SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

GYNOZOL Vaginal Soft Gelatin Capsules.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Capsule of GYNOZOL Vaginal Soft Gelatin Capsule Contains:

Miconazole Nitrate 400 mg

For a full list of excipients see Section 6.1.

3. PHARMACEUTICAL FORM

Soft Gelatin Capsules.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the local treatment of vulvovaginal candidosis and superinfections due to Gram-positive bacteria.

4.2 Posology and method of administration

GYNOZOL vaginal capsules are for intravaginal administration.

Adults (aged 18 years and older)

One soft vaginal capsule to be inserted high in the vagina at bedtime, as a single dose. This is best done in the reclining position.

Paediatrics (aged under 18 years)

The safety and efficacy of GYNOZOL vaginal capsule in children and adolescents has not been studied.

4.3 Contraindications

GYNOZOL vaginal capsule is contraindicated in individuals with a known hypersensitivity to miconazole/miconazole nitrate, other imidazole derivatives or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Severe hypersensitivity reactions, including anaphylaxis and angioedema, have been reported during treatment with GYNOZOL vaginal capsule and with other miconazole formulations (see section 4.8). If a reaction suggesting hypersensitivity or irritation should occur, the treatment should be discontinued.

Appropriate therapy is indicated when the sexual partner is also infected.

GYNOZOL vaginal capsules do not stain skin or clothes.

The concurrent use of latex condoms or diaphragms with vaginal anti-infective preparations may decrease the effectiveness of latex contraceptive agents. Therefore GYNOZOL vaginal capsules should not be used concurrently with a latex condom or latex diaphragm.

4.5 Interaction with other medicinal products and other forms of interaction

Miconazole administered systemically is known to inhibit CYP3A4/2C9. Due to the limited systemic availability after vaginal application, clinically relevant interactions occur very rarely. In patients on oral anticoagulants, such as warfarin, caution should be exercised and anticoagulant effect should be monitored. The effects and side effects of other drugs metabolized by CYP2C9 (e.g., oral hypoglycemics and phenytoin) and also CYP3A4 (e.g., HMG-CoA reductase inhibitors such as simvastatin and lovastatin and calcium channel blockers such as dihydropyridines and verapamil), when co-administered with miconazole, can be increased and caution should be exercised.

Contact should be avoided between certain latex products such as contraceptive diaphragms or condoms and GYNOZOL vaginal capsules since the constituents of the vaginal capsules may damage the latex (see section 4.4)

4.6 Pregnancy and lactation

Pregnancy

Although intravaginal absorption is limited, GYNOZOL vaginal capsules should only be used in the first trimester of pregnancy if, in the judgment of the physician, the potential benefits outweigh the possible risks.

Breastfeeding

It is not known whether miconazole nitrate is excreted in human milk. Caution should be exercised when using GYNOZOL vaginal capsules during breastfeeding.

4.7 Effects on ability to drive and use machines

None Known.

4.8 Undesirable effects

The safety of GYNOZOL was evaluated in a total of 537 women with microbiologically confirmed candidiasis and symptoms (e.g., vulvovaginal itching, burning/irritation), or signs of vulvar erythema, edema, excoriation, or vaginal erythema or edema who participated in 2 single-blind clinical trials. Subjects were treated with miconazole intravaginally, randomly assigned to either a single 1,200 mg capsule, or a 7-day application of 2% vaginal cream. Adverse reactions reported by ≥1% of GYNOZOL-treated subjects in these trials are shown in Table 1.

In the table, the frequencies are provided according to the following convention:

Very common	≥1/10
Common	≥1/100 and < 1/10
Uncommon	≥1/1,000 and <1/100

Rare	≥1/10,000 and <1/1,000
Very rare	<1/10,000

Table 1. Adverse Reactions Reported by GYNOZOL treated Subjects in 2 Single Blind Clinical Trials	
Body System/Organ Class *Frequency Category*	**Undesirable effects**
Skin and Subcutaneous Tissue Disorders	
Common	Rash
Uncommon	Rash pruritic, urticaria
Reproductive System and Breast Disorders	
Very common	Genital pruritus female, vaginal burning sensation, vulvovaginal discomfort
Common	Dysmenorrhoea

A range of additional reactions were reported during the clinical trials, such as: vaginal discharge, vaginal haemorrhage, vaginal pain, headache, dysuria, urinary tract infection, abdominal pain, rosacea, swelling of the face and nausea. However due to the design of these studies, a definitive causal relationship could not be established.

Table 2. Adverse Reactions Identified During Postmarketing Experience with GYNOZOL by Frequency Category Estimated from Spontaneous Reporting Rates	
Immune System Disorders	
Not known	Hypersensitivity including Anaphylactic and Anaphylactoid reactions
Skin and Subcutaneous Tissue Disorders	
Not known	Angioedema, Pruritus
Reproductive System and Breast Disorders	
Not known	Vaginal irritation, pelvic cramps

4.9 Overdose

Symptoms

In case of accidental ingestion, vomiting and diarrhoea may occur.

Treatment

In case of accidental ingestion, the treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic classification:
(Antiinfectives and antiseptics, excl. combinations with corticosteroids, imidazole derivative)
ATC code: G01A F04

Miconazole is a synthetic imidazole antifungal agent with a broad spectrum of activity against pathogenic fungi (including yeasts and dermatophytes) and gram-positive bacteria

(staphylococcus and streptococcus spp). Miconazole combines a potent antifungal activity against common dermatophytes and yeasts with an antibacterial activity against certain gram-positive bacilli and cocci.

Miconazole inhibits the biosynthesis of ergosterol in fungi and changes the composition of other lipid components in the membrane, resulting in fungal cell necrosis.

In general, miconazole exerts a very rapid effect on pruritus, a symptom that frequently accompanies dermatophyte and yeast infections.

5.2 Pharmacokinetic properties

After the capsule has been inserted into the vagina, the outer covering rapidly disintegrates and the active suspension is almost instantaneously released.

Absorption: miconazole persists in the vagina for up to 72 hours after a single dose. Systemic absorption of miconazole after intravaginal administration is limited, with a bioavailability of 1 to 2% following intravaginal administration of a 1200 mg dose. Plasma concentrations of miconazole are measurable within 2 hours of administration in some subjects, with maximal levels seen 12 to 24 hours after administration. Plasma concentrations decline slowly thereafter and were still measurable in most subjects 96 hours post-dose. A second dose administered 48 hours later resulted in a plasma profile similar to that of the first dose.

Distribution: Absorbed miconazole is bound to plasma proteins (88.2%) and red blood cells (10.6%).

Metabolism and Excretion: The small amount of miconazole that is absorbed is eliminated predominantly in faeces as both unchanged drug and metabolites over a four-day post-administration period. Smaller amounts of unchanged drug and metabolites also appear in urine. The apparent elimination half-life ranges from 15 to 49 hours in most subjects and likely reflects both absorption from the site of application and metabolism/excretion of the drug.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on studies of local irritation, single and repeated dose toxicity, genotoxicity, and toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Inactive Ingredients (Excipients):
Mineral Oil (Highly Viscous) (Liquid Paraffin)
White Soft Paraffin
Shell Components:
Gelatin
Sorbitol
Glycerol 85%

Sodium Ethyl Hydroxybenzoate
Sodium Propyl Hydroxybenzoate
Titanium Dioxide
Cochineal Red 70%
Purified water

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Keep at temperature not exceeding 30 °C, in a dry place.

6.5 Nature and contents of container
Carton box containing (Al/ transparent PVC) blister of 3 Vaginal Soft Gelatin Capsules + insert leaflet.

6.6 Special precautions for disposal
Not special requirements.

7. MARKETING AUTHORISATION HOLDER
PHARCO Pharmaceuticals.
31 Km. Cairo Alexandria Desert Road, Amriya, Alexandria-Egypt

8. MARKETING AUTHORISATION NUMBER(S)
23141/2017.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
04/05/2004.

10. DATE OF REVISION OF THE TEXT
July 2019.