Summary of Product Characteristics

IMAZOLE PLUS

Metronidazole, Clotrimazole & Lactobacillus Pessaries

1. NAME OF THE MEDICINAL PRODUCT:

Imazole Plus

2. QUALITATIVE & QUANTITATIVE COMPOSITION:

Each vaginal pessary contains Metronidazole BP 500mg; Clotrimazole BP 100mg; Lactobacillus spores 150 million spores

For excipients see section 6.1

3. PHARMACEUTICAL FORM:

Vaginal Pessary

White to off white bullet shaped pessaries.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

IMAZOLE PLUS pessary is indicated for vaginal infection like Trichomoniasis, bacterial vaginosis, and Vulvo – vaginal candidiosis.

4.2 Posology and Method of Administration:

One IMAZOLE PLUS vaginal pessary to be inserted preferably at bed time for 6 consecutive nights.

4.3 Contraindications:

IMAZOLE PLUS is contraindicated in women with hypersensitivity and/or allergy to any components of the product.

4.4 Special warnings and precautions for Use:

Precautions:

- Discontinue the treatment if irritation and/or sensitivity occurred
- Avoid usage in first trimester of pregnancy
- Previous history of sexually transmitted disease or exposure to partner with sexually transmitted disease
- Aged under 16 or over 60 years
- Known hypersensitivity to imidazoles or other vaginal antifungal products
- Not to be taken orally.
- Keep medicine out of reach of children

Warnings:

- Irregular vaginal bleeding
- Abnormal vaginal bleeding or a blood-stained discharge
- Vulval or vaginal ulcers, blisters or sores
- Lower abdominal pain or dysuria
- Any adverse events such as redness, irritation or swelling associated with the treatment
- Fever or chills
- Nausea or vomiting
- Diarrhoea
- Foul smelling vaginal discharge

4.5 Interaction with other medicinal products and other forms of interaction:

- Inhibits metabolism of warfarin and potentiates the anticoagulant effect
- Causes an intolerance to alcohol similar to disulfiram (therefore, avoid alcohol for 24 h after administration) abdominal cramps, nausea, vomiting, headaches and flushing occur when co-ingested with alcohol
- Cimetidine prolongs the plasma clearance by inhibiting metabolic enzymes; conversely, drugs that induce liver enzymes (e.g. Phenobarbital) may increase the elimination of metronidazole
- May impair barrier contraceptives
- Concomitant medication with vaginal Clotrimazole and oral tacrolimus might lead to increased tacrolimus plasma levels. Patients should thus be closely monitored for signs and symptoms of tacrolimus overdosage, if necessary by determination of the respective plasma levels

  Laboratory tests have suggested that, when used together, this product may cause damage to latex contraceptives.

4.6 Pregnancy and Lactation:

Metronidazole crosses the placental barrier and it effects human fetal organogenesis therefore its use in pregnancy should be carefully evaluated. Metronidazole is excreted in human milk hence unnecessary exposure to the drug should be avoided.

4.7 Effects on ability to drive and use machines:

None known

4.8 Undesirable Effects:

Digestive upsets: Abdominal cramps, nausea, vomiting, diarrhea, oral mucositis, taste disorders, loss of appetite, exceptional and reversible cases of pancreatitis.

Allergic reactions: Rash, pruritus, flushing, urticaria, fever and angioedema, exceptional anaphylactic shocks and very rare pustular eruptions.

Peripheral and central nervous system disorder: Peripheral sensory neuropathy, headache, dizziness, convulsions and ataxia.

Psychiatric disorders: Psychotic disorders including confusion and hallucinations.

Visions disorders: Transient vision disorders such as diplopia or myopia may occur.

Hematology disorders: Very rare cases of agranulocytosis, neutropenia and thrombocytopenia.

Liver: very rare cases of reversible abnormal liver function tests and cholestatic hepatitis have been reported.

4.9 Overdose:

Data not available

5. Pharmacological Properties:

5.1 Pharmacodynamic Properties:

Metronidazole has antiprotozoal and antibacterial actions and is effective against *Trichomonas vaginalis* and other protozoa including *Entamoeba histolytica* and *Giardia lamblia* and against anaerobic bacteria.

Clotrimazole has a broad antimycotic spectrum of action in vitro and in vivo, which includes dermatophytes, yeasts, moulds, etc. The mode of action of Clotrimazole is fungistatic or fungicidal depending on the concentration of Clotrimazole at the site of infection. In-vitro activity is limited to proliferating fungal elements; fungal spores are only slightly sensitive. Primarily resistant variants of sensitive fungal species are very rare; the development of secondary resistance by sensitive fungi has so far only been observed in very isolated cases under therapeutic conditions.

5.2 Pharmacokinetic Properties:

Vaginal administration of Metronidazole corresponds to the local action, where the concentration of the drug at the site of action is very high comparative to that of in the serum.

Pharmacokinetic investigations after vaginal application have shown that only a small amount of Clotrimazole (3 – 10% of the dose) is absorbed. Due to the rapid hepatic metabolism of absorbed Clotrimazole into pharmacologically inactive metabolites the resulting peak plasma concentrations of Clotrimazole after vaginal application of a 500mg

dose were less than 10 mcg/ml, reflecting that Clotrimazole applied intravaginally does not lead to measurable systemic effects or side effects.

5.3 Preclinical Safety Data:

Metronidazole has been shown to be carcinogenic in the mouse and in the rat following chronic oral administration however similar studies in the hamster have given negative results. Epidemiological studies have provided no clear evidence of an increased carcinogenic risk in humans.

Metronidazole has been shown to be mutagenic in bacteria in vitro. In studies conducted in mammalian cells in vitro as well as in rodent or humans in vivo, there was inadequate evidence of a mutagenic effect of metronidazole, with some studies reporting mutagenic effects, while other studies were negative.

There are no pre-clinical data of relevance for clotrimazole, which are additional to the information included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of Excipients:

Polyethylene Glycol 1500, Methyl paraben, Propyl paraben, Butylated Hydroxytoluene

6.2 Incompatibilities:

None Known

6.3 Shelf Life:

24 months

6.4 Special precautions for storage:

Keep in a dry place, below 30°C.

Protect from light.

6.5 Nature and contents of container:

Strip of 6 vaginal pessaries packed in PVC / PE foil in a mono carton along with pack insert.

6.6 Special precautions for disposal and other handling:

None stated.

7. MARKETING AUTHORISATION HOLDER

Bliss GVS Pharma Ltd., Saki Vihar Road, Andheri (East), Mumbai - 400 072.