PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

METROGEL V Vaginal Gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Metronidazole 37,5 mg/5g

Excipient with known effect:

Methyl hydroxybenzoate 4,0 mg/5 g (preservative)

Propyl hydroxybenzoate 1,0 mg/5 g (preservative)

Propylene glycol 150 mg /5 g

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Vaginal gel

A colourless to straw-coloured, transparent, slightly hazy, single-phase gel.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

METROGEL V is indicated for the treatment of bacterial vaginosis.

4.2 Posology and method of administration

Posology

One applicator full of METROGEL V (5 g) should be inserted into the vagina once daily, at bedtime, for 5 days. If the patient does not respond to initial therapy it is recommended that appropriate laboratory measures be used to rule out conditions other than bacterial vaginosis before repeating the treatment.

METROGEL V is not recommended for use during menses.

Paediatric population

METROGEL V is not recommended for use in children since safety and effectiveness have not been established.

Method of administration

For vaginal administration.

Pierce the sealed end of the tube and screw the end of the applicator tightly onto the tube of gel. Squeeze the tube, filling the applicator with gel. Remove applicator from the tube and gently insert the applicator into the vagina as far as it will comfortable go. Push the plunger to release the gel. Dispose of the applicator as instructed.

4.3 Contraindications

- METROGEL V is contra-indicated in patients with a prior history of hypersensitivity to metronidazole, other nitroimidazoles or parabens listed in section 6.1.

4.4 Special warnings and precautions for use

See section 4.2 above.

Approximately 6-10 % of patients treated with METROGEL V Vaginal Gel developed symptomatic Candida vaginitis during or immediately after therapy. This may be due to known or previously unrecognised vulvovaginal candidiasis which may present with more prominent symptoms during therapy. METROGEL V vaginal gel contains ingredients that may cause burning and irritation of the eye. In the event of accidental contact with the eye, rinse the eye with copious amounts of cool tap water.

Reactions seen with oral metronidazole may also occur with METROGEL V.

In patients with renal failure, there is no accumulation of metronidazole, however the hydroxy and acid metabolites are retained. Haemodialysis removes both metronidazole and the two metabolites. Although patients with severe hepatic dysfunction metabolise metronidazole slowly leading to retention of metronidazole and its metabolites, a total treatment course of 187,5 mg is unlikely to lead to excessive serum levels. Known or previously unrecognized candidiasis may present more prominent symptoms during therapy with METROGEL V and may require treatment with a candicidal medicine.

Metronidazole is a nitroimidazole and should be used with care in patients with evidence of a history of blood dyscrasias. Leukopenia has been observed during oral metronidazole administration.

Metronidazole may interfere with certain types of determination of serum chemistry values, such as aspartate aminotransferase (AST, SGOT), alanine aminotransferase (ALT, SGPT), lactic dehydrogenase (LDH), triglycerides and glucose hexokinase. Values of zero may be observed.

Seizures and peripheral neuropathy have been reported. METROGEL V should be administrated with caution in patients with central nervous system diseases.

Cases of severe hepatotoxicity/acute hepatic failure, including cases with a fatal outcome with very rapid onset after treatment initiation in patients with Cockayne syndrome have been reported with products containing metronidazole for systemic use. In this population, metronidazole should therefore be used after careful benefit-risk assessment and only if no alternative treatment is available. Liver function tests must be performed prior to the start of therapy, throughout and after end of treatment until liver function is within normal ranges, or until the baseline values are reached. If the liver function tests become markedly elevated during treatment, METROGEL V should be discontinued.

Patients with Cockayne syndrome should be advised to immediately report any symptoms of potential liver injury to their medical practitioner and stop using METROGEL V.

4.5 Interactions with other medicines and other forms of interactions

Oral metronidazole has been associated with a disulfiram-like reaction. The possibility of a similar reaction occurring with METROGEL V cannot be excluded.

Alcohol: Concurrent usage of oral metronidazole and alcohol may result in a disulfiram-like reaction. Despite the relatively low serum levels of metronidazole produced following administration of METROGEL V, the possibility of a disulfiram-like reaction to alcohol while on METROGEL V therapy cannot be excluded. Patients should be cautioned about drinking alcohol while being treated with METROGEL V vaginal gel.

Carmustine (BCNU) or cyclophosphamide: METROGEL V should be used with caution in patients receiving these medicines.

Ciclosporin and 5-Fluorouracil: Oral metronidazole has been shown to increase the plasma concentrations of ciclosporin and 5-fluorouracil. Although, vaginal administration of metronidazole results in markedly lower plasma metronidazole concentrations when compared to oral metronidazole, the possibility of these interactions cannot be ruled out.

Lithium treatment should be tapered or withdrawn prior to administrating metronidazole. Concomitant administration may lead to lithium retention and the possibility of renal damage.

Oral metronidazole has been reported to potentiate the anticoagulant effect of warfarin and other coumarin anticoagulants, resulting in a prolongation of prothrombin time. This possible drug interaction should be considered when METROGEL V is prescribed for patients on this type of anticoagulant therapy.

4.6 Fertility, pregnancy and lactation

Pregnancy

METROGEL V is contraindicated during pregnancy.

Breastfeeding

Metronidazole is secreted in milk at concentrations similar to those in serum.

4.7 Effects on ability to drive and use machines

METROGEL V, vaginal gel has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Nervous system disorders	Headache, dizziness
Gastrointestinal disorders	Abdominal cramping or pain, nausea, metallic taste in the mouth, diarrhoea, constipation, decreased appetite, gastrointestinal discomfort
Skin and subcutaneous tissue disorders	Generalised rash/pruritus
Reproductive system and breast disorders	Vaginal candidiasis, vulvovaginal itching/burning/swelling, increased pelvic pressure and abnormal vaginal discharge, yeast infection
Post-Marketing Data	
Immune system disorders	*Very rare:* Allergic reaction
Nervous system disorders	*Very rare:* Dizziness, headache, paraesthesia
Gastrointestinal disorders	*Very rare:* Vomiting, incoordination, insomnia, flushing, cystitis, incontinence and modification of taste, abdominal pain, diarroea, nausea
Skin and subcutaneous tissue disorders	*Very rare:* Pruritus genital, rash, urticaria
Reproductive system and breast disorders	*Very rare:* Leukorrhoea, vaginitis, vulvar disorder
General disorders and administration site conditions	*Very rare:* Application site reaction

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 via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

There is no human experience of overdosage with METROGEL V. Treatment is symptomatic and supportive. Metronidazole is readily removed from the plasma by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 20.2.6 Antimicrobial: medicines against protozoa.

Metronidazole is a synthetic antibacterial agent. The antimicrobial effects result from the disruption of DNA and the inhibition of nucleic acid synthesis. Metronidazole has been shown to have activity against the following pathogens: Gardnerella vaginalis, bacteroides species and Mycoplasma hominis.

5.2 Pharmacokinetic properties

After intra-vaginal administration of METROGEL V, serum concentrations of metronidazole are about 2 % of the maximum serum concentrations reached with a 500 mg tablet taken orally. Metronidazole is metabolised in the liver by side chain oxidation and glucuronide formation and a large portion of the absorbed dose is excreted as metabolites. Both unchanged drug and metabolites are excreted mainly in the urine with about 35 – 65 % of the absorbed dose recovered over 24 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Carbomer 974P

Edetate disodium

Methylparaben (preservative)

Propylene glycol

Propylparaben (preservative)

Sodium hydroxide*

Purified water

6.2 Incompatibilities

None

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 30 °C.

6.5 Nature and contents of container

Aluminium tubes with polyethylene screw caps containing 40 g product. The product is packed with five, 5 g vaginal applicators.

6.6 Special precautions for disposal and other handling

No special precautions

7. HOLDER OF CERTIFICATE OF REGISTRATION

iNOVA PHARMACEUTICALS (PTY) LTD

15 E Riley

Bedfordview

South Africa

2007

8. REGISTRATION NUMBERS

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23 October 2000

10. DATE OF REVISION OF THE TEXT

31 August 2021