SUMMARY OF THE DRUG'S CHARACTERISTICS

1. DRUG NAME

Esomed Gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The active substance is hydroquinone. Each gram of cream contains 40mg of hydroquinone (4% w/w of hydroquinone).

For the complete list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gel.

4. CLINICAL INFORMATION

4.1 Indication and usage

Esomed gel is indicated for the Lightening of skin spots. It is intended for external use only. Not for ophthalmic use.

4.2 Dosage and method of administration

Adults and children over 12 years:
Esomed gel should be as a thin layer of gel, to hyperpigmented, small surfaces.
Always avoid contact with eyes and mucous membranes.
Starting with one application per day for 10 or 15 days exclusively on the
stain and continue treatment with two applications daily, once in the morning and once in the overnight.
If improvement is not observed after 2 months of treatment, this should be
discontinued.
The duration of treatment is recommended for 60 to 90 days.
This medicine should not be used under any circumstances for more than 6 months.

4.3 Contraindications

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

Esomed gel is contraindicated for treatment of chemical hyperpigmentation such as ochronosis and colloid degeneration (colloid milium), whether of occupational or cosmetic origin.
Esomed gel is contraindicated during pregnancy as there is not enough data available about the use of hydroquinone in pregnant mothers.

4.4 Warnings and special precautions

It should not be applied on open wounds, mucous membrane, or skin affected by eczema, irritation or sunburn.

Avoid contact with the eyes and the mucous membrane. In the event of accidental contact with the eyes, wash with plenty of water to avoid possible dark patches on the cornea. If it comes into contact with the lips, you may notice a bitter taste and a slight anaesthetic effect.

If the pigmented zone is very large, it should be split up and treated in different cycles.

During treatment with hydroquinone, it is essential to protect the treated zone from the sun, given that minimum exposure to sunrays may reactivate melanin production. During the day it is recommended to use a high-protection sun block.

Wash your hands with soap after applying the product, as the hydroquinone may cause reversible brown stains on your nails.

This product cannot be used to prevent sunburn.

The effects of the hydroquinone may be less visible for people with very dark skin.

For some people, especially those with sensitive skin, hypersensitive reactions may occur. To check for such reactions, it is advisable for hypersensitive people to apply a small amount of the drug on the inside of the forearm, for at least 24 hours.
If the skin is badly irritated, stop using the drug.

In some cases a temporary darkening or irritation of the skin may occur; if this side effect continues, stop the treatment.
The depigmentation is not immediate, as the hydroquinone only interferes in the formation of new melanin, and it is a temporary reaction, so when the treatment is stopped the production of melanin is reactivated. The depigmentation may continue between 2 and 6 months after stopping the treatment. The darker the lesions, the earlier the repigmentation will occur.

4.5 Drug interactions and other forms of interaction

Concomitant use of hydroquinone with peroxides, such as oxygenated water or benzoyl peroxide, may lead to temporary colouring of the skin owing to the oxidation of the hydroquinone. This temporary colouring will disappear if you stop using these products and wash the application zone with a mild soap.

4.6 Pregnancy and breastfeeding

Animal tests have not shown teratogenic effects in non-toxic doses for mothers. However, Esomed gel is contraindicated during pregnancy as there is not enough data available about the use of hydroquinone in pregnant mothers.

4.7 Effects on the ability to drive vehicles or use machinery

There are no effects on the ability to drive vehicles or use machinery.

4.8 Undesirable effects

The undesirable effects are listed in decreasing order of severity within each frequency class.

Occasionally erythema, a burning sensation and less frequently skin sensitivity may be felt. If these symptoms do not disappear after one week, stop the treatment. In long-term treatment, hyperpigmentation skin reactions may occur.

Rarely, in long-term treatment (over 6 months), cases of ochronosis have been reported, mainly in black individuals.

There have been sporadic reports of leukodermal reactions.

No systematic adverse effects have been described.

If any of the above-mentioned undesirable side effects occur, stop the treatment.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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 according to the National Regulation by using an online form at http://sideeffects.health.gov.il
In addition, you can report to Perrigo via the following address: www.perrigo-pharma.co.il

4.9 Overdose

No cases of overdose have been described.

As an externally used drug, intoxication is unlikely. Accidental ingestion may lead to severe intoxication effects similar to hay fever. The oral ingestion of 5-15g of hydroquinone can result in tremors, seizures and haemolytic anaemia. In this case stomach pumping is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic classification: 13.8. – Other drugs used in dermatology.
Topical immunomodulators.
ATC Code: D11AX 11 Hydroquinone

The hydroquinone selectively changes the melanin production process, causing the progressive and reversible depigmenting of the skin through a tyrosinase inhibition mechanism, given that tyrosinase is the enzyme that turns tyrosine into melanin. The hydroquinone is highly selective for the melanosomes, and does not affect other cellular organelles. It has been proven that the internal structure of the melanocyte is changed through direct intracellular damage, which can lead to a reduction in the production of melamine or an increase in the degradation of the organelles or both processes simultaneously, with the consequent depigmenting of the skin.

The hydroquinone only interferes with the formation of the new melanin, so the depigmenting effect is not immediate and is only temporary, as melanin production is reactivated when the treatment with hydroquinone is stopped (see section 4.4).

5.2 Pharmacokinetic properties

The application of hydroquinone on small skin surfaces, its slow absorption through the skin and its fast urine excretion make it likely that systemic effects shall be produced.

5.3 Pre-clinical safety data

Topical toxicity studies on rabbits and guinea pigs showed depigmenting in the application zone as the most frequent finding, with the appearance of differing degrees of dermal irritation or erythema. In neither case were haematological, analytical, organic or functional changes described, apart from a slight thyroid hyperplasia.
For high concentrations (5-20%) in extensive applications (15-90%) of the shaved body, a low weight increase, lower number of lymphocytes in the blood, larger supra-renal glands and focal fibrosis in the myocardial of some guinea pigs was observed.

The teratology studies carried out on mice (oral and topical administration) and rabbits did not show toxic effects on fertility, reproduction and foetuses with non-toxic doses for mothers.

Hydroquinone has shown potential genotoxicity and carcinogenicity in long-term studies with high doses, orally administered. However, shorter studies with skin administration did not indicate carcinogenicity. Taking into account that hydroquinone is also a substance present in breastfeeding, Esomed gel administered in therapeutic doses is not believed to represent a significant increase in the risk of carcinogenicity.

Skin sensitisation tests showed that hydroquinone had moderate sensitising capacity.

6. PHARMACEUTICAL INFORMATION

6.1 List of excipients

Excipients:

Purified water, Carbomer 940, Sodium Metabisulfite, Methylparaben, Sodium Hydroxide, Edetate Disodium.

6.2 Incompatibilities

Hydroquinone reacts with peroxides (see section 4.5).

6.3 Expiry date

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

6.4 Special conservation precautions

Close the recipient after each application.

6.5 Nature and content of the recipient

Esomed gel is available in a 30g or 60 g tube. Store below 25°C. Shelf life after first opening of the tube are 2 months.

Some of the package sizes may be not marketed.

6.6 Special precautions for disposal and handling

No special requirements.

The products not used and the waste should be disposed of in compliance with the local regulations.

Wash your hands with soap after handling the product.

7. MARKETING AUTHORISATION HOLDER

Perrigo Israel Agencies Ltd.,1 Rakefet St., Shoham

8. MARKETING AUTHORISATION NUMBER

132-93-30978-00

9. MANUFACTURER
Ben Shimon Floris Ltd., Industrial park Misgav (Taradion), Israel, 2017400.

10. TEXT REVISION DATE

Revised on September 2020