Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Agisten® Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Clotrimazole 1.0% w/v.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Colourless to slightly yellowish liquid solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Skin infections caused by dermatophytes or candida species.

4.2 Posology and method of administration

To ensure complete healing, treatment should be continued for about 2 weeks after the disappearance of the subjective symptoms. The following are the usual periods of treatment:

Dermatomycoses	3-4 weeks
Erythrasma	2-4 weeks
Pityriasis versicolor	1-3 weeks
Candida vulvitis and balanitis	1-2 weeks

A thin layer should be applied to the affected sites and gently rubbed in 2-3 times daily. A few drops is sufficient to treat an area about the size of a hand.

4.3 Contraindications

Hypersensitivity to the active substance clotrimazole or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Not known

4.5 Interaction with other medicinal products and other forms of interaction

Not known

4.6 Fertility, Pregnancy and lactation

Fertility:
No human studies of the effects of clotrimazole on fertility have been performed; however, animal studies have not demonstrated any effects of the drug on fertility.

Pregnancy:
There is a limited amount of data from the use of clotrimazole in pregnant women. Animal studies with clotrimazole have shown reproductive toxicity at high oral doses (see section 5.3). At the low systemic exposures of clotrimazole following topical treatment, harmful effects with respect to reproductive toxicity are not predicted. Clotrimazole can be used during pregnancy, but only under the supervision of a physician.

Lactation:
There are no data on the excretion of clotrimazole into human milk. However, systemic absorption is minimal after administration and is unlikely to lead to systemic effects. Clotrimazole may be used during lactation. If used topically on the nipple area, wash breasts before feeding child.

4.7 Effects on ability to drive and use machines

Clotrimazole has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

As the listed undesirable effects are based on spontaneous reports, assigning accurate frequency of occurrence for each is not possible.

Immune system disorders: anaphylactic reaction, angioedema, hypersensitivity.
Vascular disorders: syncope, hypotension.
Respiratory, thoracic and mediastinal disorders: dyspnoea
Skin and subcutaneous tissue disorders: blisters, dermatitis contact, erythema, paraesthesia, skin exfoliation, pruritus, rash, urticaria ,stinging skin /burning sensation skin.
General disorders and administration site conditions: application site irritation, application site reaction, oedema, pain.

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.
Any suspected adverse events should be reported to the Ministry of Health (www.health.gov.il) according to the National Regulation by using an online form: https://sideeffects.health.gov.il
Additionally, you can also report to Padagis.co.il

4.9 Overdose

No risk of acute intoxication is seen as it is unlikely to occur following a single dermal application of an overdose (application over a large area under conditions favourable to absorption) or inadvertent oral ingestion. There is no specific antidote.

However, in the event of accidental oral ingestion, routine measures such as gastric lavage should be performed only if clinical symptoms of overdose become apparent (e.g. dizziness, nausea or vomiting). Gastric lavage should be carried out only if the airway can be protected adequately.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antifungals for topical use – imidazole and triazole derivatives

ATC Code: D01A C01

Mechanism of Action
Clotrimazole acts against fungi by inhibiting ergosterol synthesis. Inhibition of ergosterol synthesis leads to structural and functional impairment of the fungal cytoplasmic membrane.

Clotrimazole has a broad antimycotic spectrum of action in vitro and in vivo, which includes dermatophytes, yeasts, moulds, etc.

Under appropriate test conditions, the MIC values for these types of fungi are in the region of less than 0.062-8.0 µg/ml substrate. The mode of action of clotrimazole is primarily fungistatic or fungicidal depending on the concentration of clotrimazole at the site of infection. *In vitro* activity is limited to proliferating fungal elements; fungal spores are only slightly sensitive.

In addition to its antimycotic action, clotrimazole also acts on gram-positive microorganisms (Streptococci / Staphylococci / Gardnerella vaginalis), and gram-negative microorganisms (Bacteroides).

In vitro clotrimazole inhibits the multiplication of Corynebacteria and gram-positive cocci - with the exception of Enterococci – in concentrations of 0.5-10 µg/ml substrate.
Primarily resistant variants of sensitive fungal species are very rare; the development of secondary resistance by sensitive fungi has so far only been observed in very isolated cases under therapeutic conditions.

5.2 Pharmacokinetic properties

Pharmacokinetic investigations after dermal application have shown that clotrimazole is minimally absorbed from the intact or inflamed skin into the human blood circulation. The resulting peak serum concentrations of clotrimazole were below the detection limit of 0.001 mcg/ml, suggesting that clotrimazole applied topically is unlikely to lead to measurable systemic effects or side effects.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of repeated dose toxicity, genotoxicity and carcinogenicity.

Clotrimazole was not teratogenic in reproductive toxicity studies in mice, rats and rabbits. In rats high oral doses were associated with maternal toxicity, embryotoxicity, reduced fetal weights and decreased pup survival.
In rats clotrimazole and/or its metabolites were secreted into milk at levels higher than in plasma by a factor of 10 to 20 at 4 hrs after administration, followed by a decline to a factor of 0.4 by 24 hrs.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene Glycol, Isopropanol, Polyethylene Glycol 400

6.2 Incompatibilities

Not applicable

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store below 25 °C.
Shelf life after first opening: 60 days
Caution! Inflammable material. Keep away from fire.

6.5 Nature and contents of container

Plastic bottle, 20 ml.

6.6 Special precautions for disposal

Caution! Inflammable material. Keep away from fire.
Do not light a cigarette or expose to fire before the medicine has fully dried.

7 Manufacturer and Marketing Authorisation Holder

Padagis Israel Pharmaceuticals Ltd.
1 Rakefet st. Shoham.

8 Registration Number

042-26-22463

Revised on November 2024 according to MOH guidelines.