**Summary of Product Characteristics**
**(Product Data Sheet)**

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| **1.** | **Name of the Medical Product** |
| | 1.1 Product Name: **ADACIN (Adapalene and Clindamycin Phosphate Gel)** |
| | **1.2 Strength :**<br>Adapalene BP 0.1% w/w<br>Clindamycin Phosphate BP<br>Equivalent to Clindamycin 1.0%w/w |
| | **1.3 Pharmaceutical Dosage Form :** Gel |
| **2.** | **Qualitative & Quantitative Composition:**<br>Adapalene BP 0.1% w/w<br>Clindamycin Phosphate BP<br>Equivalent to Clindamycin 1.0%w/w<br>Gel base q.s.<br>For a full list of excipients, see section 6.1 of SmPC |
| **3.** | **Pharmaceutical Form:**<br>Off white coloured opaque smooth homogeneous gel with characteristic odour. |
| **4.** | **Clinical Particulars** |
| | **4.1 Therapeutic Indications:**<br>Adacin Gel is indicated for the topical treatment of mild to moderate acne vulgaris, particularly inflammatory lesions, in adults and adolescents aged 12 years and above where comedones, papules and pustules predominate. |
| | **4.2 Posology and Method of administration:**<br>Adacin Gel should be applied to the entire acne affected areas once a day in the evening on a clean and dry skin. A thin film of gel should be applied, with the fingertips, avoiding the eyes and lips.<br>If irritation occurs, the patient should be directed to apply non-comedogenic moisturizers, to use the medication less frequently (e.g. every other day), to suspend use temporarily, or to discontinue use altogether.<br>The duration of treatment should be determined by the Doctor on the basis of the clinical condition<br>*Paediatric population*<br>The safety and efficacy of Adacin Gel has not been established in children under 12 years of age, therefore Adacin Gel is not recommended for use in this population.<br>*Elderly patients*<br>No specific recommendations. |

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| | **Method of administration**<br>Adacin Gel should be applied in a thin film after washing gently with a mild cleanser and fully drying. If the gel does not rub into the skin easily, too much is being applied.<br>Hands should be washed after application. |
| | **4.3 Contraindications:**<br>Adacin Gel is contraindicated in individuals with a history of hypersensitivity to clindamycin or lincomycin or adapalene, a history of regional enteritis or ulcerative colitis, or a history of antibiotic-associated colitis. |
| | **4.4 Special warning and precautions for use:**<br>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, or to discontinue use altogether.<br>Adacin Gel should not come into contact with the eyes, mouth, nostrils or mucous membranes.<br>If product enters the eye, wash immediately with warm water. The product should not be applied to either broken (cut and abrasions) or eczematous skin, nor should it be used in patients with severe acne involving large areas of the body.<br>Adacin Gel should be used with caution in patients with a history of regional enteritis or ulcerative colitis, or a history of antibiotic-associated colitis.<br>Use of the topical formulation of clindamycin results in absorption of the antibiotic from the skin surface. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of topical and systemic clindamycin.<br>Diarrhea, colitis, and pseudomembranous colitis have been observed to begin up to several weeks following cessation of oral and parenteral therapy with clindamycin. |
| | **4.5 Interactions with other medicinal products and other forms of Interactions :**<br>There are no known interactions with other medications which might be used cutaneously and concurrently with Adapalene, however, other retinoids or drugs with a similar mode of action should not be used concurrently with adapalene.<br>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.<br>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.<br>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 (eg erythromycin up to 4%) or clindamycin phosphate (1% as the base) solutions or benzoyl peroxide water based gels up to 10% may |

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| | be used in the morning when adapalene is used at night as there is no mutual degradation or cumulative irritation.<br>Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, it should be used with caution in patients receiving such agents. |
| | **4.6 Pregnancy and Lactation:**<br>**Pregnancy**<br>There are no adequate data from the use of Adacin Gel in pregnant women<br>**Adapalene**<br>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. In case of unexpected pregnancy, treatment should be discontinued.<br>**Clindamycin**<br>A limited number of pregnancies exposed in the first trimester to clindamycin indicate no adverse effects of clindamycin on pregnancy or on the health of the foetus/new-born child. Clindamycin was not teratogenic in reproduction studies in rats and mice, using subcutaneous and oral doses of clindamycin.<br>**Breast-feeding:**<br>***Adapalene***<br>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.<br>Adapalene can be used during breastfeeding. To avoid contact exposure of the infant, application Adapalene to the chest should be avoided when used during breast-feeding.<br>***Clindamycin***<br>Oral and parenteral administration of clindamycin has been reported to result in the appearance of clindamycin in breast milk. Therefore, Adacin should not be used in women who are breast feeding. |
| | **4.7 Effects on ability to drive and use machine:**<br>No studies on the effects on the ability to drive and use machines have been performed. It is unlikely that treatment with Adacin will have any effect on the ability to drive and use machines. |
| | **4.8 Undesirable Effects:**<br>Local effects: Burning, itching, dryness, erythema and peeling.<br>Systemic effects: Cases of diarrhea, bloody diarrhea and colitis [including pseudomembranous colitis] have been reported as adverse reactions in patients treated |

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| | 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.<br>Adapalene may cause the following side effects at the site of application.<br>Common: may affect up to 1 in 10 people<br>Dry skin, irritation of the skin, burning sensation of the skin, redness of the skin (erythema).<br>Uncommon: may affect up to 1 in 100 people<br>Local skin reaction (contact dermatitis), skin discomfort, sunburn, itching of the skin (pruritus), peeling skin (exfoliation), flare up of acne. |
| | **4.9 Overdosage:**<br><br>Adapalene 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.<br>The acute oral dose of Adapalene required to produce toxic effects in mice is greater than 10 mg/kg. Nevertheless, unless the amount accidentally ingested is small, an appropriate method of gastric emptying should be considered.<br>Excessive application of topically applied clindamycin may result in absorption of sufficient amounts to produce systemic effects.<br>In the event of accidental ingestion of Adacin Gel, gastrointestinal adverse reactions similar to those seen with systemically administered clindamycin may be seen.<br>Appropriate symptomatic measures should be taken to provide relief from irritation due to excessive application.<br>Accidental ingestion should be managed clinically. |
| **5.** | **Pharmacological properties** |
| | **5.1 Pharmacodynamic Properties:**<br><br>**Adapalene**<br>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.<br>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.<br>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 |

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| | mediated inflammatory component of acne may be modified by adapalene.<br>**Clindamycin:**<br>Clindamycin is a semisynthetic derivative of the parent compound lincomycin that is produced by *Streptomyces lincolnensis* and is predominantly bacteriostatic. Clindamycin binds to the 50S ribosomal subunits of susceptible bacteria and prevents elongation of peptide chains by interfering with peptidyl transfer, thereby suppressing bacterial protein synthesis. Although clindamycin phosphate is inactive in-vitro, rapid in-vivo hydrolysis converts this compound to the antibacterial active clindamycin.<br>Clindamycin has been shown to have in vitro activity against *Propionibacterium acnes,* one pathophysiological factor that influence the development of acne vulgaris. Clindamycin also exerts an anti-inflammatory effect on the acne vulgaris lesions. |
| | **5.2 Pharmacokinetics Properties:**<br>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.<br>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.<br>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 in urine as clindamycin. |
| | **5.3 Preclinical Safety data:**<br>**Adapalene**<br>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, caridovascular 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.<br>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 |

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| | 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.<br>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.<br>**Clindamycin**<br>Systemically administered clindamycin does not affect fertility, mating ability, embryonic development, or post-natal development. In-vitro and in-vivo studies did not reveal any mutagenic potential of clindamycin. Clindamycin was not carcinogenic in mice in a 2-year dermal study with 1.2% clindamycin phosphate and a 2-year oral study in rats. |
| **6.** | **Pharmaceutical particulars** |
| | **6.1 List of Excipients:**<br>Methyl Hydroxybenzoate, Phenoxyethanol, Disodium Edetate, Carbomer 934P, Polysorbate 80, Polyethylene Glycol, Sodium Hydroxide, Propylene Glycol, Fragrance RSGR 130913 and Purified Water. |
| | **6.2 Incompatibilities:** Not applicable |
| | **6.3 Shelf life:** 2 years from date of manufacturing. |
| | **6.4 Special Precautions for storage:** Store below 30°C. Do not freeze. |
| | **6.5 Nature and contents of container:**<br>A carton containing one such laminated tube of 15 g gel along with Patient information leaflet. |
| **7.** | **Marketing Authorization Holder:**<br>Ajanta Pharma Ltd.<br>Ajanta House, Charkop<br>Kandivli (West)<br>Mumbai - 400 067<br>India.<br>Tel : +91-22-6606 1000<br>Fax : +91-22-6606 1200<br>Email : info@ajantapharma.com |
| | **Marketing Authorization Numbers:** Not Applicable |
| **8.** | **Date of first authorization/ renewal of the authorization:** Not Applicable |
| **9.** | **Date of revision of text:** Jun 13, 2019 |