DUOFILM®

Salicylic Acid and Lactic Acid Collodion

QUALITATIVE AND QUANTITATIVE COMPOSITION

Salicylic Acid IP 16.7 % w/w
Lactic Acid IP 16.7 % w/w
Flexible Collodion BP (contains Ethanol 20 to 23 % v/v) q.s.

PHARMACEUTICAL FORM

Solution for topical administration.

CLINICAL PARTICULARS

Therapeutic Indications

DUOFILM is indicated for the treatment of warts, corns and calluses.

Posology and Method of Administration

For topical use only.

- Adults the elderly and children aged 2 years and over:

DUOFILM should be applied to the affected areas only.

Use in children should be under the supervision of an adult.

DUOFILM should be applied to the wart, corn or callus once daily, preferably at bedtime. Procedure for application:

1. The wart, corn or callus should be soaked in warm water for 5 minutes and dried thoroughly with a clean towel.

2. The surface of the wart, corn or callus should be rubbed with a nail file, pumice stone, emery board or coarse washcloth, with care taken not to cause bleeding.

3. A thin layer of DUOFILM should be applied directly to the wart, corn or callus. Care should be taken to avoid the healthy surrounding skin.
4. The solution should be allowed to dry thoroughly. The wart, corn or callus should be covered with a plaster (dressing) if it is large or if it is on the foot to help penetration of ingredients.

It is recommended that treatment continues until whichever of the following occurs first:
- corns and calluses have been treated for 2 weeks
- warts have been treated for 12 weeks
- or until the wart, corn or callus is completely cleared and the normal ridgelines of the skin have been restored.

For warts, clinically visible improvement should occur in 1-2 weeks, but the maximum effect may be expected after 4-8 weeks.

If warts persist beyond 12 weeks of treatment, the patient should be advised to consult their doctor.

Consider alternative treatments if warts cover a large area of the body (more than 5 cm²) (see Special Warnings and Special Precautions for Use).

Patients should be advised to consult a doctor if skin irritation develops.

Due to the flammable nature of salicylic acid and lactic acid solution, patients should avoid smoking or being near an open flame during application and immediately after use.

- **Infants under 2 years of age**

Treatment of infants under the age of 2 years is not recommended.

- **Elderly**

No dosage adjustment is required as clinically significant systemic exposure is not expected.

- **Hepatic Impairment**

No dosage adjustment is required as clinically significant systemic exposure is not expected.

- **Renal Impairment**

No dosage adjustment is required as clinically significant systemic exposure is not expected.

**Contraindications**

*DUOFILM* is contraindicated in patients with a prior hypersensitivity reaction to salicylic acid, lactic acid or any other ingredient of the preparation.
Do not use on open wounds, irritated or reddened skin, or any area that is infected.

Do not use on moles, birthmarks, genital warts, warts on the face or mucous membranes, or warts with hair growing from them, red edges, or an unusual colour.

**Special Warnings and Special Precautions for Use**

Salicylic acid and lactic acid solution may cause eye irritation. Avoid contact with eyes and other mucous membranes. In case of accidental contact with the eyes or other mucous membranes, flush with water for 15 minutes.

Avoid exposure to healthy skin (see *Undesirable Effects*). Salicylic acid and lactic acid solution may cause skin irritation. If undue skin irritation develops treatment should be discontinued.

Consider alternative treatments if warts cover a large area of the body (more than 5 cm$^2$) due to the potential risk of salicylate toxicity.

*DUOFILM* is not recommended in patients with diabetes, circulatory problems or peripheral neuropathy except under the supervision of a doctor.

Oral salicylates taken during or immediately after a viral illness have been associated with Reye’s syndrome and hence there is a theoretical risk with topical salicylates. Therefore, do not use in children or teenagers during or immediately after chickenpox, influenza, or other viral infections.

It has been reported that salicylates are excreted via breastmilk (see *Pregnancy and Lactation*).

Patients should be advised not to inhale the vapour.

Keep out of the sight and reach of children.

**Interaction with Other Medicaments and Other Forms of Interaction**

Topical salicylic acid and lactic acid solution may increase the absorption of other topically applied medicines. Therefore, concomitant use of *DUOFILM* and other topical medicines on the treated area should be avoided. As systemic exposure of topically applied salicylic acid and lactic acid solution is low, interaction with systemically administered medicines is not anticipated.
Pregnancy and Lactation

**Pregnancy**

The safety of salicylic acid and lactic acid solution during human pregnancy has not been established. Studies in animals given salicylic acid orally demonstrated embryo-toxicity at high doses (see *Preclinical Safety Data*).

*DUOFILM* is not recommended during pregnancy.

**Lactation**

Salicylates are excreted in human milk. *DUOFILM* is not recommended during lactation.

If used or administered during lactation, care should be taken to avoid contact with the breast area in order to avoid accidental ingestion by the infant.

**Effects on Ability to Drive and Use Machines**

No effects are anticipated based on the adverse reaction profile.

**Undesirable Effects**

The following convention is used for the classification of the frequency of an adverse reaction and is based on the CIOMS guidelines:

- **Very common:** $\geq 1/10$
- **Common:** $\geq 1/100$ to $<1/10$
- **Uncommon:** $\geq 1/1000$ to $<1/100$
- **Rare:** $\geq 1/10000$ to $<1/1000$
- **Very rare:** $<1/10000$
- **Not known:** (Cannot be estimated from the available data)

**Clinical Trial Data**

**Immune system disorders**

- **Common:** Rash

**Skin and subcutaneous tissue disorders**

- **Very common:** Application site reaction, pruritus, burning sensation, erythema, scaling, dryness
- **Common:** Skin hypertrophy
Post Marketing Data

Immune system disorders

Rare: Application site hypersensitivity including inflammation

Skin and subcutaneous tissue disorders

Rare:
- Application site pain and irritation
- Application site discoloration/skin discoloration
- Exposure to healthy skin can lead to application site blistering and skin exfoliation (see Special Warnings and Special Precautions for Use).
- Allergic dermatitis

Overdose

Symptoms and Signs

In the event of accidental oral ingestion symptoms of salicylate toxicity may occur.

The risk of developing symptoms of salicylate poisoning or salicylism is increased if topical salicylic acid and lactic acid solution is used excessively or if it is used for prolonged periods of time. Therefore, duration of use and recommended frequency compliance is very important.

Treatment

Management should be as clinically indicated or as recommended by the national poisons centre, where available. There is no specific treatment for accidental oral ingestion of salicylic acid and lactic acid solution. If accidental oral ingestion occurs, the patient should be treated according to local guidelines with appropriate monitoring as necessary.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Pharmacotherapeutic group: Wart and anti-corn preparations; ATC code: D11AF.

Mechanism of Action

Topically applied salicylic acid is keratolytic. The keratolytic activity produces desquamation by solubilising the intercellular cement in the stratum corneum resulting in the shedding of skin scales.
Lactic acid affects the keratinisation process, reducing the hyperkeratosis which is characteristic of warts, corns and calluses. At high concentrations it can cause epidermolysis, leading to the destruction of the keratotic tissue, and in the case of warts, of the causative virus. It also has antiseptic properties.

Flexible collodion provides a viscous vehicle that allows accurate application of the active ingredients to the wart, corn or callus. It also forms a film that helps to hydrate and promote the destruction of hyperkeratotic tissue.

**Pharmacokinetic Properties**

*Absorption*

Salicylic acid is absorbed through the skin; where detectable, maximum plasma levels are found 6 to 12 hours after application. Systemic absorption of salicylic acid has been reported to range from 9% to 25% after topical application of other salicylic acid-containing preparations. The extent of absorption is variable depending on the duration of contact and the vehicle. Despite percutaneous absorption, the systemic exposure is low given the low dose topically administered to small, localised areas of hyperkeratotic tissue.

Human abdominal skin in a flow-through diffusion system was used to assess the *in vitro* percutaneous absorption of lactic acid. At a pH of 3, the amount of radioactivity detected in the receptor fluid, stratum corneum, epidermis, and dermis was 3.6, 6.3, 6.6, and 13.9%, respectively.

*Distribution*

Following percutaneous absorption, salicylic acid is distributed in the extracellular space; approximately half of which is protein bound to albumin.

*Metabolism*

Salicylates are metabolised in the liver by microsomal enzymes to salicyluric acid and phenolic glucuronides of salicylic acid. That which is not metabolised is excreted in the urine as unchanged salicylic acid.

*Elimination*

Within 24 hours of salicylic acid being absorbed and distributed in the intercellular space, approximately 95% of the absorbed dose can be recovered in the urine.

*Clinical Studies*

The efficacy of salicylic acid and lactic acid solution was compared with that of placebo (flexible collodion), alkyl dimethylbenzyl ammonium halide dibromide wart paint, and
podophyllin resin 50% in liquid paraffin in a study conducted in 382 subjects most of whom had plantar warts. Of 348 subjects included in the efficacy analysis, the number of subjects completing the study was 336. By the end of the 12-week treatment period, 84% of subjects treated for plantar warts with salicylic acid and lactic acid solution (n/N=64/76) had skin cleared of warts with ridgelines restored (and of those 64 subjects, 64% were cleared of warts at 6 weeks). This compared with skin clearance rates at 12 weeks of 66% for placebo [n/N=50/76], 67% for the wart paint [n/N=47/70], and 81% for podophyllin [n/N=60/74]. These results show that salicylic acid and lactic acid solution was statistically significantly more effective than the placebo and the wart paint at 12 weeks (p<0.02) for the treatment of plantar warts. For mosaic warts, the results were 50% clearance rate at 12 weeks for salicylic acid and lactic acid solution (n/N=7/14), 58% for placebo [n/N=7/12], 75% for the wart paint [n/N=9/12], and 50% for podophyllin [n/N=7/14].

A study compared salicylic acid and lactic acid solution treatment with cautery and was carried out in 85 subjects with common and plantar warts over a 12 week treatment period. Subjects were instructed to apply salicylic acid and lactic acid solution once or twice daily for 3 months after which treatment was to be discontinued (or earlier if a complete clearance had been effected, whichever occurred first). At Week 12 the percentage of subjects with complete clearance or improvement of the wart was 86.8% for those treated with salicylic acid and lactic acid solution (n/N=33/38) and 71.8% for those treated with cautery (n/N=28/39). The number of subjects with complete clearance at Week 12 was 13 and 0 in the two treatment groups, respectively. This study demonstrated statistically significant improvement for salicylic acid and lactic acid solution in efficacy, safety and acceptability rates in the treatment of warts compared with conventional cautery.

Preclinical Safety Data

Preclinical safety data on salicylic acid and lactic acid obtained from the literature and in-house have not revealed findings which are of relevance to the recommended dosage and use of the product.

Carcinogenesis and mutagenesis

No carcinogenicity or genotoxicity studies were conducted with salicylic acid (16.7%) and lactic acid (16.7%) solution. Data available on the individual ingredients are detailed below.

Carcinogenesis

Carcinogenicity studies have not been conducted with salicylic acid.

In a carcinogenicity study in rabbits (oral doses up to 0.7 g/kg/day for 16 months) lactic acid did not show evidence of tumorigenicity.
**Mutagenesis**

Salicylic acid (2 mg) exhibited specific DNA-damaging properties *in vitro* in the Rec-assay and mutagenicity *in vitro* in the Ames assay using *Salmonella typhimurium* strain TA100 with metabolic activation.

Lactic acid was negative for mutagenicity *in vitro* in the Ames, chromosomal aberration, and unscheduled DNA synthesis assays.

**Reproductive Toxicology**

No embryonic development studies were conducted with salicylic acid (16.7%) and lactic acid (16.7%) solution. Data available on the individual ingredients are detailed below.

Salicylates, including salicylic acid, cross the placental barrier in rodents, rabbits, dogs, and ferrets, and are teratogenic when administered orally at high doses. When administered to pregnant rats and rabbits orally at high doses, salicylic acid increased congenital malformations, primarily involving the skeleton and central nervous system.

In an embryo-fetal development study in mice, the only fetal effect noted following oral administration of 570 mg/kg/day lactic acid from Gestation Day 6 to 15 was an increase in delayed ossification of the parietal bones.

**PHARMACEUTICAL PARTICULARS**

**List of Excipients**

Flexible Collodion (contains Ethanol 20 to 23 % v/v).

**Incompatibilities**

No incompatibilities have been identified.

**Shelf Life**

24 months.

The expiry date is indicated on the label and packaging.

**Special Precautions for Storage**

Store in a cool place not exceeding 25°C

Keep out of reach of children.
Nature and Specification of Container

Bottle with an applicator in a carton.

Instructions for Use / Handling

There are no special requirements for use or handling of this product.

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