SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DAKTARIN 400 mg soft vaginal capsules
DAKTARIN 1200 mg soft vaginal capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One 400 mg ***soft vaginal capsule*** contains 400 mg of miconazole nitrate.
One 1200 mg ***soft vaginal capsule*** contains 1200 mg of miconazole nitrate.
For the complete list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

400 mg soft vaginal capsules
1200 mg soft vaginal capsules

4. CLINICAL INFORMATION

4.1 Therapeutic indications

Local treatment of vulvovaginal candidiasis and superinfections due to Gram-positive bacteria.

4.2 Dosage and administration method

Insert the capsule deep into the vagina.
The best way to do this is by lying on the back with knees still and separated. The ideal time to insert the capsule would be before going to bed, so as to keep it in place the entire night.

400 mg soft vaginal capsules

Insert one capsule into the vagina as deeply as possible every night, for 3 consecutive nights.
The treatment can be repeated, if necessary.
In case of pronounced infections, it may be preferable to prescribe a treatment of 6 consecutive days from the beginning.
An entire therapeutic cycle (3 or 6 days according to medical prescription) must always be completed, even if the symptoms (itching, redness or discharge) disappear quickly.
The treatment can also be carried out during the menstrual cycle.

1200 mg soft vaginal capsules

Insert one capsule into the vagina as deeply as possible, preferably in the evening.
The treatment can be repeated, if necessary.
In case of pronounced infections, it may be preferable to prescribe a longer therapeutic cycle from the beginning.
An entire therapeutic cycle (2 days) must always be completed, even if the symptoms (itching, redness or discharge) disappear quickly.
The treatment can also be carried out during the menstrual cycle.

Pediatric patients (under 18 years of age)
The safety and efficacy of DAKTARIN vaginal capsules have not been studied in children and adolescents.

4.3 Contraindications

Hypersensitivity to the active ingredient, to other imidazole derivatives or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

In the event of sensitization or an allergic reaction, treatment must be interrupted.
It is advisable to take appropriate hygienic preventive measures to limit the possibility of infection or reinfection.
Appropriate treatment is also indicated for your partner, if infected.
DAKTARIN does not stain skin or clothing.
The effectiveness of latex contraceptives, such as condoms and diaphragms, may decrease if used during treatment with anti-infective vaginal preparations. Therefore, DAKTARIN vaginal capsules must not be used concomitantly with latex condoms or diaphragms.
Severe hypersensitivity reactions, including anaphylaxis and angioedema, have been reported during treatment with Daktarin and other topical miconazole-based formulations. If you develop a reaction due to hypersensitivity or irritation, treatment must be interrupted.

Important information on some excipients
The soft vaginal capsules contain sodium ethyl-p-hydroxybenzoate and sodium propyl-p-hydroxybenzoate, which may cause allergic reactions (even delayed).

4.5 Interactions with other medicinal products and other forms of interaction

It is known that systemically administered miconazole inhibits CYP3A4/2C9. Since the presence of the medicine in the blood is limited after vaginal application, interactions considered clinically significant are very rare. However, in patients treated with oral anticoagulants, such as warfarin, caution should be exercised and anticoagulant action should be monitored. The efficacy and side effects of other medicines (such as oral hypoglycemic agents and phenytoin) can increase if administered in combination with miconazole. Therefore, special caution should be exercised.
Contact should be avoided between any latex products, such as diaphragms or condoms, and DAKTARIN soft vaginal capsules, since the latex can be damaged by the emollient base (see section 4.4 Special warnings and precautions for use).

4.6 Pregnancy and breastfeeding

Pregnancy
Although intravaginal absorption is limited, DAKTARIN should only be used during the first trimester of pregnancy if, in the doctor's opinion, the expected benefits outweigh the potential risks.

Breastfeeding

There is no known information on the excretion of miconazole nitrate in breast milk, therefore extreme care is required when DAKTARIN is administered during the lactation period (see section 4.5 Interactions with other medicinal products and other forms of interaction).

4.7 Effects on the ability to drive vehicles and use machinery

None to report

4.8 Side effects

Data from clinical studies

The safety of DAKTARIN was assessed in a total of 537 women who participated in two single-blind clinical trials. The 537 women, with microbiologically confirmed candidiasis and symptoms (e.g., vulvovaginal itching, burning sensation/irritation) or signs of vulvular erythema, edema, abrasions, vaginal erythema or edema were treated vaginally with miconazole. A single capsule of 1200 mg or a 7-day application of 2% vaginal cream was assigned at random to each of them. The Adverse Drug Reactions (ADR) ≥ 1% reported by the women involved in these studies are shown in Table 1.

Table 1. Adverse Drug Reactions (ADR) ≥ 1% reported by women treated with DAKTARIN in 2 single-blind studies

System/organ classification	Miconazole 1200 mg Soft vaginal capsules (n=272) %	Miconazole 20 mg/g Vaginal cream for 7 days (n=265) %
Reproductive system and breast disorders		
Female genital pruritus	16.5	23
Vaginal burning sensation	22.8	22.6
Vulvovaginal discomfort	16.2	14.3
Dysmenorrhea	3.3	3.4
Vaginal leakage	3.7	0.4
Vaginal hemorrhage	1.1	0.4
Vaginal pain	1.5	0.4
Nervous system disorders		
Headache	9.6	13.6
Infections and infestations		
Urinary tract infection	1.1	0.4

Gastrointestinal disorders		
Abdominal pain	1.8	2.3
Upper abdominal pain	1.5	1.1
Nausea	1.5	1.1
Lower abdominal pain	1.5	0
Skin and subcutaneous tissue disorders		
Rash	1.1	0.4
Renal and urinary disorders		
Dysuria	1.1	0.4

Other Adverse Drug Reactions (ADR) < 1% reported by the women (n=537) involved in the 2 single-blind studies are shown in Table 2.

Table 2. Adverse Drug Reactions (ADR) < 1% reported by women treated with DAKTARIN in 2 single-blind studies

System/organ classification	Miconazole 1200 mg Soft vaginal capsules (n=272) %	Miconazole 2% Vaginal cream for 7 days (n=265) %
Skin and subcutaneous tissue disorders		
Rash	0	0.4
Rosacea	0.4	0
Facial swelling	0.7	0
Urticaria	0.4	0

Most of the Adverse Drug Reactions reported during the clinical studies were of mild or moderate intensity.

Data from post-marketing reports

The Adverse Drug Reactions reported during the post-marketing experience with DAKTARIN are listed in Table 3. In this table, frequency is classified 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, including isolated cases

The reactions in Table 3 are reported according to the MedDRA classification for systems/organs and the convention on frequency, based on the evaluation of spontaneous reports.

Table 3. Adverse Drug Reactions reported during the post-marketing experience of DAKTARIN and classified in terms of frequency based on spontaneous reports

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
Systemic disorders and administration site conditions	
Very rare	Reaction at the application site

Reporting of suspected Adverse Drug Reactions
It is important to report suspected Adverse Drug Reactions that occur after the medicinal product has been authorized because it allows continued monitoring of the risk/benefit ratio of the medicinal product. Health care professionals are asked to report any suspected Adverse Drug Reactions via the national reporting system at www.agenziafarmaco.gov.it/it/responsabili.

4.9 Overdose

DAKTARIN vaginal capsules are meant for topical application and are not meant for oral use.

Treatment
In case of accidental ingestion of large quantities of DAKTARIN vaginal capsules, use appropriate supportive care (see also section 4.5 Interactions with other medicinal products and other forms of interaction).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic category: anti-infectives and antiseptics - imidazole derivatives.
ATC Code: G01AF04.
Miconazole possesses a powerful antifungal activity against common dermatophytes and yeasts, as well as an antibacterial activity against certain Gram-positive bacilli and cocci.
In fungi, miconazole inhibits the biosynthesis of ergosterol, an essential component for the integrity and functional efficiency of the fungal cell membrane, and changes the composition of other lipid components in the membrane. This mechanism of action results in fungal cell necrosis.
Miconazole exerts a very rapid effect on the itching that often accompanies dermatophyte and yeast infections, and this occurs even before the onset of therapeutic action.

5.2 Pharmacokinetic properties

Systemic absorption after intravaginal administration is limited.
8 hours after application, 90% of the medicine is still present in the vagina. Unchanged medicine cannot be traced in plasma or urine.
After insertion into the vagina, the external coating rapidly disintegrates and the active suspension is almost instantaneously released.

5.3 Preclinical safety data

TOXICOLOGY
For acute administration:
DL 50 (Miconazole nitrate in SD rat, orally): 1220 mg/kg
DL 50 (Miconazole nitrate in albino mouse, orally): 645 mg/kg
For prolonged administration:
rat, orally (miconazole nitrate, for 180 days): 25 mg/kg/day
rabbit, orally (miconazole nitrate, for 180 days): 20 mg/kg/day

- The treatment does not influence normal growth, blood composition, renal function or hepatic function. There is no negative influence on normal organ development.

FETAL TOXICITY
No fetal toxicity in either the rat or the rabbit, with oral administration.

CARCINOGENIC ACTIVITY
Ruled out due to the absence of structural similarities between miconazole and known carcinogenic substances, and due to the absence of specific findings in toxicity tests for prolonged administration.

6. PHARMACEUTICAL INFORMATION

6.1 List of excipients

400 mg soft vaginal capsules: high viscosity mineral oil (liquid paraffin), white petrolatum, gelatin, glycerin, titanium dioxide, sodium ethyl-p-hydroxybenzoate, sodium propyl-p-hydroxybenzoate.
1200 mg soft vaginal capsules: high viscosity mineral oil (liquid paraffin), white petrolatum, soy lecithin, gelatin, glycerin, titanium dioxide, sodium ethyl-p-hydroxybenzoate, sodium propyl-p-hydroxybenzoate.

6.2 Incompatibilities

None to report

6.3 Shelf life

Soft vaginal capsules: 2 years

6.4 Special precautions for storage

Do not store at temperatures above 30°C

6.5 Nature and contents of the container

Soft vaginal capsules: blister pack with 3 or 2 impressions (for the packaging of 3 capsules of 400 mg and 2 capsules of 1200 mg, respectively). Lithographed cardboard box containing the information leaflet.

6.6 Instructions for use and handling

See section 4.2 Dosage and administration method.

7. MARKETING AUTHORIZATION HOLDER

Janssen-Cilag S.p.A.
Via M. Buonarroti, 23
20093 COLOGNO MONZESE (Milan)

8. MARKETING AUTHORIZATION NUMBER(S)

400 mg soft vaginal capsules MA 024957312
1200 mg soft vaginal capsules MA 024957173

9. DATE OF FIRST AUTHORIZATION/AUTHORIZATION RENEWAL

400 mg soft vaginal capsules
Date of first authorization: October 25, 1984
Most recent renewal date: June 2005
1200 mg soft vaginal capsules
Date of first authorization: October 25, 1984
Most recent renewal date: June 2005

10. DATE OF REVISION OF THE TEXT