Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Daktacort 2% / 1% w/w Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Miconazole nitrate 2% w/w and hydrocortisone 1% w/w.

Excipients with known effect

Contains 0.2% w/w benzoic acid (E210) and 0.0052% w/w butylated hydroxyanisole (E320).

5 g: This medicine contains 10 mg benzoic acid in each tube of 5 g cream which is equivalent to 2 mg/g cream.
10 g: This medicine contains 20 mg benzoic acid in each tube of 10 g cream which is equivalent to 2 mg/g cream.
15 g: This medicine contains 30 mg benzoic acid in each tube of 15 g cream which is equivalent to 2 mg/g cream.
30 g: This medicine contains 60 mg benzoic acid in each tube of 30 g cream which is equivalent to 2 mg/g cream.
75 g: This medicine contains 150 mg benzoic acid in each tube of 75 g cream which is equivalent to 2 mg/g cream.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cream.

White, homogenous, odourless cream.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Daktacort is used for the topical treatment of skin conditions where inflammation and infection by susceptible organisms co-exist. The properties of Daktacort indicate it particularly for the initial stages of treatment. Once the inflammatory symptoms have disappeared, treatment can be continued with miconazole nitrate 20mg/g cream.

4.2 Posology and method of administration

For cutaneous administration

Apply one to three times daily to the affected area or as directed by the physician.
Daktacort cream should be rubbed in gently until it has been completely penetrated into the skin. The treatment with Daktacort cream (or subsequently with miconazole nitrate 20 mg/g cream) should be continued without interruption until the lesion has completely disappeared (usually after 2 to 6 weeks).

Elderly
Thinning of the skin occurs naturally and especially in the elderly, and is a common risk with prolonged/excessive use of corticosteroids. Corticosteroids should therefore be used sparingly and for short periods of time.

Paediatrics
In children, caution is advised when Daktacort Cream is applied to extensive surface areas or under occlusive dressings including baby napkins (diapers). In infants, use with occlusive dressings is contraindicated (see section 4.3) and the long-term continuous topical corticosteroid therapy should be avoided (see section 4.4).

4.3 Contraindications

1. Hypersensitivity to miconazole nitrate, other imidazole derivatives, hydrocortisone or to any of the excipients listed in section 6.1.

2. Use in infants in conjunction with occlusion.
3. Use in the presence of viral infections, tuberculous (skin) infections, treponemal infections, or bacterial infections due to Gram-negative organisms.
4. Daktacort cream should not be used on the eyes or face or to treat certain skin infections such as impetigo, cold sores, and acne.

4.4 Special warnings and precautions for use

Severe hypersensitivity reactions, including anaphylaxis and angioedema, have been reported during treatment with Daktacort and with other miconazole topical formulations (see section 4.8).

If a reaction suggesting hypersensitivity or irritation should occur, the treatment should be discontinued.

As with any topical corticosteroid, caution is advised with infants and children when Daktacort is to be applied to extensive surface areas or under occlusive dressings including baby napkins. Similarly, application to the face should be avoided.

Continuous treatment for longer than three weeks should be avoided in infants because of the possibility of adrenocortical suppression. Adrenal suppression can occur even without the use of occlusive dressings.

Daktacort cream contains benzoic acid, which may cause local irritation.
Benzoic acid may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old). Daktacort cream also contains butylated hydroxanisole, which may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.

Daktacort must not come into contact with the mucosa of the eyes.

Because of its corticosteroid content avoid long-term treatment with Daktacort. Once the inflammatory symptoms have disappeared treatment may be continued with miconazole nitrate 20mg/g cream (see Section 4.1)

Daktacort can damage certain synthetic materials. Therefore, it is recommended to wear cotton underwear if this clothing comes into contact with the affected area.

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

Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

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 cutaneous application, (see Section 5.2 Pharmacokinetic properties), clinically relevant interactions are unlikely to occur. 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., certain oral hypoglycemics and phenytoin), when co-administered with miconazole, can be increased and caution should be exercised.

Miconazole is a CYP3A4 inhibitor that can decrease the rate of metabolism of hydrocortisone. Serum concentrations of hydrocortisone may be higher with the use of Daktacort compared with topical preparations containing hydrocortisone alone.

4.6 Fertility, pregnancy and lactation

Pregnancy
The product should not be used during pregnancy unless considered essential by the physician. Caution is also recommended during breast-feeding. Treatment of large surfaces and the application under occlusive dressing should be avoided during that time.

Miconazole has not been observed to be teratogenic in animals, but has been shown to be embryotoxic at maternal toxic doses. In animals, corticosteroids are known to cross the placenta and consequently can affect the foetus (see section 5.3).

Breast-feeding
There are no adequate and well-controlled studies on the topical administration of Daktacort during breast-feeding. It is not known whether topical administration of Daktacort to the skin could result in sufficient systemic absorption to produce detectable quantities of hydrocortisone and miconazole in breast milk in humans. Caution is recommended during breast-feeding. Use on a patient's breast is not advised. Treatment of large surfaces and the application under occlusive dressing should be avoided during that time.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

The safety of Daktacort Cream was evaluated in 480 patients who participated in 13 clinical trials (six double-blind and seven open-label trials) of Daktacort Cream. These studies examined patients from 1 month to 95 years of age with infections of the skin caused by dermatophytes or Candida species in which inflammatory symptoms were prominent.

All Patients

No adverse reactions were reported by ≥1% of the 480 DAKTACORT Cream-treated patients (adult and paediatric patients combined).

The frequency categories use the following convention:
very common (>/10); common (>1/100 to <1/10); uncommon (>1/1,000 to <1/100); rare (>1/10,000 to <1/1,000); very rare (<1/10,000); and not known (cannot be estimated from the available clinical trial data).

Of the three adverse reactions identified from the 13 clinical trials of Daktacort Cream, skin irritation was reported in one clinical trial that included patients aged 17 to 84 years, skin burning sensation in two clinical trials that included patients aged 13 to 84 years, and irritability in one clinical trial of infants aged 1 to 34 months.

Paediatric Population

The safety of Daktacort Cream was evaluated in 63 paediatric patients (1 month to 14 years of age), who were treated with Daktacort Cream in 3 of the 13 clinical trials noted above. One adverse reaction term (irritability) was reported in these 3 trials. The frequency of irritability in Daktacort Cream-treated paediatric patients was common (3.2%).

All events of irritability occurred in one clinical trial of infants (aged 1 to 34 months) with napkin (diaper) dermatitis. The frequency, type, and severity of other adverse reactions in paediatric patients are expected to be similar to those in adults. Adverse reactions were reported by ≥1% of the 480 Daktacort Cream-treated patients (adult and paediatric patients combined).

Adverse Reactions in Adult and Paediatric Patients Treated With Daktacort Cream

System Organ Class	Adverse reactions Frequency Category	
	Uncommon (≥1/1,000 to <1/100)	Not Known
Immune System Disorders		Anaphylactic reaction, Hypersensitivity
Skin and Subcutaneous Tissue Disorders	Skin irritation, Skin burning sensation, Urticaria, Pruritus	Angioedema, Rash, Contact dermatitis, Erythema, Skin inflammation, Skin hypopigmentation, Application site reaction
Eye disorders		Vision, blurred (see also section 4.4)

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
Website: www.hpra.ie

4.9 Overdose

Prolonged and excessive use can result in skin irritation, which usually disappears after discontinuation of therapy. Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Imidazole and triazole derivatives, combinations, ATC code: D01AC20.

Miconazole nitrate is a synthetic imidazole. The clinical efficacy of miconazole has been demonstrated against dermatophytes, *Candida* spp., *Aspergillus* spp., dimorphous fungi, *Cryptococcus neoformans*, *Malassezia* spp. and *Candida glabrata*. Miconazole also has an antibacterial activity against some Gram-positive bacilli and cocci.

Hydrocortisone is an anti-inflammatory steroid. Its anti-inflammatory action is due to reduction in the vascular component of the inflammatory response, suppression of migration of polymorphonuclear leukocytes, and reversal of increased capillary permeability. The vasoconstrictor action of hydrocortisone may also contribute to its anti-inflammatory activity.

Miconazole in combination with hydrocortisone acts very rapidly on pruritus, which frequently accompanies dermatophyte and yeast infections. This symptomatic improvement is seen before the first signs of healing are observed. However, treatment with hydrocortisone is symptomatic and lesions may flare up again after a discontinuation of the treatment.

5.2 Pharmacokinetic properties

Absorption

Miconazole remains in the skin for up to 4 days after topical application. Systemic absorption of miconazole is limited, with a bioavailability of less than 1% following topical application of miconazole. Plasma concentrations of miconazole and/or its metabolites were measurable 24 and 48 hours after application. Systemic absorption has also been demonstrated after repeated application of miconazole to infants with napkin dermatitis. Plasma levels of miconazole were undetectable or low. Approximately 3% of the dose of hydrocortisone is absorbed after application on the skin.

Distribution

Absorbed miconazole is bound to plasma proteins (88.2%) and red blood cells (10.6%). More than 90% of hydrocortisone is bound to plasma proteins.

Metabolism and elimination

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 half-life of hydrocortisone is about 100 minutes. Metabolism takes place in the liver and tissues and the metabolites are excreted with the urine, mostly as glucuronides, together with a very small fraction of unchanged hydrocortisone.

5.3 Preclinical safety data

Preclinical data on the drug product (miconazole nitrate + hydrocortisone) revealed no special hazard for humans based on conventional studies of ocular irritation, dermal sensitization, single dose oral toxicity, primary dermal irritation toxicity, and 21-day repeat dose dermal toxicity. Additional preclinical data on the individual active ingredients in this drug product reveal

no special hazard for humans based on conventional studies of local irritation, single and repeated dose toxicity, genotoxicity, and for miconazole toxicity to reproduction. Reproductive effects and developmental abnormalities have been reported with hydrocortisone in various animal models.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Macrogol ester
Oleoyl macroglycerides
Liquid paraffin
Benzoic acid (E210)
Disodium edetate
Butylated hydroxyanisole (E320)
Purified water

6.2 Incompatibilities

Contact should be avoided between latex products such as contraceptive diaphragms or condoms and Daktacort since the constituents of Daktacort may damage the latex.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C)

6.5 Nature and contents of container

Aluminium tube lined on the inside with heat-polymerized epoxy-phenol resin, with a latex cold-seal ring. Cap: polypropylene

Daktacort cream is supplied in tubes of 5 g, 10 g, 15 g, 30 g and 75 g.

Not all pack sizes are marketed.

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 Sciences Ireland UC
Barnahely
Ringaskiddy
Cork
P43 FA46
Ireland

8 MARKETING AUTHORISATION NUMBER

PA22612/003/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 16 December 2006

10 DATE OF REVISION OF THE TEXT

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