Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT (FPP)

Duoskin.

Isoconazole - Diflucortolone

1.1 Strength

10 mg/g – 1 mg/g

1.2 Pharmaceutical form

Cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 Qualitative declaration

For the full list of excipients: see 6.1

Excipient with known effect: cetostearyl alcohol.

2.2 Quantitative declaration

Each gram of cream contains 10 mg isoconazole nitrate and 1 mg diflucortolone valerate.

3. PHARMACEUTICAL FORM

Hydrophilic Cream.

Semi-solid preparation for cutaneous application.

White, odourless homogeneous cream

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Initial or interim treatment of those superficial fungal infections of the skin which are accompanied by highly inflammatory or eczematous skin conditions, e.g. in the

region of the hands, the interdigital spaces of the feet and in the inguinal and genital regions.

Duoskin is not suitable for the treatment of perioral dermatitis and rosacea.

4.2. Posology and mode of administration

4.2.1. Posology

Duoskin should be applied twice daily to the diseased areas of skin.

Treatment with Duoskin must be terminated after regression of the inflammatory or eczematous skin conditions or at the latest after 2 weeks.

4.2.2. Special populations

No additional information.

4.2.3. Paediatric population

- Dose adjustments are not required when Duoskin is administered to children aged 2 years or older and adolescents.
- Only limited data on the safety of Duoskin in children aged below 2 years are available.

4.2.4. Method of administration

- For cutaneous use only.
- Always wash the hands before and after applying Duoskin.
- Apply in a thin layer on the cutaneous areas affected, by means of a light massage.
- To treat the affected interdigital spaces in the fingers and toes, it is often recommended to apply a gauze compress coated with Duoskin between the fingers or toes.
- Regular hygiene measures are essential to the success of Duoskin treatment.

4.3. Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Tuberculous or syphilitic processes in the area to be treated; virus diseases (e.g. varicella, herpes zoster), rosacea, perioral dermatitis and post vaccination skin reactions in the area to be treated.

4.4. Special warning and precautions for use

4.4.1. General information

- Duoskin should not come in contact with wounds or mucous membranes. When applying on the face, it must be ensured that Duoskin does not come into contact with the eyes.
- Extensive application of topical glucocorticoids to large areas of the body or for prolonged periods of time, in particular under occlusion, may increase the risk of systemic side effects.
- As known from systemic glucocorticoids, glaucoma may also develop from using local glucocorticoids (e.g. after large-dosed or extensive application over a prolonged period, occlusive dressing techniques, or application to the skin around the eyes).
- Visual disturbances may occur during systemic or local corticosteroid therapy. In case of blurred vision or any other visual symptom appearing during a corticosteroid treatment, an ophthalmological examination is required in particular for cataract, glaucoma, or a rarer lesion such as Central serous chorioretinopathy, described with systemic or local administration of corticosteroids.
- In case of mixed bacterial infections with Gram-negative organisms, additional specific treatment may be necessary.
- Regular hygiene measures are very important for effective treatment with Duoskin.
- In case of mycosis of the feet, the interdigital spaces must be carefully dried after washing, and socks changed daily.

- Duoskin contains a strong corticosteroid and can therefore only be applied for a short period of time: in no case more than 2 weeks.
- In case of improper use, worsening of the clinical symptoms is possible.
- The cream contains cetostearyl alcohol which may cause local skin reactions (e.g. contact dermatitis).

4.4.2. Pediatric population

Only limited data on the safety of Duoskin in children aged below 2 years are available.

4.5. Interactions with other medicinal products and other forms of interactions

No interaction is known between topical forms of isoconazole nitrate and diflucortolone valerate and other medicines.

4.6. , Pregnancy, lactation and fertility

4.6.1 Pregnancy

Duoskin should be avoided during the first trimester of pregnancy.

The clinical indication for treatment with Duoskin must be carefully reviewed and the benefits weighed against the risks in pregnant women. In particular, application on a large surface during an extended period has to be avoided during pregnancy

4.6.2 Lactation

Nursing mothers should not be treated on the breasts. Also any contact of the infant with any other part of the skin treated with Duoskin cream should be avoided.

4.6.3 Fertility

No data available

4.7. Effects on the ability to drive and use machines

Duoskin has no effects on the ability to drive and to use machines.

4.8. Undesirable effects

- Duoskin is generally very well tolerated; in rare cases, it is possible to observe irritative skin phenomena, such as pruritus, burning sensation, erythema or appearance of vesicles.
- The application of Duoskin over a large area (approximately 10% of the body surface area and above) and / or for a long period (more than 4 weeks) may cause local adverse effects, such as skin atrophy, telangiectasia, stretch marks and acneiform lesions, as well as a systemic action of the corticosteroid due to resorption.
- As with other glucocorticoids for topical application, the following local adverse reactions may occur (rarely): folliculitis, hypertrichosis, perioral dermatitis, skin discolouration, allergic skin reactions to any of the ingredients of the formulation.
- Eye disorders (uncommon): blurred vision.
- Adverse reactions cannot be excluded in neonates whose mothers have been treated extensively or for a prolonged period of time during pregnancy or while lactating (for example, reduced adrenocortical function).

4.9. Overdose

There are no reports of cases of intoxication in humans.

Therefore, no particular therapeutic measures can be recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: imidazoles/triazoles in combination with corticosteroids.

ATC code: D01AC20.

Duoskin is a broad-spectrum antimycotic (isoconazole nitrate) supplemented with a corticosteroid (diflucortolone valerate).

- **Isoconazole nitrate** is a broad-spectrum antifungal agent belonging to the group of imidazoles. It inhibits the synthesis of ergosterol which is the main compound

of sterol playing a vital role in maintaining and functioning of the fungal cell membrane. This inhibition is achieved via inhibition of cytochrome P450-dependent 14α-demethylase and blockade of the conversion of lanesterol to ergosterol.

It acts on dermatophytes, yeasts and moulds (including the agent responsible for pityriasis versicolor).

It also acts on the agent responsible for erythrasma and on Gram-positive bacteria (such as Staphylococcus aureus, Staphylococcus / Micrococcus species, Streptococcus faecalis, and Corynebacterium species (aerobic). Isoconazole nitrate does not result in the selection of resistant germs.

- **Diflucortolone valerate** is a potent corticosteroid (class II) and has an anti-inflammatory effect by inhibiting phospholipase A2. It relieves the signs of pain, burning and sting by inhibiting inflammation during the inflammatory process and allergic diseases. It does not work against the underlying mycotic infection.

5.2. Pharmacokinetic properties

- **Isoconazole** quickly passes from the cream into the skin. At the latest after 1 hour, the maximum concentrations of active substance are reached in all skin layers. Isoconazole is not inactivated by metabolism in the skin. The systemic load resulting from percutaneous resorption is low. The active substance that reaches the body through the skin is metabolised completely and eliminated rapidly, 33% by renal route and 66% by bile duct.
- **Diflucortolone valerate** also quickly passes from the cream into the skin. Peak concentrations in the stratum corneum were measured after 1 hour. Diflucortolone valerate undergoes only slight hydrolysis in the skin, so that the active substance absorbed into the skin is totally active locally. After exposure for 4 hours, less than 1% of the amount of corticosteroid from the cream is resorbed. In the body, diflucortolone valerate is rapidly split into diflucortolone and valerian acid. Valeric acid is incorporated into the metabolism of fatty acids.

Diflucortolone is eliminated 75% renal and 25% in the bile, with a half-life of about 4 hours.

5.3. Preclinical safety data

Single dose toxicity

There is no risk of poisoning after ingestion of the complete tube of cream (equivalent to 150 mg of isoconazole nitrate and 15 mg of diflucortolone valerate).

Repeated dose toxicity

Isoconazole Nitrate: Repeated dose ingestion reveals no systemic effects.

Diflucortolone valerate: repeated ingestion of doses may reveal the typical effects of glucocorticoids. Effects have been observed in animals only at exposures considered to be sufficiently greater than the maximum exposure observed in humans, and have little clinical significance.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

- Liquid paraffin
- Polysorbate 60
- Disodium edetate
- White soft paraffin
- Cetostearyl alcohol
- Sorbitan stearate
- Purified water.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

36 months

6.4. Special precautions for storage

Store below 30°C

6.5. Nature and contents of container

Tube of lacquered aluminium closed with a HDPE screw-cap.

15 g of cream.

6.6. Special precautions for disposal and other handlings

No special requirements for disposal.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER AND MANUFACURING SITE ADDRESS

7.1. Marketing Authorisation Holder

Dafra Pharma GmbH, Mühlenberg 7, 4052 Basel, Switzerland.

7.2. Manufacturer

Bilim Ilaç San.ve Tic. A.Ş (Bilim Pharmaceuticals)

GOSB 41480 Gebze-Kocaeli, Turkey.

8. MARKETING AUHORISATION NUMBER

See list of MAs per country

9. DATE OF FIRST REGISTRATION

See list of MAs per country

10. DATE OF REVISION OF TEXT

March 2019