted as glucuronide conjugates.
No pharmacologically active metabolites are known.

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.

Following ingestion of one tablet of levonorgestrel the mean value of SHBG was approximately 40 nmol/l. Serum levels of SHBG tend to stay at these levels (or slightly increased) for up to 24 hours, and then gradually decrease to reach levels of approximately 30 nmol/l at 192 hours.

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

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium

Lactose monohydrate

Magnesium stearate

Microcrystalline cellulose

Poloxamer 188

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 25 ºC.

Store in the original packaging.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

A pack size of 1 tablet packed in a blister pack consisting of aluminium push-through foil and clear, transparent PVC/PVDC film, in an outer unit carton box with a leaflet.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Unicorn Pharmaceuticals (Pty) Ltd

Corner of Searle and Pontac Streets

Woodstock, Cape Town

8001

enquiries@unicornpharma.co.za

8. REGISTRATION NUMBER(S)

53/21.8.2/0608

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

24 October 2023

10. DATE OF REVISION OF THE TEXT

Not applicable.