Professional Information for NORLEVO 1,5

SCHEDULING STATUS: **S2**

1. NAME OF THE MEDICINE

NORLEVO 1,5 tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 1,5 mg levonorgestrel.

Excipients with known effect:

Contains sugar: Each tablet contains 90,9 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

White, round, biconvex tablet with the code ‘NL 1.5’ engraved on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

NORLEVO 1,5 is indicated for the prevention of pregnancy within 72 hours of unprotected sexual intercourse or the recognisable failure of mechanical methods.

NORLEVO 1,5 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

Take one NORLEVO 1,5 tablet in a single administration as soon as possible, preferably within 12 hours, but not later than 72 hours after unprotected sexual intercourse.

The earlier NORLEVO 1,5 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.

All further unprotected sexual intercourse must be avoided until the next menstrual period; until then, only mechanical and/or chemical methods (condom, foam and pessary) of contraception may be used. The use of NORLEVO 1,5 does not contraindicate the continuation of regular hormonal contraception.

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

NORLEVO 1,5 can be used at any time during the menstrual cycle unless menstrual bleeding is overdue.

Paediatric population

NORLEVO 1,5 is not recommended in children.
Very limited data are available in women under 16 years of age.

Method of administration

Oral administration.

4.3 Contraindications

- Hypersensitivity to levonorgestrel or to any of the excipients listed in section 6.1.
- NORLEVO 1,5 should not be used if there is a possibility that pregnancy already exists, e.g. if unprotected sexual intercourse has already taken place in the same cycle or if the last menstrual period failed to occur (see section 4.6).
- NORLEVO 1,5 should not be given to patients with undiagnosed vaginal bleeding, or to those with a history, or current high risk of arterial disease.
- Severe hepatic impairment.
- Women with hormone-dependent neoplasms.
- Active trophoblastic disease.
- The repeated use of NORLEVO 1,5 within a monthly cycle is to be avoided, since it constitutes undesirable hormonal stress and may result in severe cycle disturbances.
- Porphyria.
- NORLEVO 1,5 is not recommended for women who are at risk of an ectopic pregnancy.
- Depression not well controlled with treatment.
- A history of depression with the use of hormonal contraceptives.

4.4 Special warnings and precautions for use

Pregnancy, puerperium and perinatal conditions

Emergency contraception is an **occasional** method. NORLEVO 1,5 is intended for emergencies only and is completely unsuitable for regular contraception.

Emergency contraception does not prevent a pregnancy to occur in every instance, especially if uncertainty about the timing of the unprotected intercourse. In case of doubt (menstrual periods delayed by more than five days or abnormal bleeding at the expected date of menstrual periods, symptoms of pregnancy), it is mandatory to check the absence of pregnancy by performing a pregnancy test.

If the woman has had unprotected intercourse more than 72 hours earlier in the same menstrual cycle, conception may have occurred. Treatment with NORLEVO 1,5 following the second act of

intercourse may therefore be ineffective in preventing pregnancy.

Limited and inconclusive data suggest that there may be reduced efficacy of NORLEVO 1,5 with increasing body weight or body mass index (BMI) (see section 5.2). In all women, emergency contraception should be taken as soon as possible after unprotected intercourse, regardless of the woman’s body weight or BMI.

Patients who become pregnant despite emergency contraception should be carefully evaluated for ectopic pregnancy.
The absolute risk of ectopic pregnancy is likely to be low as NORLEVO 1,5 prevents ovulation and fertilisation. Ectopic pregnancy may continue, despite the occurrence of uterine bleeding.
Therefore, NORLEVO 1,5 is not recommended for patients who are at risk of ectopic pregnancy (previous history of salpingitis or of ectopic pregnancy) (see section 4.3).
The effect of NORLEVO 1,5 on the conceptus in the event of a failure to prevent conception is not definitely known. Therefore, a pregnancy test must be performed if there is any doubt.
Its reliability is not as high as that of the familiar "pill", which is taken for at least 21 days of the menstrual cycle.
NORLEVO 1,5 should not be used diagnostically for pregnancy testing and should not be given in missed or incomplete abortion.

After NORLEVO 1,5 intake, menstrual periods are usually of normal abundance and occur at the expected date. They can sometimes occur earlier or later than expected by a few days. It is recommended to have a medical visit to initiate or adapt a method of regular contraception. In case no menstrual period occurs in the next pill-free period following the use of NORLEVO 1,5 after regular hormonal contraception, pregnancy should be ruled out.

Repeated administration within a menstrual cycle is not advisable, because of an undesirable high load of hormones for the patient and the possibility of severe disturbances of the cycle. Women

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

The use of emergency contraception does not replace the necessary precautions against sexual transmitted diseases.

Mood changes and depression

Mood changes and depression are side effects reported with the use of hormonal contraceptives including NORLEVO 1,5. 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 NORLEVO 1,5.

Endocrine disorders

The next menstrual period may occur earlier or later than usual. A health care professional should be consulted 3 weeks after taking NORLEVO 1,5 regardless of whether bleeding has occurred or not.

Other

NORLEVO 1,5 should be used with caution in women with:

- Malabsorption syndromes such as Crohn’s disease. These disorders might impair the efficacy of NORLEVO 1,5. Prescribers should exercise caution and counsel patients accordingly.
- Liver dysfunction.
- Functional ovarian cyst.
- Diabetes mellitus.
- Hypertension.

- Migraine.
- Thromboembolic disorder, especially personal or family history of thrombophilia.
- Epilepsy.
- Asthma.
- Cardiac and renal impairment.
- Conditions being treated with medicines containing ulipristal acetate (see section 4.5).

NORLEVO 1,5 contains lactose

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

4.5 Interaction with other medicines and other forms of interaction

The metabolism of NORLEVO 1,5 is enhanced by the concomitant use of liver enzyme inducers , mainly CYP3A4 enzyme inducers. Concomitant administration of efavirenz has been found to reduce plasma levels of levonorgestrel (area under curve (AUC)) by around 50 %. Medicines suspected of having similar capacity to reduce plasma levels of levonorgestrel include anticonvulsants (phenobarbitone, phenytoin, primidone and carbamazepine); rifabutin, rifampicin, griseofulvin, ritonavir, and herbal medicines containing *Hypericum perforatum* (St John's wort). The efficacy of NORLEVO 1,5 may be decreased in cases of concomitant intake of the above-mentioned medicines.

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 levonorgestrel (i.e. 3 000 µg 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 levonorgestrel during concomitant use of an enzyme inducer) has not been studied.

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

Ulipristal acetate is a progesterone receptor modulator that may interact with the progestational activity of levonorgestrel. Therefore, the concomitant use of levonorgestrel and medicines containing ulipristal acetate is not recommended.

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

4.6 Fertility, pregnancy and lactation

Pregnancy

NORLEVO 1,5 is contraindicated in pregnancy (see section 4.3).

NORLEVO 1,5 cannot interrupt an ongoing pregnancy.

In case of failure of this emergency contraception with a persisting pregnancy, epidemiological studies indicate no malformative effects of progestins on the foetus.

There is no data available on the consequences for the child if doses higher than 1,5 mg levonorgestrel are taken.

Lactation

Levonorgestrel is excreted into breast milk. Therefore, it is suggested to breastfeed immediately before taking NORLEVO 1,5 and to skip nursing at least 8 hours following NORLEVO 1,5 administration (see section 4.3).

Fertility

A rapid return to fertility is likely following treatment with NORLEVO 1,5 for emergency contraception; therefore, regular contraception should be continued or initiated as soon as possible following the use of NORLEVO 1,5 to ensure ongoing prevention of pregnancy.

4.7 Effects on ability to drive and use machines

NORLEVO 1,5 may cause drowsiness and dizziness. Patients should be advised not to drive or operate machines until it is established that their ability to perform such activities is not affected. Patients should be advised to use caution when driving a car or operating hazardous machinery until they are reasonably certain that their performance is not affected by NORLEVO 1,5.

4.8 Undesirable effects

The following undesirable effects have been reported.

MedDRA system organ class	Side Effects
Immune system disorders	
Less frequent:	Anaphylaxis or anaphylactoid reactions.
Endocrine disorders	
Frequent:	Premenstrual syndrome-like symptoms, altered menstrual cycles or irregular menstrual bleeding, spotting.
Less frequent:	Cushing's syndrome, hot flushes.
Frequency unknown:	Certain progesterones such as NORLEVO 1,5 may have an adverse effect on serum lipids.
Metabolism and nutrition disorders	
Frequent:	Changes in weight, oedema, hyperglycaemia.
Frequency unknown:	Changes in appetite.
Psychiatric disorders	
Frequent:	Nervousness, mood changes.
Less frequent:	Mental depression.
Nervous system disorders	
Frequent:	Drowsiness, dizziness, headache.
Less frequent:	Insomnia.
Vascular disorders	
Less frequent:	Adrenal suppression or insufficiency or hypotension; thromboembolism or thrombus formation.
Gastrointestinal disorders	

Frequent:	Lower abdominal pain or cramping, diarrhoea, nausea, vomiting.
Frequency unknown:	Gastrointestinal disturbances.
Hepato-biliary disorders	
Less frequent:	Alterations in liver function tests, jaundice.
Skin and subcutaneous tissue disorders	
Less frequent:	Acne, melasma or chloasma, allergic skin reactions, hair loss, hirsutism.
Musculoskeletal and connective tissue disorders	
Frequency unknown:	Loss of bone mineral density, osteoporosis, osteoporotic fracture.
Reproductive system and breast disorders	
Frequent:	Breast tenderness, uterine pain, delay of menses more than 7 days, heavy menses, bleeding not related to menses, irregular menses, spotting. Bleeding patterns may be temporarily disturbed, but most women will have their next menstrual period within 5 days of the expected time. If the next menstrual period is more than 5 days overdue pregnancy should be excluded.
Less frequent:	Galactorrhoea, breast changes including gynaecomastia, changes in libido.
General disorders and administration site conditions	
Frequent:	Fatigue, fever.

In post-marketing experience, the following additional undesirable effects have been reported.

MedDRA system organ class	Side Effects
Psychiatric disorders	
Frequency unknown:	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 of suspected adverse reactions after authorisation of NORLEVO 1,5 is important. It allows continued monitoring of the benefit/risk balance of NORLEVO 1,5. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website or to Cipla Medpro (Pty) Ltd. by email: drugsafetysa@cipla.com or telephone: 080 222 6662 (toll free).

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. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Pharmacotherapeutic groups:

ATC code: G03AD01.

Levonorgestrel is a progesterone and acts as a contraceptive by inhibiting ovulation and preventing the nidation of a fertilised ovum in the uterine mucosa.

5.2 Pharmacokinetic properties

Absorption

Oral bioavailability of levonorgestrel is approximately 100 %. The maximal plasma concentration

(approximately 40 nmol/ℓ) is reached within 3 hours.

Distribution

In the plasma levenorgestrel is strongly bound to SHBG (sex hormone binding globulin).

Biotransformation

Levonorgestrel is hydroxylated in the liver and the metabolites are excreted as glucuronide conjugates.

Elimination

After oral administration of 1,5 mg levonorgestrel the plasma terminal half-life is estimated to be 43 hours. Levonorgestrel is eliminated metabolically via the kidney (60 – 80 %) and liver (40 – 50 %).

Pharmacokinetics in obese women:

A pharmacokinetic study showed that total 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. Another study also reported a decrease of total levonorgestrel maximum serum concentration (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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal anhydrous silica

Lactose monohydrate

Magnesium stearate

Maize starch

Povidone.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

Store at or below 25 °C.

6.4 Special precautions for storage

Protect from light and moisture.

Keep the blister strip in the outer carton until required for use.

6.5 Nature and contents of container

NORLEVO 1,5 contains 1 tablet in PVC complex (PVC/PE/PVDC orange) and aluminium foil blister strip. The blister strip is enclosed in an outer cardboard**.**

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

CIPLA MEDPRO (PTY) LTD.

Building 9

Parc du Cap

Mispel Street

Bellville

7530

Customer Care: 080 222 6662

8. REGISTRATION NUMBERS

NORLEVO 1,5 mg - 44/21.8.2/0809

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 26 November 2015

10. DATE OF REVISION OF THE TEXT

23 October 2026