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. The use of VONEL does not contraindicate the continuation of regular hormonal contraception.
Women who have used enzyme-inducing drugs during the last 4 weeks and need emergency contraception are recommended to use a non-hormonal EC, i.e. Cu-IUD or take a double dose of levonorgestrel (i.e. 4 tablets taken together) for those women unable or unwilling to use Cu-IUD (see section 4.5).

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 or suspected 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.
- Repeated administration within a menstrual cycle is not advisable because of the possibility of disturbance of the cycle.
- The use of emergency contraception, such as VONEL, does not protect against sexually transmitted diseases (STDs).
- Limited and inconclusive data suggest that there may be reduced efficacy of VONEM 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.
- 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. Prescribers should inform their patients to contact their doctor for advice if they experience mood changes and depression whilst on treatment with VONEL. VONEL is not recommended for use in patients with depression (see section 4.3).
- 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):

- Concomitant administration of efavirenz has been found to reduce plasma levels of levonorgestrel (AUC) by around 50 %.
- 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 foetus.

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 8 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.

After treatment with levonorgestrel a rapid return to fertility is expected and therefore, regular contraception should be continued or initiated as soon as possible after the use of VONEL.

4.7 Effects on ability to drive and use machines

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

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

a. Summary of the safety profile

The most frequently reported side effect is nausea.

b. Tabulated summary of adverse reactions

System Organ Class	Frequency	Undesirable effect

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:

System Organ Class	**Frequency**	**Undesirable effect**
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
Psychiatric disorders	Frequency unknown	Severe depression with a higher risk of suicidal thoughts/behaviour and suicide

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 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.

Suspected adverse reactions can also be reported directly to the HCR via email: pharmacovigilance.africasme@sunpharma.com or tel: +27(0) 12 643 2000.

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 is 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 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.

Levonorgestrel is not effective once the process of implantation has begun.

Results from a study on 1,50 mg levonorgestrel, taken within 72 hours of unprotected sex, prevents 84 % of expected pregnancies. At the recommended regimen, levonorgestrel is not expected to induce significant modification of blood clotting factors, and lipid and carbohydrate metabolism.

5.2 Pharmacokinetic properties

Absorption

Orally administered levonorgestrel is rapidly and almost completely absorbed.
The oral bioavailability of levonorgestrel is approximately 100 %.
Maximum plasma concentration (approximately 40 nmol/L) is reached within 2 hours.

Distribution

Levonorgestrel is strongly 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. Levonorgestrel is hydroxylated in the liver and the metabolites are excreted as glucuronide conjugates. 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 AUC0-24), 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.

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

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8. REGISTRATION NUMBER

49/21.8.2/0574

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30 September 2016.

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26 January 2026.

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