**Summary of Product Characteristics for Pharmaceutical Products**

## 1. Name of the medicinal product

Derivex Acne Gel

## 2. Qualitative and quantitative composition

Each 1.0 gram of gel contains;
Adapalene BP 0.1% w/w
Clindamycin phosphate BP 1.0% w/w
Excipients with known effect
Sodium metabisulphite 7.14mg
For the full list of excipients, see section 6.1.

## 3. Pharmaceutical form

Topical gel

White to off white translucent homogenous gel

## 4. Clinical particulars

### 4.1 Therapeutic indications

Differin 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

Derivex 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 (see 4.4 Special Warnings and Special Precautions for Use, below). 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 Derivex 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 Derivex Gel have not been studied in children below 12 years of age. Derivex gel should not be used in patients with severe acne.

## 4.3 Contraindications

Pregnancy (see section 4.6).

Women planning a pregnancy

History of hypersensitivity to clindamycin or lincomycin or adapalene, a history of regional enteritis or ulcerative colitis, or ahistory of antibiotic-associated colitis.

## 4.4 Special warnings and precautions for use

Use of the topical formulation of clindamycin results in absorption of the antibiotic from the skinsurface. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of topical and systemic clindamycin. Diarrhea, colitis, and pseudomembranous colitis have been observed to begin up to several weeks following cessation of oral and parenteral therapy with clindamycin. Adapalene should not be used on areas which have cuts or scrapes or on sunburnt skin or in eczema. Contact with the eyes, mouth or angles of the nose and other very sensitive areas of the body should be avoided. If accidental contact does occur, immediately wash with warm water.General: Clindamycin should be prescribed with caution in atopic individuals. Avoid exposure to strong sunlight and artificial UV light. Use of sunscreen products and protective clothing over the treated area is recommended. Stop the use of Derivex acne gelin case of sensitivity or irritation. Pediatric Use: Safety and effectiveness of Derivex acne gelin children under the age of 12 havenot been established.

## 4.5 Interaction with other medicinal products and other forms of interaction

Clindamycin has been shown to have neuromuscular blocking properties that may enhance theaction of other neuromuscular blocking agents. Therefore, it should be used with caution inpatients receiving such agents.

There are no known interactions with other medications which might be used cutaneously andconcurrently with Adapalene, however, other retinoid or drugs with a similar mode of actionshould 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.

**4.6 Fertility, pregnancy, and lactation**

General: Clindamycin should be prescribed with caution in atopic individuals. Pregnancy: Category B: Reproduction studies have been performed in rats and mice using subcutaneous and oral doses of clindamycin ranging from 100 to 600 mg/kg/day and have revealed no evidence of impaired fertility or harm to the fetus due to clindamycin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, Clindamycin should be usedduring pregnancy only if clearly needed. Derivex acne gel should not be used during pregnancy. Nursing Mothers: It is not known whether clindamycin is excreted in human milk following useof Derivex acne gel. However, orally and parenterally administered clindamycin has been reported toappear in breast milk. Because of the potential for serious adverse reactions in nursing infants, adecision should be made whether to discontinue nursing or to discontinue the drug, taking intoaccount the importance of the drug to the mother. Adapalene can be used during breast-feeding.

**4.7 Effects on ability to drive and use machines.**

Derivex Acne gel has no influence on the ability to drive and use machines

**4.8 Undesirable effects**

Local effects: Burning, itching, dryness, erythema and peeling. Systemic effects: Cases of diarrhea, bloody diarrhea and colitis [including pseudomembranouscolitis] have been reported as adverse reactions in patients treated with oral and parenteral formulations of clindamycin and rarely with topical clindamycin. Abdominal pain and gastrointestinal disturbances as well as gram-negative folliculitis have also been reported in association with the use of topical formulations of clindamycin. Adapalene 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), flare up of acne.

**Reporting of suspected adverse reactions:** Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

**4.9 Overdose**

Derivex acne 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

Derivex acne gel contains two active ingredients, Clindamycin and Adapalene, with different mechanisms of action which are thought to act complementary to each other in the treatment of mild to moderate inflammatory and non-inflammatory Acne. Clindamycin phosphate an inactive compound, is an antibiotic belonging to the lincomycin group of antibiotics that blocks protein synthesis in the bacteria responsible for causing infection of acne affected skin, and thus kills the bacteria, by rapidly converting in vivo into active form -Clindamycin. Propionibacterium acnes are bacteria that normally exist on the skin without causing any problems, living on fatty acids in the sebum (oil) secreted by the sebaceous glands. Over production of sebum causes the pores of the skin to become blocked and the pimples, whiteheads and blackheads (comedones) are formed. Clogged pores attract bacteria which thenovergrow and cause infection. Clindamycin phosphate gets into the blackheads and blocks the growth of the bacteria, while at the same time free fatty acids on the skin surface are decreasedfrom approximately 14% to 2% following application of clindamycin. These actions ofClindamycin phosphate reduces bacterial growth that contributes to formation acne skin lesionsand prevents the spread of infection. Adapalene is a retinoid-like compound has been demonstrated to possess anti-inflammatory properties. Adapalene is essentially stable to oxygen and light and is chemically non-reactive. Mechanistically, adapalene binds like tretinion to specific retinoic acid nuclear receptors. Adapalene applied cutaneously is comedolytic in the rhino mouse model and also has effects onthe abnormal processes of epidermal keratinization and differentiation, both of which are presentin the pathogenesis of acne vulgaris. The mode of action of adapalene is suggested to be anormalisation of differentiation of follicular epithelial cells resulting in decreased microcomedone formation. It inhibits the metabolism by lipoxidation of arachidonic acid to pro-inflammatory mediators. The profile suggests that the cell mediated inflammatory component ofacne may be modified by adapalene. Studies in human patients provide clinical evidence thatcutaneous adapalene is effective in reducing the inflammatory components of acne (papules andpustules). Adapalene removes dead skin cells as well as enhances the follicular penetration of Clindamycin.

### 5.2 Pharmacokinetic properties

Following multiple topical applications of clindamycin phosphate at a concentration equivalent to 10 mg clindamycin per mL in an isopropyl alcohol and water solution, very low levels of clindamycin are present in the serum (0-3 ng/mL) and less than 0.2% of the dose is recovered inurine as clindamycin. Absorption of adapalene through human skin

is low: in clinical trials measurable plasma adapalene levels were not found following chronic cutaneous application to large areas of acneicskin. There are no data which define the pharmacokinetics of Derivex acne gel, following topical administration in man.

**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**

Carbomer 940
Sodium metabisulphite
Polysorbate 80
Sodium hydroxide pellets
Methyl paraben
Propyl paraben
Propylene glycol
D.M. Water

**6.2 Incompatibilities**

None known

**6.3 Shelf life**

36 months

**6.4 Special precautions for storage:**

Store in a below 30˚C. Protect from light and freezing.

**6.5 Nature and contents of container**

15 g lamitube placed in a carton with an insert.

**6.6 Special precautions for disposal and other handling:**

No special requirements.

**7. Marketing authorization holder and manufacturing site addresses**

**Marketing authorization holder:**

Avetina Life sciences limited

**Manufacturing site address:**

LexineTechnochem Pvt. Ltd Survery No. 373, Opp. Ramakaka Deri, Chhani - 391740, Vadodara, Gujarat, India

**8. Marketing authorization number**

CTD9835

**9. Date of first registration**

02/07/2022

**10. Date of revision of the text:**

16/09/2023

**11. Dosimetry:**

Not Applicable

**12. Instructions for Preparation of Radiopharmaceuticals:**

Not Applicable