SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Adapalene + Clindamycin phosphate Gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of gel contains Adapalene BP……1 mg Clindamycin phosphate USP Equivalent to Clindamycin……10 mg

3. PHARMACEUTICAL FORM

Gel

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Fixed Dose Combination of Adapalene + Clindamycin phosphate Gel is indicated 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

Fixed Dose Combination of Adapalene + Clindamycin phosphate 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 + Clindamycin 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 Fixed Dose Combination of Adapalene + Clindamycin phosphate Gel have not been studied in children below 12 years of age. Fixed Dose

Combination of Adapalene + Clindamycin phosphate Gel should not be used in patients with severe acne.

4.3 Contraindications

 Pregnancy Women planning a pregnancy. Hypersensitivity to the active substances or to any of the excipients listed in section 6.1. Although cross-sensitisation to lincomycin has not been demonstrated, it is recommended that Adapalene + Clindamycin phosphate Gel should not be used in patients who have demonstrated lincomycin sensitivity.

4.4 Special warnings and precautions for use

Adapalene 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. Clindamycin Oral and parenteral clindamycin, as well as most other antibiotics, have been associated with severe pseudomembranous colitis. Topical clindamycin has very rarely been associated with pseudomembranous colitis; however, if diarrhoea occurs the product should be discontinued immediately. Studies indicate a toxin(s) produced by Clostridium difficile is the major cause of antibioticassociated colitis. Colitis is usually characterised by severe persistent diarrhoea and abdominal cramps. Should antibiotic associated colitis occur appropriate diagnostic and therapeutic measures (such as stopping clindamycin and if necessary, antibiotic treatment such as metronidazole or vancomycin treatment) should be taken immediately. Responses may not be seen for 4-6 weeks. Although the risk of systemic absorption following the administration of clindamycin is low, the potential

for the development of gastrointestinal adverse effects should be taken into account when considering treatment in patients with a previous history of antibioticassociated colitis, enteritis, ulcerative colitis or Crohn's disease. Prolonged use of clindamycin may cause resistance and/or overgrowth of non-susceptible bacteria or fungi although this is a rare occurrence. Cross resistance may occur with other antibiotics such as lincomycin and erythromycin. Contact with the eyes or the mucous membranes of the nose and mouth should be avoided. In the event of accidental contact with the eyes or mucous membranes bathe the affected area with copious amounts of cool water. Pediatric Use Safety and effectiveness of Fixed Dose Combination of Adapalene + Clindamycin phosphate Gel in children under the age of 12 have not been established. This product contains propylene glycol which may cause skin irritation.

4.5 Interaction with other medicinal products and other forms of interaction

No formal drug-drug interaction studies were conducted with Adapalene + Clindamycin phosphate Gel. Adapalene 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 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 is used at night as there is no mutual degradation or

cumulative irritation. Clindamycin No interactions have been reported with topical clindamycin.

4.6 Fertility, pregnancy and lactation

Pregnancy:

Adapalene 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. Adapalene 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. Clindamycin For clindamycin applied cutaneously no clinical data on exposed pregnancies are available. Data on a limited number of pregnancies exposed to clindamycin administered by other routes indicate no adverse effects on pregnancy or on the health of the foetus/newborn child. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Caution should be exercised when prescribing to pregnant women.

Breastfeeding:

Adapalene No study on animal or human milk transfer was conducted after cutaneous application of adapalene gel. 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. Clindamycin Orally and parenterally administered

clindamycin has been reported to appear in breast milk. It is not known whether clindamycin is excreted in human milk following use of clindamycin. As a general rule, patients should not breastfeed while taking a drug since many drugs are excreted in human milk. Sensitisation and diarrhoea cannot be ruled out in nursed infants. For use during pregnancy and lactation, benefit and possible risks have to be weighed carefully against each other. Fertility There are no data on the effect of Adapalene + Clindamycin phosphate Gel on fertility in humans.

4.7 Effects on ability to drive and use machines

Adapalene and clindamycin phosphate gel has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Adapalene

Adapalene may cause the following adverse drug reactions:

Body Frequency Adverse Drug Reaction System (MeDRA) Skin and Common (≥1/100 to Dry skin, skin irritation, skin burning sensation, subcutaneous <1/10) erythema tissue disorders Uncommon (≥1/1000 Dermatitis contact, skin discomfort, sunburn, to <1/100) pruritus, skin exfoliation, acne Unknown* Dermatitis allergic (allergic contact dermatitis), pain of skin, skin swelling, application site burn**, skin hypopigmentation, skin hyperpigmentation Eye Unknown* eyelid irritation, eyelid erythema, eyelid pruritus, disorders eyelid swelling Immune Unknown* Anaphylactic reaction, angioedema system disorders *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 Clindamycin Approximately 10% of patients can be expected to experience an adverse reaction. These reactions are typical of irritant dermatitis. The incidence of these is likely to increase if an excess of gel is used. Should irritation occur, the use of a moisturizer may be of benefit. The table below shows all adverse reactions reported with clindamycin in clinical trials. They are listed in decreasing order of incidence. Organ Common Uncommon System (>1/100, <1/10) (>1/1000, <1/100) Skin and subcutaneous Dry skin Painful skin tissue disorder Erythema Scaly rash Skin burning Irritation around eyes Acne exacerbation Pruritis Whilst no case of

severe diarrhoea or pseudomembranous colitis has been reported in clinical trials with clindamycin, and only a small amount of clindamycin is absorbed percutaneously, pseudomembranous colitis has very rarely been reported with the use of other topical clindamycin products. Therefore, a theoretical risk of pseudomembranous colitis with clindamycin exists. Reporting of suspected adverse reactions Healthcare professionals are requested to report any suspected adverse reactions via national regulatory portal or systems.

4.9 Overdose

Adapalene 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. Clindamycin It is not expected that overdose would occur in normal use. Irritant dermatitis may occur when excessive quantities of clindamycin are applied. The use of a suitable moisturiser may be of benefit in these cases. In subsequent applications a thin film of clindamycin should be applied in accordance with the dosage instructions.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Anti-Acne Preparations for Topical Use ATC code: D10A Adapalene 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. Clindamycin This gel combination contains clindamycin phosphate which is hydrolysed in the skin to the active constituent clindamycin. Clindamycin is a lincosamide antibiotic with primarily bacteriostatic action against Gram positive aerobes and wide range of anaerobic bacteria. When clindamycin phosphate is applied cutaneously, clindamycin is found in comedone samples at sufficient levels to be active against most strains of Propionibacterium (P. acnes). It thus reduces the number of surface and follicular P. acnes, one of the aetiological factors of the disease. As with all antibiotics, the long-term use of cutaneous clindamycin may lead to resistance.

5.2 Pharmacokinetic properties

Adapalene 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 [14C] 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. Clindamycin In clindamycin gel, clindamycin phosphate binds with zinc to form a complex in a formulation which results in a reduced extent of absorption. A study with clindamycin gel in vitro with human skin has shown penetration of radiolabeled clindamycin phosphate from the clindamycin gel formulation to be less than 5% of the applied dose. When applied topically to patients with acne at the maximum anticipated clinical dose a very small amount, (median less than 2ng/ml) of clindamycin was measured in plasma.

5.3 Preclinical safety data

Adapalene 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 circukating levels of adapalene at least 300 times those demonstrated in clinical use developed normally. Clindamycin phosphate Preclinical data for clindamycin reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity or toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium Edetate, Carbomer 940, Sodium Hydroxide, Propylene Glycol, Methyl Hydroxy Benzoate, Poloxamer 407, Phenoxyethanol, Purified water.

6.2 Incompatibilities

Not Applicable.

6.3 Shelf life

18 Months.

6.4 Special precautions for storage

Store below 30°C. Do not freeze.

6.5 Nature and contents of container

A printed carton containing a leaflet and a printed Lami tube containing white to yellow smooth homogenous gel.

6.6 Special precautions for disposal and other handling

No special requirements. Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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

Manufactured at:

Glenmark Pharmaceuticals Ltd. Plot No. E-37, 39, D-Road, MIDC, Satpur, Nashik 422007 Maharashtra State, India

8. MARKETING AUTHORISATION NUMBER(S)

17487/R1

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

2026 August 22

10. DATE OF REVISION OF THE TEXT

2026 August 22