ÆSCULAPIUS
FARMACEUTICI

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF MEDICINAL PRODUCT

ECOMESOL 1% cream
ECOMESOL 1% skin solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ECOMESOL 1% **cream**:
100 grams of cream contains:
Active ingredient: Econazole nitrate g 1.00

ECOMESOL 1% **skin solution**:
100 ml of solution contains:
Active ingredient: Econazole nitrate g 1.00

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream – Skin solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cutaneous mycoses caused by dermatophytes, yeasts and moulds, also accompanied by infections caused by gram-positive bacteria.

4.2 Posology and method of administration

One application in the morning and one in the evening on the infected skin areas with a gentle massage.

In the case of humid intertriginous areas (interdigital areas in feet, folds in glutei), it is recommended to clean with gauze or bandages before the application of ECOMESOL.

4.3 Contraindications

ECOMESOL is contraindicated in patients who have shown hypersensitivity to the active ingredient or to any of the excipients.

4.4 Special warnings and precautions for use

Only for external use. ECOMESOL is not for ophthalmic or oral use.
Whenever a sensitisation or irritation reaction occurs, the use of the product should be interrupted.

4.5 Interaction with other medicinal products and other forms of interaction

Econazole is a known inhibitor of cytochromes CYP3A4 and CYP2C9. In spite of the poor systemic availability after application on the skin, there may be clinically relevant interactions that have been reported in patients treated with oral anticoagulants, such as warfarin and acenocoumarol. In these patients, caution must be exercised, and the INR must be monitored more frequently. It may be necessary to adjust the dose of the oral anticoagulant during the treatment with econazole and after its interruption.

4.6 Pregnancy and lactation

Use during pregnancy

Animal studies have shown that econazole nitrate does not have teratogenic effects, but it has been demonstrated that it is fetotoxic in rodents at maternal subcutaneous doses of 20mg/Kg/day and at oral maternal doses of 10mg/Kg/day. The relevance of such effect on human beings is not known.

In human beings, the systemic absorption of econazole is low (< 10%) after its topical application on unharmed skin. There are no suitable, controlled studies on the undesirable effects deriving from the use of ECOMESOL during pregnancy, and there are no other relevant epidemiological data available. Based on the limited amount of post-marketing data, no undesirable effects of ECOMESOL on pregnancy or on the health of the foetus or of the newborn have been identified.

Due to systemic absorption, ECOMESOL must not be used in the first trimester of pregnancy, unless the doctor considers it necessary for the patient's health.

ECOMESOL may be used during the second and third trimesters of pregnancy if the potential benefits for the mother outweigh the possible risks for the foetus.

Use during lactation

After the oral administration of econazole nitrate in female rats during lactation, econazole and/or its metabolites have been excreted in milk, and have been found in the baby breast-fed rats.

It is not known whether the skin administration of ECOMESOL may cause such a systemic absorption of econazole that would produce detectable amounts in human breast milk.

Caution must be exercised when ECOMESOL is administered to women during lactation.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Data deriving from clinical studies

The safety of econazole nitrate cream (1%) and econazole nitrate emulsion (1%) has been assessed on 470 individuals participating in 12 clinical studies, who have been administered at least one of the formulations. Based on the safety data collected from these clinical studies, the most commonly reported (incidence ≥ 1%) Adverse Drug Reactions (ADRs) have been (with incidence in %): pruritus (1.3%), skin burning sensation (1.3%), and pain (1.1%).

The table below shows the ADRs that have been reported with the use of dermatological formulations of econazole in clinical studies or in post-marketing experience. The frequency classes have been reported 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) and not known (frequency cannot be estimated from the available data coming from clinical studies).

In the table below, all the ADRs with known incidence (common or uncommon) come from clinical studies, and all the ADRs with unknown incidence come from post-marketing data.

Table 1: Adverse Drug Reactions (ADRs)

Systemic-organic classification	**Adverse Drug Reactions**		
	Frequency class		
	Common (from ≥ 1/100 to <1/10)	**Uncommon** (from ≥ 1/1,000 to < 1/100)	**Not known**
Skin and subcutaneous tissue disorders	Pruritus Skin burning sensation	Erythema	Angioedema Contact dermatitis Skin eruption Urticaria Blister Skin exfoliation
General disorders and administration site conditions	Pain	Discomfort Swelling	

This product may cause sensitisation, especially when used for a prolonged period. In case of hypersensitivity reactions, the treatment should be discontinued and a suitable therapy should be followed; similar measures should be adopted in case of development of non-susceptible micro-organisms.

Reporting suspected adverse reactions
Reporting suspected adverse reactions seen after the authorisation of the medicinal product is important. It allows continued monitoring of benefit/risk balance of the medicinal product.
Healthcare professionals are asked to report any suspected adverse reaction via the Italian national reporting system to this address: http://www.agenziafarmaco.gov.it/it/responsabili.

4.9 Overdose

ECOMESOL is to be exclusively used for application on the skin. In case of accidental ingestion, there may be nausea, vomiting and diarrhoea; treat with symptomatic therapy. Given the available pharmaceutical forms, which are intended for topical application, cases of acute overdose due to ingestion are extremely unlikely and have never been reported so far. If the product accidentally comes into contact with the eyes, wash with clean water or saline, and consult the doctor if symptoms persist.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group:
Cream and skin solution: antifungals for topical use – ATC Code D01AC03

Econazole is an antifungal for topical use. It is effective against dermatophytes, yeasts and moulds, therefore including all human pathogenic fungi.
Econazole is also active against gram-positive bacteria, which constitutes an advantageous property in case of mixed infections.
Econazole exerts its action both at the level of the cell membrane of the pathogenic agent, and by interfering with the biosynthesis connected to it.

Exposing fungal cells to the drug causes, in temporal succession, the appearance of the following phenomena:
increase in the permeability of the cell wall
entrance of the drug into cytoplasm
alteration of all membranous systems
appearance of decomposition products grouped in blisters; accumulation of lipid substances. This causes a blocking effect on the metabolism of the RNA, of proteins and of lipids.

5.2 Pharmacokinetic properties

As it is a product for topical use, tests have been conducted to check for a possible systemic absorption. In no case, a clinically significant absorption of the econazole active ingredient has been demonstrated, neither in animals nor in human beings, after application either on the skin or on the vagina.

5.3 Preclinical safety data

Toxicological tests on different animal species have demonstrated that ECOMESOL is well tolerated. In addition, it is not teratogenic or mutagenic.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

ECOMESOL 1% **cream**:
polyglycerol ester of fatty acids, propylene glycol, methyl parahydroxybenzoate, propyl parahydroxybenzoate, deionised water.
ECOMESOL 1% **skin solution**:
ethyl alcohol, propylene glycol, methyl parahydroxybenzoate, propyl parahydroxybenzoate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years, unopened package.

6.4 Special precautions for storage

No special precautions for storage.

6.5 Nature and contents of container

1% Cream: 30 g aluminium tube.
1% Skin solution: 30 ml bottle.

6.6 **Special precautions for disposal**

Medicines no longer used or medical waste should be disposed of in compliance with the local regulations in force.

7. MARKETING AUTHORISATION HOLDER

Aesculapius Farmaceutici S.r.l. – Via Cefalonia, 70 – 25124 Brescia

8. MARKETING AUTHORISATION NUMBERS

ECOMESOL 1% cream	025055017
ECOMESOL 1% skin solution	025055031

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of renewal: June 2010

10. DATE OF REVISION OF THE TEXT

March 2017