SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Deriva Aqueous gel (Adapalene 0.1% w/w Gel)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition:
Adapalene BP 0.1% w/w
In aqueous cream base
Methyl Paraben BP (0.1 % w/w)
Phenoxyethanol BP (0.25 % w/w)

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Topical Gel

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Adapalene Gel 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

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

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.

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.

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

4.3. Contraindications

Pregnancy.

Women planning a pregnancy.

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

4.4. 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 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.

The excipient propylene glycol may cause skin irritation and methyl parahydroxybenzoate may cause allergic reactions which can possibly be delayed.

4.5. 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, 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.

Adapalene Gel 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 (e.g. 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 is used at night as there is no mutual degradation or cumulative irritation.

4.6. Fertility, pregnancy and lactation

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.

Pregnancy:
Adapalene gel 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 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.

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

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

Fertility
No clinical trial data are available on the effects of adapalene on human fertility.

4.7. Effects on ability to drive and use machines

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

4.8. Undesirable effects

Adapalene 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
Eye disorders	Unknown*	eyelid irritation, eyelid erythema, eyelid pruritus, eyelid swelling

*Post marketing surveillance data

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.

4.9. Overdose

Adapalene Gel 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 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.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: D10A Anti-Acne Preparations for Topical Use

ATC code: D10AD03

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.

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.

5.2. Pharmacokinetic properties

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.

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

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.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Inactive material are Di-Sodium Edetate,Carbomer 940, Propylene Glycol, Methyl hydroxyl benzoate, Phenoxyethanol, Poloxamer 407, Sodium Hydroxide & Purified Water.

6.2. Incompatibilities

None

6.3. Shelf life

36 months

6.4. Special precautions for storage

Do not store above 30°C. Protect from Freezing and Light.

6.5. Nature and contents of container

A printed carton containing a leaflet and a printed aluminium collapsible tube containing opaque white smooth gel.

6.6. Special precautions for disposal and other handling

Not Applicable

7. MARKETING AUTHORISATION HOLDER

Glenmark Pharmaceuticals Limited
B/2, Mahalaxmi Chambers,
22, Bhulabhai Desai road, Mumbai – 400 026

8. MARKETING AUTHORISATION NUMBER(S)

FDA/SD.203-04160

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04.02.2005

10. DATE OF REVISION OF THE TEXT

Dec 2018

PATIENT INFORMATION LEFALET
Adapalene 0.1% w/w Gel

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

In this leaflet

1. What is Adapalene Gel and what is it used for?

- The active substance in Adapalene Gel is adapalene, which has an anti-inflammatory effect reducing soreness and irritation.
- It is used on the face, chest or back for acne, where the skin has lots of blackheads, spots and pimples.
- Adapalene is only absorbed into the body in very small amounts and has little effect, except on the surface of the skin.

2. What you need to know before you use Adapalene Gel

Do not use Adapalene Gel:

- If you are pregnant
- If you are planning a pregnancy
- If you are allergic to adapalene or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

- Do not use this medicine on areas where you have cuts or scrapes or if you have a skin condition called eczema.
- Avoid contact with the eyes, mouth or nostrils, and avoid other very sensitive areas of the body. If accidental contact does occur, immediately wash with warm water.
- If you experience sensitivity or irritation when applying this medicine, stop using it and tell your doctor. You may be asked to use the gel less often, or to stop using it until symptoms subside.

- You should avoid exposure to sunlight and artificial UV light whilst using Adapalene Gel.
- Talk to your doctor or pharmacist if you are not sure.

Other medicines and Adapalene Gel

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
Other acne products (containing benzoyl peroxide, erythromycin or clindamycin) may be used with Adapalene Gel but they must be applied in the morning and Adapalene Gel at night.
Cosmetics may be used but they must not cause blackheads or dry the skin.

Pregnancy, breast-feeding and fertility

- **DO NOT use Adapalene Gel if you are pregnant or thinking of becoming pregnant**. Your doctor can give you more information.
- If you fall pregnant while using Adapalene Gel, the treatment must be discontinued and you should inform your doctor as soon as possible for a further follow-up.
- Adapalene Gel can be used during breast-feeding. To avoid contact exposure of the infant, application of Adapalene Gel to the chest should be avoided.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Adapalene Gel contains:

- propylene glycol which may cause skin irritation
- methyl parahydroxybenzoate which may cause allergic reactions (possibly delayed)

3. How to use Adapalene Gel

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

- Adapalene Gel is only intended for use in adults and adolescents aged 12 years and over.
- **This medicine is for EXTERNAL USE ONLY.**
- Adapalene Gel is applied at night before going to bed, unless your doctor has told you otherwise.
- Thoroughly wash the areas to be treated with water. Make sure the skin is clean and dry before using this medicine.
- Put on a thin film of the gel with your fingertips to the affected areas and rub in gently.
- Don't forget to wash your hands afterwards.

- How long you will have to use this medicine will depend on how quickly your acne improves. After you have used this medicine for three months, it is important that you see your doctor. He or she can then check the improvement of your acne.

If you use more Adapalene Gel than you should or accidentally swallow the gel
If you put too much Adapalene Gel on your skin, you will not get rid of your acne any quicker, but your skin may become irritated and red. Some peeling or discomfort could also occur.
In the rare event that you accidentally swallow any of this medicine, seek medical advice.
If you forget to use Adapalene Gel
Don't worry if you forget to apply your Adapalene Gel at the right time. When you remember, start using this medicine again, in the same way as before.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Adapalene Gel may cause the following side effects at the site of application.

Common: may affect up to 1 in 10 people
- dry skin
- irritation of the skin
- burning sensation of the skin
- redness of the skin (erythema)

Uncommon: may affect up to 1 in 100 people
- local skin reaction (contact dermatitis)
- skin discomfort
- sunburn
- itching of the skin (pruritus)
- peeling skin (exfoliation)
- acne

Not known: frequency cannot be estimated from the available data
- allergic contact reaction
- pain or swelling of the skin
- irritation, redness, itching or swelling of the eyelids

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store

Do not store above 30°C. Protect from Freezing and Light.

6. Contents of the pack and other information

A printed carton containing a leaflet and a printed aluminium collapsible tube containing opaque white smooth gel.

Date of Revision of the Text:

Dec 2018