Summary of Product Characteristics

1. Name of the medicinal product
METROGYL V GEL
(Metronidazole Gel USP)

2. Qualitative and quantitative composition
Each gram of gel contains:
Metronidazole USP……..10 mg
Water soluble gel base……q.s.

3. Pharmaceutical form
Vaginal gel

4. Clinical particulars
4.1 Therapeutic indications
Metrogyl V gel is indicated in the treatment of bacterial vaginosis (formerly referred to as *Haemophilus vaginitis*, *Gardnerella vaginitis*, non-specific vaginitis, *Corynebacterium* vaginitis, or anaerobic vaginosis).
NOTE: For purposes of this indication, a clinical diagnosis of bacterial vaginosis is usually defined by the presence of a homogeneous vaginal discharge that (a) has a pH of greater than 4.5, (b) emits a "fishy" amine odor when mixed with a 10% KOH solution, and (c) contains clue cells on microscopic examination. Gram's stain results consistent with a diagnosis of bacterial vaginosis include (a) markedly reduced or absent *Lactobacillus* morphology, (b) predominance of *Gardnerella* morphotype, and (c) absent or few white blood cells.
Other pathogens commonly associated with vulvovaginitis, e.g., *Trichomonas vaginalis*, *Chlamydia trachomatis*, *N. gonorrhoeae*, *Candida albicans*, and *Herpes simplex* virus should be ruled out.

4.2 Posology and method of administration
The recommended dose is one applicator full of Metrogyl V-Gel (approximately 5 grams containing approximately 50 mg of metronidazole) intravaginally twice daily for 5 days. The medication should be applied once in the morning and once in the evening.

4.3 Contraindications
Metrogyl V-Gel is contraindicated in patients with a prior history of hypersensitivity to metronidazole, parabens, other ingredients of the formulation, or other nitroimidazole derivatives.

4.4 Special warnings and precautions for use
General
Patients with severe hepatic disease metabolize metronidazole slowly. This results in the accumulation of metronidazole and its metabolites in the plasma. Accordingly, for such patients, metronidazole get should be administered cautiously. Known or previously unrecognized vaginal candidiasis may present more prominent symptoms during therapy with metronidazole vaginal gel. Approximately 6% of patients' vaginitis during or immediately after therapy.
The patient should also be instructed to not to engage in vaginal intercourse during treatment with this product.
Warning
- If significant irritation develops from the use of this medication. Discontinue use and consult your physician.

- Do not use during pregnancy except under the supervision of a physician.
- Keep this and all medications out of reach of children.
- For vaginal use only. Not for use in the eyes or on the skin or mouth.

4.5 Interaction with other medicinal products and other forms of interaction

Disulfiram-like reactions to alcohol has been reported with oral metronidazole, thus the possibility of such a reaction occurring while on metronidazole vaginal gel therapy cannot be excluded.

The patient should be informed not to drink alcohol while being treated with metronidazole vaginal gel. While blood levels are significantly lower with Metrogyl V-gel than with usual doses of oral metronidazole, a possible interaction with alcohol cannot be excluded.

Oral metronidazole has been shown to increase the plasma concentrations of warfarin and other coumarin anticoagulants resulting in a prolongation of prothrombin time. The effect of topical metronidazole on prothrombin time is unknown. It has also been shown to increase the plasma concentrations of lithium, cyclosporin and 5-fluorouracil. Similar effects after vaginal administration of metronidazole are not expected due to the low plasma concentrations but cannot be completely ruled out.

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 hexokinase glucose. Values of zero may be observed.

4.6 Fertility, pregnancy and breastfeeding

Pregnancy

There are, however, no adequate and well- controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

Breast-feeding

Specific studies of metronidazole levels in human milk following administered metronidazole have not been performed. However, metronidazole is secreted in human milk in concentration similar to those found in plasma following oral administration of metronidazole. Because of the potential for tumorigenicity shown for metronidazole in mouse and rat studies, a decision should be made whether to discontinue nursing or to discontinue the drug taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

Metrogyl V Gel has no influence on the ability to drive and use machines.

4.8 Undesirable effects

In controlled clinical trials involving 759 patients, the most commonly reported ADRs were urogenital (26%) and gastrointestinal (14%).

The following spontaneous adverse experiences have been reported, and within each system organ class, are ranked by frequency, using the following convention:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)

Infections and infestations	
Common:	Vaginal candidiasis.

Metabolism and nutrition disorders	
Common:	Decreased appetite
Psychiatric Disorders	
Uncommon:	Depression, difficulty sleeping.
Nervous system disorders	
Common:	Headache, dizziness.
Uncommon:	Paraesthesia, hypoesthesia, dysgeusia (metallictaste).
Gastrointestinal disorders	
Common:	GI discomfort/abdominal cramps, vomiting,unpleasant taste/unusual feeling on tongue.
Uncommon:	Diarrhoea, constipation, abdominal bloating/noises,nausea, dry mouth.
Skin and subcutaneous tissue disorders	
Common:	Dry skin, erythema, pruritus, skin discomfort(burning, pain of skin/stinging), skin irritation.
Not known	Urticaria
Musculoskeletal and connective tissue disorders	
Uncommon:	Cramp.
Renal and urinary disorders	
Uncommon:	Urine discolouration, urinary tract infection symptoms.

4.9 Overdose

There is no human experience of overdosage with Metrogyl V gel. There is no specific treatment. Metronidazole is readily removed from the plasma by haemodialysis

5. Pharmaceutical properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Gynecological anti-infectives and antiseptics

ATC code: G01 AF01

Metronidazole is a synthetic antibacterial agent which also possesses amoebicidal activity. Metrogyl V gel has been shown *in vivo* to be active against the vaginal pathogens Gardnerella vaginalis and bacteroides species.

Significant increases in lactobacilli are observed in bacterial vaginosis patients following therapy with Metrogyl V gel.

5.2 Pharmacokinetic properties

Bioavailability studies on the administration of a single 5 gram dose of Metrogyl V gel into the vagina of 12 normal subjects showed a mean C_{max} serum concentration of 237 nanogram/ml or about 2% of the mean maximum serum concentration of a 500 mg tablet taken orally (mean C_{max} = 12,785 ng/ml). Under normal usage, the formulation therefore affords minimal serum concentrations of metronidazole.

Metronidazole has a large apparent volume of distribution and has the ability to penetrate the blood brain barrier and blood cerebro-spinal fluid barrier at concentrations similar to serum concentrations.

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.

5.3 Preclinical safety data
At high doses metronidazole has been found to be mutagenic in bacteria but not in mammalian cells *in vitro* or *in vivo*. A carcinogenic potential has been demonstrated in mouse and rat but not in hamster. In epidemiological studies, no evidence of increased risk of cancer as a consequence of exposure to metronidazole has been observed.

6. Pharmaceutical particulars
6.1 List of excipients
Propyl Hydroxybenzoate BP
Propylene Glycol BP
Polyacrylic Acid Polymer (Carbomer 940) NF
Disodium Edetate BP
Sodium Hydroxide (Pellets) BP
Purified Water BP

6.2 Incompatibilities
Not Applicable

6.3 Shelf life
3 years

6.4 Special precautions for storage
Store at a temperature not exceeding 30°C. Protect from light.

6.5 Nature and content of container
30 g Laminated tube packed in a carton along with leaflet.

6.6 Special precautions for disposal and other handling
Not Applicable

7. Marketing authorization holder

UNIQUE PHARMACEUTICAL LABORATORIES
(A Div. of J. B. Chemicals and Pharmaceuticals Ltd.)
Neelam Centre, B wing, 4th Floor, Hind Cycle Road,
Worli Mumbai – 400 030

8. Marketing Authorization Number
06833/5892/NMR/2018

9. Date of First Authorization/Renewal of the Authorization
28/11/2021

10. Date of revision of the text
27/07/2023