173mm

400mm

MetroGel® V

VAGINAL GEL / VAGINALE GEL
metronidazole / metronidasool 0,75 %

SCHEDULING STATUS

S2

PROPRIETARY NAME AND DOSAGE FORM

METROGEL® V, Vaginal Gel.

COMPOSITION

Metronidazole 37,5 mg/5 g
Preservatives: Methyl hydroxybenzoate 0,08 % *m/m*
Propyl hydroxybenzoate 0,02 % *m/m*
Excipients include carbomer 974P, edetate disodium, propylene glycol and purified water.

PHARMACOLOGICAL CLASSIFICATION

A 20.2.6 Antimicrobial: medicines against protozoa.

PHARMACOLOGICAL ACTION

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.

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.

INDICATIONS

METROGEL® V is indicated for the treatment of bacterial vaginosis.

CONTRAINDICATIONS

METROGEL® V is contraindicated in patients with a prior history of hypersensitivity to metronidazole, other nitroimidazoles or parabens.

PREGNANCY AND LACTATION

METROGEL® V is contraindicated during pregnancy.

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

WARNINGS

See **DOSAGE AND DIRECTIONS FOR USE**.

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 unrecognised candidiasis may present more prominent symptoms during therapy with **METROGEL® V** and may require treatment with a candicidal agent.

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 physician and stop using **METROGEL® V**.

DOSAGE AND DIRECTIONS FOR USE

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 comfortably go. Push the plunger to release the gel. Dispose of the applicator as instructed.

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.

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

SIDE EFFECTS AND SPECIAL PRECAUTIONS

Adverse reactions are: vaginal candidiasis, vulvovaginal itching/burning/swelling, increased pelvic pressure and abnormal vaginal discharge. Abdominal cramping or pain, nausea, metallic taste in the mouth, diarrhoea, constipation, decreased appetite, decreased/increased white blood cells, headache, dizziness, and generalised rash/pruritis may occur.

Leukopenia was observed in some patients, but this was not clinically significant.

In addition, post-marketing experience revealed the following adverse events: vomiting, incoordination, insomnia, flushing, cyctitis, incontinence and modification of taste.

Interaction with other medication

Oral metronidazole has been associated with a dissulfiram-like reaction.

The possibility of a similar reaction occurring with **METROGEL® V** cannot be excluded.

Lithium treatment should be tapered or withdrawn prior to administering 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.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

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

IDENTIFICATION

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

PRESENTATION

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

STORAGE INSTRUCTIONS

Store at or below 30 °C.

KEEP OUT OF REACH OF CHILDREN

REGISTRATION NUMBER

33/20.2.6/0243

NAME AND BUSINESS ADDRESS OF APPLICANT

iNova Pharmaceuticals (Pty) Ltd
15E Riley Road, Bedfordview 2007

DATE OF PUBLICATION OF THIS PACKAGE INSERT

23 October 2000

BOTSWANA
Scheduling status: S2
Pharmacological classification: ATC: GOIA F01-Anti-infectives and antiseptics excl. combinations with corticosteroids, imidazole derivatives
Registration number: BOT 0200490

ZIMBABWE
Scheduling status: Prescription Preparation (PP)
Pharmacological classification: 14.17 Dermatological and topical preparations: Vaginal preparations
Registration numbers: 2000/14.17/3648

NAMIBIA
Scheduling status: NS1
Registration number: 10/20.2.6/0472

HOW TO USE THE APPLICATORS

Your tube of **METROGEL® V** vaginal gel is packed in a box which also contains five throw away vaginal applicators.

When filled with gel, each applicator contains one single dose of **METROGEL® V** gel for application into the vagina.

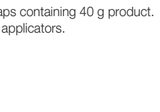
Hygiene

To ensure maximum hygiene, always

- wash your hands before opening the tube or touching the applicators
- use a new applicator for each dose
- immediately throw away the used applicator in the waste bin

Opening the tube

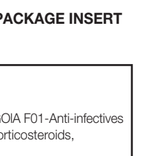
Before using **METROGEL® V** vaginal gel for the first time, you will need to puncture the metal seal on the tube. To do this, simply unscrew the cap from the tube and pierce the seal using the pointed tip of the cap [1].



Filling the applicator

Remove an applicator from the wrapper. Unscrew the cap from the tube and screw the open end of the applicator onto the tube [2].

Squeeze the tube slowly from the bottom to fill the applicator with gel: the plunger will move as the applicator fills and will stop moving when the applicator contains the correct amount of gel [3].



Unscrew the applicator and replace the cap on the tube.

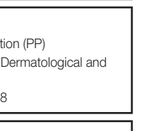
Inserting the applicator

Hold the filled applicator by its barrel and gently insert it into your vagina as far as it will comfortably go [4].

You may find it easier to do this whilst lying on your back with your knees bent; alternatively, choose any position you find comfortable.

Applying the gel

Slowly press the plunger to deposit the gel into your vagina; continue pressing until the plunger stops (this will ensure you have released the correct amount of gel) [5].



Remove the applicator from the vagina and throw it in the waste bin immediately.

YOU MAY WANT TO READ THIS LEAFLET AGAIN. PLEASE DO NOT THROW IT AWAY UNTIL YOU HAVE FINISHED YOUR MEDICINE.

iNova Pharmaceuticals (Pty) Ltd
15E Riley Road, Bedfordview 2007
128413-0206 6203 5539 2

LT027603

LT054.03.17

MetroGel® V

VAGINAL GEL / VAGINALE GEL
metronidazole / metronidasool 0,75 %

SKEDULERINGSTATUS

S2

EIENDOMSNAAM EN DOSEERVORM

METROGEL® V, Vaginale Gel.

SAMESTELLING

Metronidasool 37,5 mg/5 g
Preserveermiddels: Metielhidroksiebensoaat 0,08 % *m/m*
Propielhidroksiebensoaat 0,02 % *m/m*
Ander onaktiewe bestanddele sluit karbomeer 974P, dinatriumedetaat, propileenglikool en gesuiwerde water in.

FARMAKOLOGIESE KLASSIFIKASIE

A 20.2.6 Antimikrobies: middels teen protosoë.

FARMAKOLOGIESE WERKING

Metronidasool is 'n sintetiese antibakteriese middel. Die antimikrobiese effekte is die resultaat van die versteuring van DNA en die inhibisie van nukleïensuur sintese. Metronidasool toon aktiwiteit teen die volgende patogene: Gardnerella vaginalis, bakterioïed spesies en Mikoplasma hominis.

Na intra-vaginale toediening van **METROGEL® V**, is die serum konsentrasies van metronidasool ongeveer 2 % van die maksimum serum konsentrasies wat bereik word na 'n oraal geneemde 500 mg tablet.

Metronidasool word gemetaboliseer in die lewer deur syketting oksidasie en glukoronied formasie en 'n groot gedeelte van die geabsorbeerde dosis word uitgeskei as metaboliete. Beide onveranderde geneesmiddel en metaboliete word hoofsaaklik in die urien uitgeskei en omtrent 35 - 65 % van die geabsorbeerde dosis word herwin oor 24 uur.

INDIKASIES

METROGEL® V is aangedui vir die behandeling van bakteriële vaginose.

KONTRA-INDIKASIES

METROGEL® V is gekontra-indikeerd in pasiënte met 'n bestaande geskiedenis van hipersensitiwiteit vir metronidasool, ander nitroimidasole of parabene.

SWANGERSKAP EN BORSVOEDING

METROGEL® V is gekontra-indikeerd gedurende swangerskap. Metronidasool word uitgeskei in borsmelk in konsentrasies gelykstaande aan dié gevind in serum.

WAARSKUWINGS

Sien **DOSIS EN GEBRUIKSAANWYSINGS.**

Reaksies waargeneem tydens die orale inname van metronidasool mag ook voorkom met **METROGEL® V**.

Daar is geen akkumulasie van metronidasool in pasiënte met nierversaking nie maar die hidroksie- en suurmetaboliete word teruggehou. Hemodialiese verwyder beide metronidasool en die twee metaboliete.

Ten spyte daarvan dat pasiënte met erge lewerfunksie inkorting metronidasool stadig metaboliseer en metronidasool en sy metaboliete behou word, is dit onwaarskynlik dat 'n totale behandelings kurses van 187,5 mg tot uitermatige serum vlakke sal lei.

Bekende of voorheen, ongediagnoseerde kandidiase mag meer prominente simptome tot gevolg hê gedurende die behandeling met **METROGEL® V** en mag behandeling met 'n kandida teenmiddel vereis.

Metronidasool is 'n nitroimidasool en moet met omsigtigheid gebruik word in pasiënte met 'n geskiedenis van bloedsiektes. Leukopenie is al waargeneem gedurende orale metronidasool toediening.

Metronidasool mag sekere bepalings van chemiese serum waardes, soos aspartaat aminotransferase (AST, SGOT), alanien aminotransferase (ALT, SGPT), laktiese dehidrogenase (LDH), trigliseriedes en glukose heksokinase belemmer. Nul waardes mag waargeneem word.

Konvulsies en perifere neuropatie is al gerapporteer. **METROGEL® V** moet met omsigtigheid gebruik word in pasiënte wat aan sentrale senuweestelsel siektes lei.

Na die sistemiese gebruik van metronidasool bevattende produkte, was gevalle van erge hepatotoksisiteit of akute lewerversaking, insluitend fatale gevalle, met 'n baie vinnige aanvang, in pasiënte met Cockayne sindroom gerapporteer.

Die risiko moet dus vasgestel word in hierdie pasiënte en metronidasool moet slegs gebruik word indien geen alternatiewe behandeling beskikbaar is nie.

Lewerfunksie toetse moet voor, tydens en na die behandeling uitgevoer word totdat die lewerfunksie terugkeer na normaal of totdat die basislynwaarde verkry is.

As die lewerfunksie toetse merkbaar verhoog gedurende die gebruik van **METROGEL® V**, moet die behandeling gestaak word.

Pasiënte met Cockayne sindroom moet aangeraai word om enige potensiële simptome van lewer beskadiging onmiddelik by hul dokters aan te meld en onmiddelik **METROGEL® V** te staak.

DOSIS EN GEBRUIKSAANWYSINGS

Vir vaginale toediening.

Deursteek die geseëlde deel van die buis en skroef die punt van die applikator styf aan die buis van gel vas. Druk die buis om die toediener met gel te vul. Verwyder die toediener van die buis af en plaas die toediener sagkuns in die vagina in so ver as wat dit gemaklik sal ingaan. Druk die dompelaar om die gel vry te stel. Gooi die toediener weg soos aangedui.

Een vol toediener van **METROGEL® V** (5 g) behoort intra-vaginaal toegedien te word, een maal per dag, voor slaaptyd, vir 5 dae.
Indien die pasiënte nie op die behandeling reageer nie, word dit aanbeveel dat die toepaslike laboratoriese maatstawwe geneem word om toestande, anders as bateriële vaginose, uit te skakel voordat die behandelings kursus herhaal word.

METROGEL® V word nie aanbeveel vir gebruik gedurende menstruasie nie.

METROGEL® V word nie aanbeveel vir gebruik in kinders nie aangesien die veiligheid en effektiwiteit nie vasgestel is nie.

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS

Newe-effekte is as volg: vaginale kandidiase, vulvovaginale jeuk/brand/swelling, verhoogde pelviese druk en abnormale vaginale afskeiding. Abdominale krampe of pyn, naarheid, metaal smaak in die mond, diaree, konstipasie, verminderde aptyt, verlaagde/verhoogde witbloedselle, hoofpyn, lighoofdigheid en algemene uitslag/pruritis mag voorkom.

Leukopenie is al waargeneem in sommige pasiënte maar dit was nie klinies relevant nie.

Bykomend het na-bemarkings ondervinding die volgende newe-effekte onthul: braking, gebrek aan koördinasie, slapeloosheid, blosing, sistitis, inkontinensie en verandering van smaak.

Interaksie met ander medikasie

Orale metronidasool is al geassosieer met 'n disulfiram-tipe reaksie. Die moontlikheid van 'n soortgelyke reaksie met **METROGEL® V** kan nie uitgesluit word nie.

Litium behandeling behoort ooreenkomstig verminder of onttrek te word voordat metronidasool toegedien word. Gelyktydige toediening mag lei tot litium retensie en die moontlikheid van nierskade.

Orale metronidasool is al gerapporteer om die antikoagulant effek van warfarien en ander coumarin antikoagulante te verhoog, met gevolglike verlenging van protrombien tyd. Hierdie interaksie behoort in ag geneem te word indien **METROGEL® V** aan pasiënte voorgeskryf word wat op hierdie tipe antikoagulant behandeling is.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN

Daar is geen menslike ondervinding van oordosering met **METROGEL® V** nie. Behandeling is simptomaties en ondersteunend.

Metronidasool is maklik verwyderbaar uit die plasma deur middel van hemodialiese.

IDENTIFIKASIE

'n Kleurlose tot strooikleurige, deurskynende, effe wasige, enkel fase gel.

AANBIEDING

Aluminium buise met polipropileen aanskroef doppies wat 40 g gel bevat. Die produk is verpak met vyf, 5 g vaginale toedieners.

BERGINGSAANWYSINGS

Bewaar teen of benede 30 °C.

HOU BUITE BEREIK VAN KINDERS

REGISTRASIENOMMER

33/20.2.6/0243

NAAM EN BESIGHEIDSADRES VAN DIE APPLIKANT

iNova Pharmaceuticals (Pty) Ltd
Rileyweg 15E, Bedfordview 2007

DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET

23 Oktober 2000

HOE OM DIE TOEDIENERS TE GEBRUIK

U buisie **METROGEL® V** word in 'n kartonhouer verpak wat ook 5 wegdoenbare vaginale toedieners bevat. Wanneer met gel gevul is, bevat elke toediener 'n enkel dosis **METROGEL® V** vir toediening in die vagina.

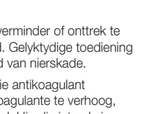
Higiëne

Doen altyd die volgende om maksimum higiëne te verseker:

- Was u hande voordat u die buisie oopmaak of aan die toedieners raak.
- Gebruik 'n nuwe toediener vir elke dosis.
- Gooi die toediener onmiddellik na gebruik weg.

Hoe om die buisie oop te maak

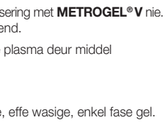
Voordat u **METROGEL® V** vir die eerste keer gebruik, is dit nodig om die metaal seël op die buisie te prik. Doen dit deur eenvoudig die proppie van die buisie te verwyder en die seël met die skerp punt op die proppie te prik [1].



Hoe om die toediener te vul

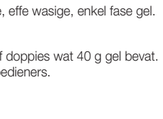
Verwyder 'n toediener uit die omhulsel, Verwyder die proppie van die buisie en skroef die oop kant van die toediener op die buisie. Druk die buisie stadig vanaf die onderkant om die toediener te vul. Namate die toediener opvul, sal die plunjer beweeg. Die plunjer sal stop wanneer die toediener die korrekte hoeveelheid gel bevat [2].

Skroef die toediener af en plaas die proppie terug op die buisie [3]



Hoe om die gevulde toediener te gebruik

Hou die toediener aan die silinder vas en druk dit versigtig in u vagina in tot so diep as wat dit gemaklik sal gaan [4].



Dit mag makliker wees om dit te doen wanneer u op u rug lê met u knieë gebuig; alternatiewelik kan u enige posisie gebruik wat vir u gemaklik is.

Hoe om die gel toe te dien

Druk die plunjer stadig in om die gel in u vagina te deponeer; hou aan druk totdat die plunjer nie meer verder wil beweeg nie (dit sal verseker dat u die korrekte hoeveelheid gel vrygestel het) [5].

Verwyder die toediener van die vagina en gooi dit onmiddellik weg.

U MAG MOONTLIK HIERDIE BLAADJIE WEER WIL LEES. MOET DIT DAAROM NIE WEGGOOI VOORDAT U NIE U MEDISYNE KLAAR GEBRUIK HET NIE.

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