Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Gyno-Daktarin 1200 mg vaginal capsule.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 1200 mg miconazole nitrate.

Also contains ethyl parahydroxybenzoate (E215) and sodium propyl parahydroxybenzoate (E217)

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Vaginal capsule, soft.
White to off white egg shaped soft vaginal capsule containing a white to cream coloured hydrophobic mass.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Adult females only.

For the local treatment of vulvo-vaginal Candida infections, including those with superinfection due to susceptible gram positive bacteria.

4.2 Posology and method of administration

Gyno-Daktarin vaginal capsule is for vaginal administration.

Adults (aged 18 years and older)
One soft vaginal capsule inserted high into the vagina before retiring at night. This is best done in the reclining position.

Paediatrics (aged under 18 years)
The safety and efficacy of Gyno-Daktarin vaginal capsule in children and adolescents has not been studied.

4.3 Contraindications

Gyno-Daktarin 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 Gyno-Daktarin 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.

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

Gyno-Daktarin vaginal capsule does not stain skin or clothes.

4.5 Interaction with other medicinal products and other forms of interactions

Miconazole administered systemically is known to inhibit CYP3A4/2C9. Due to the limited systemic availability after vaginal application, clinically relevant interactions occur very rarely. However, in patients on oral anticoagulants, such as warfarin, caution should be exercised and anticoagulant effect should be monitored.
The effects and side effects of some other drugs (e.g., oral hypoglycemics and phenytoin), when co-administered with miconazole, can be increased and caution should be exercised.

Contact should be avoided between latex products such as contraceptive diaphragms or condoms and Gyno-Daktarin vaginal capsules since the constituents of the vaginal capsules may damage the latex. (See Section 4.4, Special warnings and precautions for use).

4.6 Fertility, pregnancy and lactation

Pregnancy
Although intravaginal absorption is limited, Gyno-Daktarin vaginal capsule should only be used in the first trimester of pregnancy if, in the judgement 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 Gyno-Daktarin vaginal capsule during breastfeeding (see

Section 4.5, Interactions with other medicinal products and other forms of interaction).

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Clinical trial data
Adverse events, regardless of causality, reported in 2 Phase 3 clinical trials are shown in Table 1. 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 were treated with miconazole intravaginally: randomly assigned to either a single 1200 mg capsule, or a 7-day application of 2% vaginal cream. There was no placebo reference. Safety was self-assessed daily on a diary card.

Included in the table are adverse events reported by ≥1% of subjects in either treatment group.

Table 1: Adverse events, regardless of causality, reported by ≥1% of patients in either treatment group in 2 Phase 3 clinical trials.

System Organ Class Preferred terms	Miconazole 2% Vaginal Cream 7-days (n= 265), %	Miconazole 1200 mg Capsule (n=272), %
Nervous system disorders		
Headache	13.6	9.6
Renal and urinary disorders		
Urinary tract infections	0.4	1.1
Reproductive system and breast disorders		
Genital pruritus female	23.0	16.5
Vaginal burning sensation	22.6	22.8
Vaginal discomfort	14.3	16.2
Dysmenorrhea	3.4	3.3
Vaginal discharge Vaginal haemorrhage Vaginal pain	0.4 0.4 0.4	3.7 1.1 1.5

System Organ Class Preferred terms	Miconazole 2% Vaginal Cream 7-days (n= 265), %	Miconazole 1200 mg Capsule (n=272), %
Gastrointestinal disorders		
Abdominal pain	2.3	1.8
Abdominal pain upper	1.1	1.5
Nausea	1.1	1.5
Abdominal pain lower	0	1.5
Skin and Subcutaneous Tissue Disorders		
Rash	0.4	1.1
Renal and urinary disorders		
Dysuria	0.4	1.1

Additional adverse reactions that occurred in < 1% of Gyno-Daktarin-treated subjects (n=527) in the single-blind clinical datasets are listed in Table 2:

Table 2: Adverse Reactions Reported by < 1% of GYNO-DAKTARIN-treated Subjects in 2 Single-blind clinical Trials

System Organ Class Preferred terms	Miconazole 2% Vaginal Cream 7-days (n= 265), %	Miconazole 1200 mg Capsule (n=272), %
Skin and Subcutaneous Tissue Disorders		
Rash pruritic	0.4	0
Rosacea	0	0.4
Swelling face	0	0.7
Urticaria	0	0.4

The majority of adverse reactions reported in clinical trials were mild to moderate in severity.

Postmarketing data

Adverse reactions first identified during post-marketing experience with Gyno-Daktarin are included in Table 3. The adverse drug reactions are ranked by frequency according to using 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, including isolated reports

In Table 3, adverse reactions are presented by MedRA System organ class and frequency category based on spontaneous rates.
The frequencies provided below reflect reporting rates for adverse reactions from spontaneous reports, and do not represent more precise estimates of incidence that might be obtained in clinical or epidemiological studies.

Table 3. Postmarketing reports of adverse reactions

Immune system disorders
Very rare Hypersensitivity including Anaphylactic and anaphylactoid reactions

Skin and subcutaneous tissue disorders
Very rare Angioedema, Pruritus

Reproductive system and breast disorders
Very rare Vaginal irritation

General disorders and administration site conditions
Very rare Application site reactions

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via: HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2, Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; E-mail: medsafety@hpra.ie

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 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.

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 20 to 45 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 conventional studies of local irritation, single and repeated dose toxicity, genotoxicity, and toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule:
Liquid paraffin
White petrolatum
Lecithin

Capsule shell:
Gelatin
Glycerol
Titanium dioxide (E171)
Sodium ethyl parahydroxybenzoate (E215)
Sodium propyl parahydroxybenzoate (E217)
Medium chain triglycerides

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Do not store above 30^{o}C. Store in the original package to protect from moisture.

6.5 Nature and contents of container

Gyno-Daktarin vaginal capsule is supplied in a blister strip (PVC-LDPE-PVDC/ALU) containing one soft vaginal capsule.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Janssen-Cilag Ltd.
50-100 Holmers Farm Way
High Wycombe
Buckinghamshire
HP12 4EG
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA0748/020/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 09 June 1989
Date of last renewal: 09 June 2009

10 DATE OF REVISION OF THE TEXT

November 2018