SUMMARY OF PRODUCT CHARACTERISTICS

Deriva Aqueous Gel

(Adapalene Gel 0.1% w/w)

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1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

1.1 Strength

0.1% w/w

1.2 Pharmaceutical form

Topical Gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 Qualitative declaration

Ingredients	Specifications
Adapalene (Micronised)	BP
Di-Sodium Edetate	BP
Carbomer 940 (Carbopol 940)	USP-NF
Propylene Glycol	USP
Methyl Hydroxybenzoate	BP
Phenoxyethanol	BP
Poloxamer 407	USP-NF
Sodium Hydroxide	BP
Purified Water	BP

2.2 Quantitative declaration

Ingredients	Specifications	Quantity (% w/w)	Function
Adapalene (Micronised)	BP	0.1@	Active Ingredient
Di-Sodium Edetate	BP	0.050	Chelating Agent
Carbomer 940 (Carbopol 940)	USP-NF	0.550	Viscolizer / Gelling agent
Propylene Glycol	USP	8.000	Solvent/Humectant
Methyl Hydroxybenzoate	BP	0.100	Preservative
Phenoxyethanol	BP	0.250	Preservative
Poloxamer 407	USP-NF	0.100	Surfactant
Sodium Hydroxide	BP	0.068	Neutralizer
Purified Water	BP	91.000#	Solvent

@, # Quantity depends upon potency of drug.

3. PHARMACEUTICAL FORM

Topical Gel

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Adapalene Gel 0.1% is proposed for the cutaneous treatment of mild to moderate acne where comedones, papules and pustules predominate. Acne of the face, chest or back is appropriate for treatment.

4.2 Posology and method of administration

Posology

Adapalene Gel 0.1% should be applied to the acne affected areas once a day before retiring and after washing.

Since it is customary to alternate therapies in the treatment of acne, it is recommended that the physician assess the continued improvement of the patient after three months of treatment with Adapalene Gel 0.1%.

With patients for whom it is necessary to reduce the frequency of application or to temporarily discontinue treatment, frequency of application may be restored or therapy resumed once it is judged that the patient can again tolerate the treatment.

If patients use cosmetics, these should be non-comedogenic and non-astringent.

Special populations

a) ***Elderly population:*** No data available

b) ***Renal impairment:*** No data available

c) ***Hepatic impairment:*** No data available

d) ***Patients with a particular genotype:*** No data available

e) ***Other relevant special population:*** No data available

Paediatric population

The safety and effectiveness of Adapalene Gel 0.1% have not been studied in children below 12 years of age. Adapalene Gel 0.1% should not be used in patients with severe acne.

4.3 Method of administration

A thin film of gel should be applied, with the fingertips, avoiding the eyes and lips. Ensure that the affected areas are dry before application.

4.4 Contraindications

Pregnancy.

Women planning a pregnancy.

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

4.5 Special warnings and precautions for use

If a reaction suggesting sensitivity or severe irritation occurs, use of the medication should be discontinued. If the degree of local irritation warrants, patients should be directed to use the medication less frequently, to discontinue use temporarily until symptoms subside, or to discontinue use altogether. Adapalene Gel 0.1% should not come into contact with the eyes, mouth, angles of the nose or mucous membranes.

If product enters the eye, wash immediately with warm water. The product should not be applied to either broken (cut and abrasions) sunburnt or eczematous skin, nor should it be used in patients with severe acne involving large areas of the body.

Exposure to sunlight and UV light irradiation should be minimised during use of Adapalene Gel 0.1%.

Adapalene Gel 0.1% contains methyl parahydroxybenzoate (E218). It may cause allergic reactions which can possibly be delayed.

This medicine also contains 40mg propylene glycol (E1520) in each gram which is equivalent to 4% w/w. It may cause skin irritation

4.6 Paediatric population

No data available.

4.7 Interaction with other medicinal products and other forms of interaction

There are no known interactions with other medications which might be used cutaneously and concurrently with Adapalene Gel 0.1%, however, other retinoids or drugs with a similar mode of action should not be used concurrently with adapalene.

Adapalene is essentially stable to oxygen and light and is chemically non-reactive. Whilst extensive studies in animals and man have shown neither phototoxic nor photoallergic potential for adapalene, the safety of using adapalene during repeated exposure to sunlight or UV irradiation has not been established in either animals or man. Exposure to excessive sunlight or UV irradiation should be avoided.

Absorption of adapalene through human skin is low and therefore interaction with systemic medications is unlikely. There is no evidence that the efficacy of oral drugs such as contraceptives and antibiotics is influenced by the cutaneous use of Adapalene Gel 0.1%.

Adapalene Gel 0.1% has a potential for mild local irritation, and therefore it is possible that concomitant use of peeling agents, abrasive cleansers, strong drying agents, astringents or irritant products (aromatic and alcoholic agents) may produce additive irritant effects. However, cutaneous antiacne treatment (eg erythromycin up to 4%) or clindamycin phosphate (1% as the base) solutions or benzoyl peroxide water based gels up to 10% may be used in the morning when Adapalene Gel 0.1% is used at night as there is no mutual degradation or cumulative irritation.

4.8 Additional information on special populations

No data available.

4.9 Paediatric population

No data available.

4.10 Fertility, pregnancy and lactation

4.10.1 General principles

Orally administered retinoids have been associated with congenital abnormalities. When used in accordance with the prescribing information, topically administered retinoids are generally assumed to result in low systemic exposure due to minimal dermal absorption. However, there could be individual factors (e.g. damaged skin barrier, excessive use) that contribute to an increased systemic exposure.

4.10.2 Women of childbearing potential / Contraception in males and females

No data available.

4.10.3 Pregnancy

Adapalene Gel 0.1% is contraindicated in pregnancy, or in women planning a pregnancy.

Animal studies by the oral route have shown reproductive toxicity at high systemic exposure. Clinical experience with locally applied adapalene in pregnancy is limited but the few available data do not indicate harmful effects on pregnancy or on the health of the foetus exposed in early pregnancy. Due to the limited available data and because a very weak cutaneous passage of adapalene is possible, Adapalene Gel 0.1% should not be used during pregnancy. If the product is used during pregnancy, or if the patient becomes pregnant while taking this drug, treatment should be discontinued.

4.10.4 Breastfeeding

No study on animal or human milk transfer was conducted after cutaneous application of Adapalene Gel 0.1%. No effects on the suckling child are anticipated since the systemic exposure of the breast-feeding woman to Adapalene Gel 0.1% is negligible.

Adapalene Gel 0.1% can be used during breastfeeding. To avoid contact exposure of the infant, application of Adapalene Gel 0.1% to the chest should be avoided when used during breast-feeding.

4.10.5 Fertility

No data available.

4.11 Effects on ability to drive and use machines

Adapalene Gel 0.1% has no influence on the ability to drive and use machines.

4.12 Undesirable effects

a) Summary of the safety profile

No data available.

b) Tabulated list of adverse reactions

Adapalene Gel 0.1% may cause the following adverse drug reactions:

Body System (MeDRA)	Frequency	Adverse Drug Reaction
Skin and subcutaneous tissue disorders	Common (≥1/100 to <1/10)	Dry skin, skin irritation, skin burning sensation, erythema
	Uncommon (≥1/1000 to <1/100)	Dermatitis contact, skin discomfort, sunburn, pruritus, skin exfoliation, acne
	Unknown*	Dermatitis allergic (allergic contact dermatitis), pain of skin, skin swelling, application site burn**, skin hypopigmentation, skin hyperpigmentation
Eye disorders	Unknown*	eyelid irritation, eyelid erythema, eyelid pruritus, eyelid swelling
Immune system disorders	Unknown*	Anaphylactic reaction, angioedema

*Post marketing surveillance data
** Most of the cases of "application site burn" were superficial burns but cases with second degree burn reactions have been reported.

c) Description of selected adverse reactions

No data available.

d) Paediatric population

No data available.

e) Other special populations

No data available.

f) Further guidance on the estimation of frequency of adverse reactions

Adverse reactions from clinical trials: No data available.

Adverse reactions from safety studies: No data available.

Adverse reactions from spontaneous reporting: No data available.

Reporting of suspected adverse reactions

Reporting suspected adverse reaction after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via national reporting system.

4.13 Overdose

Adapalene Gel 0.1% is not to be taken orally and is for cutaneous use only. If the medication is applied excessively, no more rapid or better results will be obtained and marked redness, peeling or discomfort may occur.

The acute oral dose of Adapalene Gel 0.1% required to produce toxic effects in mice is greater than 10 g/kg. Nevertheless, unless the amount accidentally ingested is small, an appropriate method of gastric emptying should be considered.

Additional information on special populations

No data available.

Paediatric population

No data available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-Acne Preparations for Topical Use

ATC code: D10AD03

Mechanism of action

Adapalene is a retinoid-like compound which in, in vivo and in vitro models of inflammation, has been demonstrated to possess anti-inflammatory properties. Adapalene is essentially stable to oxygen and light and is chemically non-reactive. Mechanically, adapalene binds like tretinoin to specific retinoic acid nuclear receptors but, unlike tretinoin not to cytosolic receptor binding proteins.

Adapalene applied cutaneously is comedolytic in the rhino mouse model and also has effects on the abnormal processes of epidermal keratinization and differentiation, both of which are present in the pathogenesis of acne vulgaris. The mode of action of adapalene is suggested to be a normalisation of differentiation of follicular epithelial cells resulting in decreased microcomedone formation.

Pharmacodynamic effects

Adapalene is superior to reference retinoids in standard anti-inflammatory assays, both in vivo and in vitro. Mechanistically, it inhibits chemotactic and chemokinetic responses of human polymorphonuclear leucocytes and also the metabolism by lipoxidation of arachidonic acid to pro-inflammatory mediators. This profile suggests that the cell mediated inflammatory component of acne may be modified by adapalene.

Clinical efficacy and safety

No data available.

Paediatric population: No data available.

5.2 Pharmacokinetic properties

a) General introduction

No data available.

b) General characteristics of the active substance(s) after administration of the medicinal product

Absorption:

Absorption of adapalene through human skin is low, in clinical trial measurable plasma adapalene levels where not found following chronic cutaneous application to large areas of acneic skin with an analytical sensitivity of 0.15 ng/ml.

Distribution:

After administration of [^{14}C] adapalene in rats (IV, IP, oral and cutaneous), rabbits (IV, oral and cutaneous) and dogs (IV and oral), radioactivity was distributed in several tissues, the highest levels being found in liver, spleen, adrenals and ovaries.

Biotransformation and Elimination:

Metabolism in animals has been tentatively identified as being mainly by O-demethylation, hydroxylation and conjugation, and excretion is primarily by the biliary route.

Linearity/non-linearity:
No data available.

c) Characteristics in specific groups of subjects or patients

No data available.

d) Pharmacokinetic/pharmacodynamic relationship(s)

No data available.

Paediatric population: No data available.

5.3 Preclinical safety data

In animal studies, adapalene was well tolerated on cutaneous application for periods of up to six months in rabbits and for up to two years in mice. The major symptom of toxicity found in all animal species by the oral route were related to a hypervitaminosis A syndrome, and included bone dissolution, elevated alkaline phosphatase and a slight anaemia. Large oral doses of adapalene produced no adverse neurological, cardiovascular or respiratory effects in animals. Adapalene is not mutagenic. Lifetime studies with adapalene have been completed in mice at cutaneous doses of 0.6,2 and 6 mg/kg/day and in rats at oral doses of 0.15, 0.5 and 1.5 mg/kg/day. The only significant finding was a statistically significant increase of benign phaeochromocytomas of the adrenal medulla among male rats receiving adapalene at 1.5 mg/kg/day. These changes are unlikely to be of relevance to the cutaneous use of adapalene.

Adapalene produces teratogenic effects by the oral route in rats and rabbits. At cutaneous doses up to 200-fold the therapeutic dose, producing circulating plasma levels of adapalene at least 35 to 120 times higher than plasma levels demonstrated in therapeutic use, adapalene increased the incidence of additional ribs in rats and rabbits, without increasing the incidence of major malformations.

It is not known whether adapalene is secreted in animal or human milk. In animal studies, infant rats suckled by mother with circulating levels of adapalene at least 300 times those demonstrated in clinical use developed normally.

Environmental Risk Assessment (ERA)

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

1) Di-Sodium Edetate
2) Carbomer 940 (Carbopol 940)
3) Propylene Glycol

4) Methyl Hydroxybenzoate
5) Phenoxyethanol
6) Poloxamer 407
7) Sodium Hydroxide
8) Purified Water

6.2 Incompatibilities
Not Applicable

6.3 Shelf life
36 months

6.4 Special precautions for storage
Store below 30°C. Protect from freezing and light.

6.5 Nature and contents of container
The proposed marketed packs for Adapalene Gel 0.1% w/w is a printed carton containing a leaflet and a printed aluminium collapsible tube.

6.6 Special precautions for disposal and other handling
A thin film of the gel should be applied, avoiding eyes, lips and mucous membranes. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES
Glenmark Pharmaceuticals Limited
B/2 Mahalaxmi Chambers,
22, Bhulabhai Desai Road, Mumbai-400026, (India).
At: Plot no. E-37, 39, D-Road, MIDC, Satpur,
Nashik 422007, Maharashtra State, India.

8. MARKETING AUTHORISATION NUMBER
Rwanda FDA-HMP-MA-0608

9. DATE OF FIRST REGISTRATION/ RENEWAL OF THE REGISTRATION
Not applicable

10. DATE OF REVISION OF THE TEXT
January 2024

11. DOSIMETRY (IF APPLICABLE)
Not applicable

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)
Not applicable

13. DOCUMENT REVISION HISTORY
January 2024