SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Gyno-Daktarin 20mg/g vaginal cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Miconazole nitrate 2% w/w.
(Each gram of cream contains 20mg miconazole nitrate)

Excipients: Each gram of cream contains 2mg benzoic acid and 5 micrograms of butylated hydroxyanisole.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Vaginal cream.
The cream is white and homogeneous.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications
For the treatment of mycotic vulvovaginitis and superinfections due to gram-positive bacteria.

4.2 Posology and method of administration
Gyno-Daktarin vaginal cream is for vaginal administration.

Adults (aged 18 years and older)
Administer the contents of one applicator (about 5g of cream) once daily deeply into vagina for 10 – 14 days or twice daily for 7 days. For vulvitis the cream should be applied topically twice daily. Continue the course of treatment even after pruritus and leukorrhoea have disappeared or menstruation begins.

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

4.3 Contraindications
Gyno-Daktarin vaginal cream 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 cream 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.
Gyno-Daktarin vaginal cream does 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 Gyno-Daktarin vaginal cream should not be used concurrently with a latex condom or latex diaphragm.

Gyno-Daktarin vaginal cream contains benzoic acid and butylated hydroxyanisole, which may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.

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 Gyno-Daktarin vaginal cream since the constituents of the cream may damage the latex (see section 4.4).

4.6 Fertility, pregnancy and lactation
Pregnancy
Although intravaginal absorption is limited, Gyno-Daktarin vaginal cream should be used in the first trimester of pregnancy only 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 cream during breastfeeding.
4.7. Effects on ability to drive and use machines

None known.

4.8. Undesirable effects

The safety of GYNO-DAKTARIN 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 GYNO-DAKTARIN-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>
<thead>
<tr>
<th>Body System/Organ Class</th>
<th>Frequency Category</th>
<th>Undesirable effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin and Subcutaneous Tissue Disorders</td>
<td>Common</td>
<td>Rash</td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Rash pruritic, urticaria</td>
</tr>
<tr>
<td>Reproductive System and Breast Disorders</td>
<td>Very common</td>
<td>Genital pruritus female, vaginal burning sensation, vulvovaginal discomfort</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Dysmenorrhoea</td>
</tr>
</tbody>
</table>

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 Gyno-Daktarin by Frequency Category Estimated from Spontaneous Reporting Rates

<table>
<thead>
<tr>
<th>Immune System Disorders</th>
<th>Not known</th>
<th>Hypersensitivity including Anaphylactic and Anaphylactoid reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin and Subcutaneous Tissue Disorders</td>
<td>Not known</td>
<td>Angioedema, Pruritus</td>
</tr>
<tr>
<td>Reproductive System and Breast Disorders</td>
<td>Not known</td>
<td>Vaginal irritation, pelvic cramps</td>
</tr>
</tbody>
</table>

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms

Gyno-Daktarin vaginal cream is intended for local application and not for oral use. In case of accidental ingestion, no problems are expected.

Treatment

In the event of accidental ingestion of large quantities, use appropriate supportive care.

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.

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

5.2 Pharmacokinetic properties

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**
PEG-6, PEG-32 and glycol stearate
Oleoyl macroglycerides
Liquid paraffin
Benzoic acid (E210)
Butylated hydroxyanisole (E320)
Purified water

6.2. **Incompatibilities**
None known.

6.3. **Shelf Life**
24 months.

6.4 **Special precautions for storage**
Do not store above 25°C.

6.5 **Nature and contents of container**
Tube containing 15 g, 40 g or 78 g of cream*.
The aluminium tube inner is lined with heat polymerised epoxy-phenol resin with a white polypropylene cap.
The cream is supplied with disposable cardboard vaginal applicators.
*Not all pack sizes may be marketed

6.6. Instructions for Use/Handling

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Janssen-Cilag Limited
50-100 Holmers Farm Way
High Wycombe
Buckinghamshire
HP12 4EG
UK

8. MARKETING AUTHORISATION NUMBER(S)

PL 0242/0015

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13/05/1974 / 12/12/2008

10 DATE OF REVISION OF THE TEXT

11/12/2015