Professional Information for VONEL

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

VONEL 0,75 mg tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 0,75 mg levonorgestrel.

Excipient with known effect:

Contains sugar (84,5 mg lactose monohydrate per tablet).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

White to off-white, circular, flat faced, bevelled edge, uncoated tablet, debossed with “403” on one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

VONEL is indicated for the prevention of pregnancy within 72 hours of unprotected sexual intercourse or the recognisable failure of mechanical methods.

VONEL is intended for emergencies only and is completely unsuitable for regular contraception. The reliability of VONEL is not as high as that of the contraceptive, which is taken for at least 21 days of the menstrual cycle.

4.2 Posology and method of administration

Posology:

Take 2 tablets as soon as possible in a single administration.

VONEL should be taken preferably within 12 hours, but not later than 72 hours after unprotected sexual intercourse.

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

Even extremely high doses of the 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 and only mechanical and/or chemical methods of contraception (condoms, foam, pessary) may be used until the next menstrual period.

If the patient vomits within three to four hours of taking the tablet, another tablet should be taken immediately. VONEL can be used at any time during the menstrual cycle unless menstrual bleeding is overdue.

Paediatric population:

VONEL 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

- Hypersensitivity to levonorgestrel or any of the ingredients of VONEL (see section 6.1).
- Pregnancy. VONEL should not be used if there is a possibility that pregnancy already exists (e.g. if the last menstrual cycle failed to occur or if unprotected sexual intercourse has already taken place during the same cycle) (see section 4.6).
- Undiagnosed vaginal bleeding.
- History or current high risk arterial disease.
- Severe hepatic impairment.
- Depression not well controlled with treatment.
- A history of depression with the use of hormonal contraceptives.
- The repeated use of VONEL should be avoided as it constitutes undesirable hormonal stress and may result in severe cycle disturbances.

4.4 Special warnings and precautions for use

- VONEL is only intended for emergencies and is unsuitable for regular contraception use. The reliability of VONEL is not as high as that of the contraceptive, which is taken for at least 21 days of the menstrual cycle. VONEL 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 VONEL 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.
- VONEL is not recommended in patients who are at high risk of developing an ectopic pregnancy (patients with a history of salpingitis, fallopian tube surgery, pelvic inflammatory disease or ectopic pregnancy).
- Patients who become pregnant despite the use of emergency contraception, should be carefully evaluated for ectopic pregnancy.
- VONEL is not recommended in patients with severe hepatic disease, including benign or malignant liver disease (see section 4.3). The metabolism of VONEL may be impaired and VONEL may worsen the condition.
- Severe malabsorption syndromes, such as Crohn's disease, might impair the efficacy of VONEL.
- The effect of VONEL on the conceptus, in the event of a failure to prevent conception, is not definitively known. If there is any doubt, a pregnancy test must be performed.
- VONEL should not be used diagnostically for pregnancy testing and should not be given in the event of missed or incomplete abortion.
- After VONEL 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. It is recommended to make a medical appointment 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 VONEL 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.
- Women who present for repeated courses of emergency contraception should be advised to consider long-term methods of contraception.
- The use of emergency contraception, such as VONEL, does not protect against sexually transmitted diseases (STDs).
- Mood changes and depression are side effects reported with the use of hormonal contraceptives including VONEL. 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. VONEL is not recommended for use in patients with depression (see section 4.3).
- A health care provider should be consulted 3 weeks after taking VONEL, whether or not bleeding has occurred. The next menstrual cycle may occur earlier or later than usual after the use of VONEL.
- Caution is advised in patients with known or suspected breast malignancies or tumours, as VONEL may worsen conditions in some nonresponsive patients.
- The use of VONEL in patients with undiagnosed urinary tract bleeding may delay the diagnosis by masking the underlying condition.
- Caution is advised in patients with hypertension, cardiac or renal impairment, asthma, epilepsy, migraine, or any other condition which may be aggravated by fluid retention.
- VONEL may alter the metabolism of carbohydrates and decrease glucose tolerance in patients. Caution is advised in patients with diabetes mellitus.
- VONEL may be associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Lactose monohydrate:

VONEL contains lactose monohydrate (see section 6.1). Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take VONEL.

4.5 Interaction with other medicines and other forms of interaction

Efficacy may be decreased, and metabolism may be enhanced during the concomitant intake of VONEL and the following hepatic enzyme-inducing medication (mainly CYP3A4 enzyme inducers):

- Anticonvulsants (phenobarbitones, phenytoin, primidone and carbamazepine).
- Ampicillin and other antibiotics, including medicines used to treat tuberculosis (e.g. rifabutin or rifampicin).
- Griseofulvin.
- Ritonavir.
- Herbal medicines containing *Hypericum perforatum* (St John's wort).

VONEL may inhibit ciclosporin metabolism, leading to increased plasma ciclosporin concentrations and a risk of toxicity.

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 (e.g. 3 000 micrograms 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.

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

4.6 Fertility, pregnancy and lactation

Pregnancy:

VONEL is not indicated during pregnancy and should not be given to pregnant women (see section 4.3). 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 fetus. In case of unprotected coitus more than 72 hours earlier, the patient may be pregnant. In these cases, pregnancy should be excluded.

Breastfeeding:

VONEL is excreted into breast milk.

Potential exposure of an infant to VONEL can be reduced if the breastfeeding woman takes the tablet immediately after feeding and avoids nursing for at least 6 hours following VONEL administration.

Fertility:

Levonorgestrel increases the possibility of cycle disturbances which can sometimes lead to an 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

VONEL may cause side effects such as drowsiness or dizziness. Patients should only drive a vehicle or operate machinery once the effects of VONEL are known.

4.8 Undesirable effects

Immune system disorders:

Less frequent: Anaphylaxis, anaphylactoid reactions.

Endocrine disorders:

Frequent: Bleeding (not related to menses), delay of menses (more than 7 days), spotting, amenorrhoea, menometrorrhagia, menorrhagia, hyperglycaemia.

Less frequent: Adrenal insufficiency, Cushing's syndrome, premenstrual syndrome-like symptoms, alterations in serum lipid profiles.

Metabolism and nutrition disorders:

Frequency unknown: Changes in appetite, changes in weight, unusual or rapid weight gain.

Psychiatric disorders:

Frequent: Drowsiness, mood changes, nervousness.

Less frequent: Insomnia.

Frequency unknown: Mental depression.

Nervous system disorders:

Frequent: Dizziness, headache.

Vascular disorders:

Less frequent: Hypotension, thromboembolism.

Gastrointestinal disorders:

Frequent: Nausea, diarrhoea, lower abdominal pain, cramping, vomiting.

Less frequent: Gastrointestinal disturbances.

Hepato-biliary disorders:

Less frequent: Jaundice, alterations in liver function tests.

Skin and subcutaneous tissue disorders:

Less frequent: Skin rash, melasma, hot flushes, hair loss, hirsutism, acne, urticaria.

Musculoskeletal and connective tissue disorders:

Frequency unknown: Loss of bone mineral density, osteoporosis, osteoporotic fracture.

Reproductive system and breast disorders:

Frequent: Breast tenderness, ovarian enlargement, ovarian cyst formation.

Less frequent: Galactorrhoea, breast pain, decreased libido, breast changes, gynaecomastia.

General disorders and administration site conditions:

Frequent: Fatigue, oedema, unusual tiredness or weakness.

Less frequent: Fluid retention, fever.

Post-marketing experience:

The following post-marketing experiences have been reported:

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 VONEL is important. It allows continued monitoring of the benefit/risk balance of VONEL. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Overdose may cause nausea and withdrawal bleeding may occur. There are no specific antidotes and treatment is symptomatic and supportive (see section 4.8).

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.

Levonorgestrel acts as a contraceptive by inhibiting ovulation to some degree, creating changes in

the cervical mucus that inhibit fertilisation and prevent nidation of a fertilised ovum in the uterine mucosa.

5.2 Pharmacokinetic properties

Absorption

The oral bioavailability of levonorgestrel is approximately 100 %.

Maximum plasma concentration (approximately 40 nmol/L) is reached within 3 hours.

Distribution

It is strongly bound to sex hormone-binding globulin (SHBG) within the plasma.

Biotransformation

The biotransformation follows the known pathways of steroid metabolism. Levonorgestrel is hydroxylated in the liver and the metabolites are excreted as glucuronide conjugates. No pharmacologically active metabolites are known.

Elimination

Levonorgestrel is metabolically eliminated via the kidneys (60 – 80 %) and the liver (40 – 50 %). After oral administration, the plasma terminal half-life is approximately 43 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silicon dioxide

Corn starch

Hypromellose

Lactose monohydrate

Magnesium stearate

Talcum.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from light.

Keep blister strip in outer carton until required for use.

6.5 Nature and contents of container

Silver aluminium/clear PVC blister strip containing 2 tablets. One blister strip is packed into an outer carton.

Pack size: 2 tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Ranbaxy Pharmaceuticals (Pty) Ltd

14 Lautre Road

Stormill, Ext. 1

Roodepoort

Johannesburg 1724

8. REGISTRATION NUMBER

49/21.8.2/0574

9. DATE OF FIRST AUTHORISATION

30 September 2016.

10. DATE OF REVISION OF THE TEXT

03 May 2023

Namibia NS1 20/18.7/0105

Signed: