For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

Diclofenac Diethylamine, Methyl Salicylate, Menthol and Absolute Alcohol, Topical Solution (Non-Aqueous)

Tapal-D

टेपल-डी

Composition: Each ml contains:

Diclofenac Diethylamine I.P.	2.32% w/v
(Eq. to Diclofenac Sodium I.P. 2.00% w/v)	
Methyl Salicylate I.P.	10.00% w/v
Menthol I.P.	5.00% w/v
Absolute Alcohol I.P.	10.00% v/v
In topical solution base (non aqueous)	q.s.

Description:

Tapal-D is available in 30 ml bottle with metered dose spray having 360° rotatable nozzle for topical application. Each actuation delivers 0.1 ml of the solution, containing 2.32 mg of diclofenac diethylamine equivalent to 2 mg of diclofenac sodium. Diclofenac diethylamine has chemical formula $C_{18}H_{23}C_{12}N_2O_2$ with molecular weight of 369.3.

Pharmacodynamics: Diclofenac inhibits the cyclooxygenase (COX) enzyme, an early component of the arachidonic acid cascade, resulting in the reduced formation of prostaglandins, thromboxanes and prostacyclin. Diclofenac, the active component has anti-inflammatory, anti-nociceptive and antipyretic effects.

Pharmacokinetics: The quantity of diclofenac absorbed through the skin after topical application is proportional to the area of drug application, and depends on both the total dose applied and the degree of skin hydration. The concentration of diclofenac in plasma is considerably lower after topical application as compared with oral administration. Diclofenac is more than 99% bound to human serum proteins, primarily to albumin. It diffuses into and out of the synovial fluid. The major diclofenac metabolite, 4'hydroxy-diclofenac, has very weak pharmacological action. The formation of 4'-hydroxy diclofenac is primarily mediated by CPY2C9. Both diclofenac and its metabolites undergo glucuronidation or sulfation followed by biliary excretion. CYP3A4 is responsible for the formation of minor metabolites, 5-hydroxy and 3'-hydroxy-diclofenac. Diclofenac is eliminated through urinary and biliary excretion of the glucuronide and the sulphate conjugates of the metabolites. Little or no free unchanged diclofenac is excreted in the urine.

Indications: Tapal-D is indicated for the local symptomatic relief of mild to moderate pain and inflammation associated with:

- Low backache, sprain and strain
- Blunt trauma of the tendons, ligaments, muscles and joints
- Localized forms of soft tissue rheumatism
- Arthritis of superficial joints such as knees, hands.

Contraindications:

Diclomist is contraindicated in the following conditions:

- Hypersensitivity to diclofenac, any of the excipients, acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs)
- Patient with asthma or in patient, when attacks of asthma, urticaria or acute rhinitis are precipitated by acetylsalicylic acid or other NSAID
- Third trimester of pregnancy
- Application to the breast area of nursing mothers.
- Paediatric population: the use in children and adolescents aged less than 14 yrs is not recommended.

Precautions and Warnings:

The possibility of systemic adverse events from application of **Tapal-D** cannot be excluded if the preparation is used on large areas of skin and over a prolonged period.

Tapal-D 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.

Tapal-D can be used with non-occlusive bandages but should not be used with an airtight occlusive dressing.

Patients should be warned against excessive exposure to sunlight in order to reduce the incidence of photosensitivity. Discontinue the treatment if a skin rash develops after applying the product.

The concomitant use of **Tapal-D** with oral NSAIDs should be cautioned as the incidence of systemic side effects may increase. Where **Tapal-D** is applied to a relatively large area of skin (i.e. more than 600 square centimetres of the body surface) and over a prolonged period (i.e. more than 4 weeks), the possibility of systemic side-effects cannot be completely excluded. If such usage is envisaged, the data sheet on diclofenac oral dosage forms should be consulted (for example, there is the potential for hypersensitivity, asthmatic and renal adverse reactions).

Bronchospasm may be precipitated in patients suffering from or with previous history of bronchial asthma or allergenic disease.

Tapal-D should only be used with caution in patients with a history of peptic ulcer, hepatic or renal insufficiency, bleeding diathesis or inflammatory bowel disease as isolated cases with topical diclofenac have been reported. No overall difference in effectiveness or safety is expected between elderly and younger patients, but because elderly patients are more likely to have decreased renal function, care should be taken when using **Tapal-D** in the elderly and it may be useful to monitor renal function. Do not mix or apply **Tapal-D** with any other topical agent.

Usage in Pregnancy & Lactation: Pregnancy: No data is available for use of **Tapal-D** in pregnant women. Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fetal development. Data from epidemiological studies suggest an increased risk of miscarriage, cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation increased from less than 1% to approximately 1.5%. The risk increases with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been found to increase pre- and post-implantation loss and embryo/fetal lethality. In addition, increased incidence of various malformations including cardiovascular have been reported in animals administered with prostaglandin synthesis inhibitor during organogenesis.

During the first and second trimester of pregnancy, **Tapal-D** should not be given unless clearly necessary. If **Tapal-D** 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:

- Cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- Renal dysfunction, which may progress to renal failure with oligo-hydroamniosis;

The mother and the neonate, at the end of pregnancy, to:

- Possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.
- Inhibition of uterine contractions resulting in delayed or prolonged labour.Consequently, diclofenac is
- Contraindicated during the third trimester of pregnancy.

Lactation: Like other NSAIDs, diclofenac passes into breast milk in small amounts. However, at therapeutic doses of **Tapal-D** 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, **Tapal-D** should not be applied on the breasts of nursing mothers, nor elsewhere on large areas of skin or for a prolonged period of time

Drug Interactions: Since systemic absorption of diclofenac from topical application is very low as compared to oral diclofenac, such interactions are very unlikely. Concurrent acetylsalicylic acid or other NSAIDs may result in an increased incidence of adverse reaction.

Possible Side Effects:

Like all medicines, this medicine can cause side-effects, although not everybody gets them.

- Discontinue use of **Tapal-D** if any skin rash develops. Following the use of topical (applied to the skin) diclofenac preparations reactions at the site of application have been reported commonly. These include rashes, itching, reddening, burning sensations or scaling of the skin.
- If you experience any of the following signs of allergy, STOP using Diclofenac Sodium Spray and tell a doctor or pharmacist immediately:
  - Skin rash with blisters; hives (may affect between 1 and 10 in every 10,000 people).
  - Wheezing, shortness of breath or feeling of tightness in the chest (asthma) (may affect less than 1 in every 10,000 people).
  - Swelling of the face, lips, tongue or throat (may affect less than 1 in every 10,000 people).
- **Some side effects are common** (may affect between 1 and 10 in every 100 people): Skin rash, itching, reddening or smarting of the skin.
- **Some side effects are very rare** (may affect less than 1 in every 10,000 people):The skin may be more sensitive to the sun. Possible signs are sunburn with itching, swelling and blistering.
- **Some side effects have unknown frequency** (frequency of occurrence in patients cannot be estimated from the available data): Application site reaction, dry skin, burning sensation

Dosage and Administration: Tapal-D is for external use only and not to be administered orally. It should not be applied on any mucosa, open wound, cut or diseased skin. Patient should be advised to ensure that the site of application is clean and dry before applying **Tapal-D** . Depending on the size of the affected site to be treated, 1-6 actuations (0.1-0.6 ml equivalent to 2-12 mg of diclofenac sodium) should be applied 3-4 times in a day. The maximum daily dose is 40 actuations (4 ml equivalent to 80 mg of diclofenac sodium). It should be sprayed from a distance of 4-5 inches from the site of application. Patient should be instructed not to massage the treated area after application. Patient should be advised to avoid washing or corning in contact of treated area with clothes or other objects for 8-10 minutes after application. It is recommended that lowest effective dose for shortest duration should be used. The treatment may be discontinued when the symptoms (pain and/or swelling) have subsided. For acute painful musculoskeletal conditions, patient should be advised to consult the doctor if no improvement is seen after 3 days and treatment should not be continued beyond 7 days without review. For chronic pain, if symptoms do not improve by day 7, or if they worsen within the first 7 days, a consultation with the doctor is recommended and use for more than 14 days is not recommended without review.

Overdosage: The low systemic availability of diclofenac from topical diclofenac makes overdose very unlikely. However, undesirable effects, similar to those observed following overdose of diclofenac tablets, can be expected if **Diclomist** is inadvertently ingested (1 bottle of 30 ml contains the equivalent of 600 mg of diclofenac sodium). In the event of accidental ingestion, resulting in significant systemic adverse effects, general therapeutic measures, normally adopted to treat poisoning with NSAIDs should be used. Management of overdosage with. NSAIDs essentially consists of supportive and symptomatic measures. Gastric decontamination and the use of activated charcoal should be considered. Supportive and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastro-intestinal irritation, and respiratory depression; specific therapies such as forced diuresis, dialysis or hemoperfusion are probably of no help in eliminating NSAIDs due to their high rate of protein binding and extensive metabolism.

Presentation: 30 ml in a glass bottle, Actuator and Pack insert.

Storage conditions: Store below 25°C, protected from light.

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