SUMMARY OF PRODUCTS CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MUSCOLEVE
Linseed Oil, Diclofenac Diethylamine, Methyl Salicylate and Menthol Gel

Strength

Linseed Oil BP	3.0 % w/w
Diclofenac Diethylamine	1.16 % w/w
Equivalent to Diclofenac Sodium BP	1.0 % w/w
Methyl Salicylate BP	10.0 % w/w
Menthol BP	5.0 % w/w

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition:

Linseed Oil BP	3.0 % w/w
Diclofenac Diethylamine	1.16 % w/w
Equivalent to Diclofenac Sodium BP	1.0 % w/w
Methyl Salicylate BP	10.0 % w/w
Menthol BP	5.0 % w/w
Gel Base q.s.	

Excipient with known effect
Each gram of gel contents

Benzyl Alcohol BP	10 mg
Butylated Hydroxy Toluene	0.100 mg
Butylated Hydroxy Anisole	0.100 mg
Polyoxyl 40 Hydrogenated Caster Oil	40.00 mg
Propylene Glycol	120.00 mg

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Gel
White to off white smooth gel

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Linseed Oil, Diclofenac Diethylamine, Methyl Salicylate and Menthol Gel is indicated in adults and adolescents aged 14 years and over as anti-inflammatory and analgesic agent in the treatment of:
- mild to moderate muscle pain;
- contusions;
- post-traumatic pain.

4.2 Posology and method of administration

Posology

Adults and children over 14 years: apply the formulation on the skin 3-4 times in a day and rub in gently. The quantity of formulation to be used depends upon the size of the painful area. A single dose is 2-4 g (4-8 cm when the tube neck is fully open).

There are insufficient data on efficacy and safety available for the children and adolescents below 14 years of age.

The duration of treatment without consulting a physician should not exceed 7 days.

The possibility of a long-term use of medicine the doctor decides individually.

Method of administration

Cutaneous use.

Apply on healthy skin only.

After application, the hands should be washed, unless these are being treated.

Linseed Oil, Diclofenac Diethylamine, Methyl Salicylate and Menthol 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 used in the formulation.

- 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

Linseed Oil, Diclofenac Diethylamine, Methyl Salicylate and Menthol Gel should be applied only on unbroken skin and not on open wounds. Occlusive dressing is not recommended after application. Care should be taken to avoid contact with the eyes and mucous membranes.

Use with caution in: severe disorders of the liver and kidney functions, bronchial asthma, pregnancy (first and second trimesters), elderly patients.

- Muscoleve contains Benzyl alcohol which may cause mild local irritation;
- Muscoleve contains Butylated Hydroxy Toluene and Butylated Hydroxy Anisole which may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.
- Muscoleve contains Polyoxyl 40 Hydrogenated Caster Oil which may cause skin reactions;
- Muscoleve contains propylene Glycol which may cause skin irritation. Do not use this medicine in babies less than 4 weeks old with open wounds or large area of broken or damaged skin (such as burn) without talking to you doctor or pharmacist.

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

The systemic concentration of diclofenac is lower after topical administration, compared to oral formulations.
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 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.

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
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
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to **TMDA**

4.9 Overdose
The low systemic absorption of topical diclofenac renders overdoses 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
Pharmacodynamics
Pharmacotherapeutic group: Topical products for joint and muscular pain, Anti-inflammatory preparations, non-steroids for topical use, ATC code: M02AA15

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 faeces.

5.3 Preclinical safety data

Not Applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl Alcohol

Polysorbate 80

Butylated Hydroxy Toluene

Butylated Hydroxy Anisole

Polyoxyl 40 Hydrogenated Castor Oil

Citric Acid Monohydrate

Disodium EDTA

Carbopol 940

Isopropyl Alcohol

Propylene Glycol

Triethanolamine

Purified Water

6.2 Incompatibilities

None known

6.3 Shelf life

36 months

Use within one month after opening the tube.

6.4 Special precautions for storage

Do not store above 30°C, do not freeze.
Protect from light.

6.5 Nature and contents of container
10, 15, 20 & 30 gm printed collapsible lami tube.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
Keep the tube tightly closed when not in use.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES

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8. MARKETING AUTHORISATION NUMBER(S)

TAN 22 HM 0503

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

05th December, 2022

10. DATE OF REVISION OF THE TEXT