Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

RUFENAC GEL (Diclofenac Diethyl Ammonium Gel)

2. Qualitative and quantitative composition

1.16 % w/w Diclofenac Diethylammonium Salt BP
equivalent to 1% w/ w Diclofenac Sodium BP.

For the full list of excipients, see section 6.1

3. Pharmaceutical form

Topical Gel

4. Clinical particulars

4.1 Therapeutic indications

Rufenac Gel contains diclofenac diethylamine, methyl salicylate and menthol that relieve the pain and swelling in joints and muscles in the following conditions:

- Rheumatoid arthritis (body's immune system attacks its own tissue, including joints that can cause joint pain and damage throughout body),
- Osteoarthritis (pain and stiffness of joints),
- Spondylitis (pain, stiffness and weakness of spines),
- Sprains and strains, Bursitis (pain of small, fluid-filled sacs around a joint),
- Tendinitis (swelling of a tendon-the thick fibrous cords that attach muscle to bone)
- Dysmenorrhoea (pain during menses), and
- Acute gout (sudden, severe attacks of pain, swelling, redness and tenderness in the joints). Components in Rufenac Gel have the following actions:
- Diclofenac diethylamine reaches in deeper tissues and inhibits the formation of chemicals that are responsible for the production of pain and swelling.
- Methyl salicylate increases the blood flow to flush the harmful chemicals and decreases the pain in muscles and joints.
- Menthol provides the cooling sensation and suppresses the pain

4.2 Posology and method of administration

Posology

Adults and adolescents aged 14 years and over

Apply thin layers of Diclofenac 1% Gel in the affected area, 3-4 times daily according to the need of the situation (about 2-4 g, quantity as big as a cherry or a walnut) and rub gently.

The treatment duration depends on the indications and the patient's response to the treatment. It is recommended that the treatment should be evaluated 7 days after its beginning.

In adolescents aged 14 years and over, if this product is required for more than 7 days for pain relief or if the symptoms worsen the patients/parents of the adolescent is/are advised to consult a doctor.

Diclofenac 1% Gel can be used as additional treatment to the oral administration of non-steroidal anti-inflammatory drugs.
Children and adolescents aged below 14 years
There are insufficient data on efficacy and safety available for the children and adolescents below 14 years of age (see also section 4.3).
Hepatic and renal impairment
No dosage adjustment is required in patients with hepatic impairment. Diclofenac 1% Gel is contraindicated in patients with renal impairment.
Elderly
The usual adult dosage may be used.
Method of administration
Cutaneous use.
Apply on healthy skin only.
After application, the hands should be washed, unless these are being treated.
Diclofenac 1% Gel can be used as additional treatment to the oral administration of non-steroidal anti-inflammatory drugs.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Patients with or without chronic asthma in whom attacks of asthma, urticaria or acute rhinitis are precipitated by acetylsalicylic acid or other non-steroidal anti- inflammatory drugs (NSAIDs).
- The use in children and adolescents aged less than 14 years is contraindicated.
- Third trimester of pregnancy.
- Patients with renal impairment.

4.4 Special warnings and precautions for use
The occurrence of systemic undesirable effects with the topical use of diclofenac is low when compared with the frequency of undesirable effects with the oral use of diclofenac.
The possibility of systemic adverse events from application of topical diclofenac cannot be excluded if the preparation is used on large areas of skin and over a prolonged period (see the product information on systemic forms of diclofenac).
Cutaneous safety of NSAIDs: Serious skin reactions, some of them fatal, have been reported very rarely, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, associated with the administration of NSAIDs (see section 4.8.). Apparently the risk of occurrence of these reactions is higher at the beginning of the treatment and in most cases these reactions are manifested during the first month of treatment. Concomitant use of oral NSAID's should be cautioned as the incidence of untoward effects, particularly systemic side effects, may increase.
Diclofenac 1% Gel should be discontinued at the first signs of rash, mucosal injuries or other hypersensitivity manifestations.
Topical diclofenac should be applied only to intact non-diseased skin, and not to skin wounds or open injuries. It should not be allowed to come into

contact with the eyes or mucous membranes and should not be ingested.
The area treated with Diclofenac 1% Gel should not be exposed to sunlight.
Topical diclofenac can be used with non-occlusive bandages but should not be used with an airtight occlusive dressing

4.5 Interaction with other medicinal products and other forms of interaction

Diuretics, Angiotensin Converting Enzyme Inhibitors (ACE inhibitors) and Angiotensin II Antagonists (AAII): NSAIDs may decrease the effectiveness of diuretics and other antihypertensive medicinal products. In some patients with impaired renal function (e.g., dehydrated patients or elderly with impaired renal function) the co-administration of an ACEI or AIIA and cyclooxygenase inhibitor agents may result in the progression of renal function deterioration, including the possibility of acute renal insufficiency, which is usually reversible. The occurrence of these interactions should be considered in patients applying diclofenac, particularly if in large areas of the skin and for prolonged periods, in combination with ACEI or AIIA. Consequently, this drug combination should be used with caution, especially in elderly patients. Patients should be properly hydrated and the need to monitor the renal function after the beginning of the concomitant therapy and periodically thereafter should be analysed.
Since systemic absorption of diclofenac from a topical application is very low such interactions are very unlikely.

4.6 Pregnancy and Lactation

Pregnancy
There are no clinical data from the use of Diclofenac 1% Gel during pregnancy. Even if systemic exposure is lower compared with oral administration, it is not known if the systemic Diclofenac 1% Gel exposure reached after topical administration can be harmful to an embryo/fetus. During the first and second trimester of pregnancy, Diclofenac 1% Gel should not be used unless clearly necessary. If used, the dose should be kept as low and duration of treatment as short as possible.
During the third trimester of pregnancy, systemic use of prostaglandin synthetase inhibitors including diclofenac may induce cardiopulmonary and renal toxicity in the fetus. At the end of the pregnancy prolonged bleeding time in both mother and child may occur, and labour can be delayed. Therefore, Diclofenac 1% Gel is contraindicated during the last trimester of pregnancy (see Section 4.3).

The systemic concentration of diclofenac is lower after topical administration, compared to oral formulations. With reference to experience from treatment with NSAIDs with systemic uptake, the following is recommended:
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early

pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. During the first and second trimester of pregnancy, diclofenac should not be given unless clearly necessary. If diclofenac is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.
During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose
• the foetus to:
o cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
o renal dysfunction, which may progress to renal failure with oligo-hydroamniosis;
• the mother and the neonate, at the end of pregnancy, to:
o possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.
o inhibition of uterine contractions resulting in delayed or prolonged labour.
Consequently, diclofenac is contraindicated during the third trimester of pregnancy (see section 4.3).

Breast-feeding

Like other NSAIDs, diclofenac passes into breast milk in small amounts. However, at therapeutic doses of topical diclofenac no effects on the suckling child are anticipated. Because of a lack of controlled studies in lactating women, the product should only be used during lactation under advice from a healthcare professional. Under this circumstance, this medicinal product should not be applied on the breasts of nursing mothers, nor elsewhere on large areas of skin or for a prolonged period of time (see section 4.4).

4.7 Effects on ability to drive and use machines

Cutaneous application of topical diclofenac has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions (Table 1) are ranked under heading of frequency, the most frequent first, using the following convention: very common (> 1/10); common ≥(1/100, <1/10); uncommon ≥(1/1,000, < 1/100); rare (≥ 1/10,000, <1/1,000); very rare (<1/10,000), not known: cannot be estimated from the available data.

Table 1
Immune system disorder:
Very rare: Hypersensitivity (including urticaria), angioneurotic oedema.
Infections and infestations:

Very rare: Rash pustular.
Respiratory, thoracic and mediastinal disorders
Very rare: Asthma.
Skin and subcutaneous tissue disorders
Common: Rash, eczema, erythema, dermatitis (including dermatitis contact), pruritus
Rare: Dermatitis bullous
Very rare: Photosensitivity reaction
Not known: Burning sensation at the application site Dry skin
Although less likely with the topical administration, some side effects normally associated with systemically administered diclofenac may also occur.
The prolonged use of diclofenac in a relatively extensive area can cause systemic side effects such as nausea, vomiting, diarrhoea or epigastric pain.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via the relevant national regulatory authority pharmacovigilance.

4.9 Overdose
The low systemic absorption of topical diclofenac renders overdose very unlikely.
However, undesirable effects similar to those observed following an overdose of Diclofenac tablets can be expected if Topical diclofenac is inadvertently ingested (1 tube of 100 g contains the equivalent of 1,000 mg diclofenac sodium).
In the event of accidental ingestion resulting in significant systemic adverse effects, general therapeutic measures normally adopted to treat poisoning with non-steroidal anti-inflammatory medicines should be used. Gastric decontamination and the use of activated charcoal should be considered, especially within a short time of ingestion.

5. Pharmacological properties
5.1 Pharmacodynamic properties
Pharmacological category: Topical products for joint and muscular pain, anti-inflammatory preparations,
ATC code: M02A A15
Diclofenac is a phenylacetic acid derivative. It leads to the inhibition of cyclooxygenase activity, which then leads to the inhibition of the synthesis of prostaglandin and other mediators of inflammation. Diclofenac acts as anti-inflammatory and analgesic agent in the treatment of topical symptoms of rheumatic and non-rheumatic pains of the locomotor apparatus.

5.2 Pharmacokinetic properties
Absorption
After topical application, diclofenac is well-absorbed into the subcutaneous layers of the skin. In healthy volunteers, the maximum level of diclofenac after a 7.5 g dose of 1% of concentration was, on average, approximately 3.9 ng/ml. After several days of treatment, the

concentration on skin and soft tissues of patients with arthrosis reached values 30 to 40 times higher than the ones from plasma. The diclofenac absorption in the 1% concentration applied on the healthy skin reached 6 to 7% in healthy individuals.

Distribution

The diclofenac concentration was measured on plasma and tissue and synovial fluid after topical administration in the hands and knees joints. Maximum plasma concentration was about 100 times lower than after oral administration. Diclofenac binds 99.7% to plasma proteins, mainly albumin (99.5%).

Biotransformation

Biotransformation of diclofenac involves partly glucuronidation of the intact molecule, and mainly single and multiple hydroxylations, most of which are converted to glucuronide conjugates (hydroxyl-gluconates). The main metabolite is 4-hydroxy-diclofenac (30%-40%). All the metabolites are biologically active, but to a much smaller extent than diclofenac.

Elimination

Diclofenac and its metabolites are excreted mainly in the urine. Total clearance of diclofenac from plasma is 263 ± 56 ml/min. The terminal plasma half-life is of 1-2 hours. Its metabolites have similar plasma half-lives of 1-3 hours. Approximately 60% of the dose administered is eliminated in the urine
in the form of metabolites, only 1% in the form of diclofenac. The remaining is eliminated as metabolites by bile and in feces.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and reproductive toxicity, at the intended therapeutic doses.

At high systemic levels of diclofenac, not observed following topical application of Diclofenac 1% Gel, toxicity of diclofenac took the form mainly of lesions and ulcers in the gastro-intestinal tract. Increased duration of gestation, dystocia and increased resorptions were observed at maternally toxic doses.

6. Pharmaceutical Particulars

6.1 List of Excipients

Acrypol 980 In-House, Acrysol 140 USP/NF, Disodium Edetate BP, Methyl Hydroxy Benzoate (Methyl Paraben) BP, Propyl Hydroxy Benzoate (Propyl Paraben) BP, Triethanolamine BP and Purified water (q.s) BP**.**

6.2 Incompatibilities

None

6.3 Shelf-Life

36 months

6.4 Special Precautions for storage

Do not store above 30°C. Protect from sunlight. Keep out of reach of children

6.5 Nature and Content of container
20 & 30 gm aluminium collapsible tube packed in inner carton along with a leaflet.

6.6 Special precautions for disposal and other handling
None

7. Marketing Authorization Holder
SHALINA HEALTHCARE DMCC
30th Floor, Almas Towers,
Jumeirah Lakes Towers Dubai-UAE.

8. Marketing Authorization Number
H2013/CTD545/387/R1

9. Date of first authorization/renewal of the authorization
2025 September 15

10. Date of revision of the text
2025 September 15