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

Diclogesic® Gel

Oleum-lini, Diclofenac, Methyl salicylate, Menthol and Capsaicin Gel

Composition:
Diclogesic® Gel
Oleum-lini
(Containing Predominantly -α-Linolenic acid) B.P. 3.00 % w/w
Diclofenac Diethylamine B.P. 1.16%w/w (eq. To Diclofenac Sodium I.P. 1.00 % w/w)
Methyl salicylate I.P. 10.00 % w/w
Menthol I.P. 5.00 % w/w
Capsaicin U.S.P. 0.025 % w/w
Gel Base q.s.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMIC PROPERTIES

Diclogesic Gel is an analgesic, anti-inflammatory preparation for topical application. Its active substances include Oleum-lini, diclofenac diethylamine, capsaicin, methyl salicylate and menthol. The gel is applied to the skin. The properties of the combination of all four active ingredients in Diclogesic Gel have not been evaluated directly in clinical efficacy studies.

Oleum lini - contains predominantly essential fatty acids i.e. a - linolenic acid. When it is absorbed percutaneously, alpha - linolenic acid gets converted to eicosapentaenoic acid (EPA). EPA is acted upon by cyclo-oxygenase enzyme to produce prostaglandin E_3 which is a weak inflammatory agent. Presence of EPA prevents the action of cyclooxygenase on Arachidonic acid which reduces its conversion to PGE_2 (a highly inflammatory agent)

Diclofenac has been shown in experiments to inhibit prostaglandin biosynthesis; and this is regarded as an important factor in its mechanism of action.

Capsaicin gels and creams (in concentrations ranging from 0.025% - 0.075%) have been used as topical analgesics in painful conditions such as post-herpetic neuralgia after the lesions have healed, diabetic neuropathy, osteoarthritis and rheumatoid arthritis. The mechanism of analgesic effect of capsaicin is believed to result from stimulation of the release of substance P from local sensory C-type nerve fibers and subsequent depletion of substance P from the entire neuron, reducing the transmission of pain impulses to the CNS. Capsaicin is not considered to be a traditional counter-irritant, because it does not rely on vasodilation in the skin for its mechanism of action, but it has been included in various rubefacient preparations for the relieve of muscular and rheumatic pain. Local application may result in a transient warm, burning or stinging sensation corresponding to transient excitation of the pain fibres, followed by hypoalgesia due to inactivation of the pain fibres.

Methyl salicylate is a salicylic acid derivative that is irritant to the skin and is used topically as a counter-irritant in rubefacient preparations for the relief of pain in musculoskeletal, joint and soft tissue disorders. Like other salicylates, methyl salicylate may be absorbed through intact skin. A

study evaluating other commercial formulations containing 20% methyl salicylate indicated that the methyl salicylate is extensively metabolized to salicylic acid in the dermal and subcutaneous tissues following topical administration.

Menthol is a common counter-irritant in various topical analgesic preparations. When applied to the skin, menthol dilates the blood vessels, causing a sensation of coldness followed by an analgesic effect.

PHARMACOKINETIC PROPERTIES

Absorption

Diclofenac

The amount of diclofenac absorbed through the skin is proportional to the contact time and skin area covered with Diclofenac sodium gel, and depends on the total topical dose and on skin hydration. About 6% of the active substances is absorbed after topical application of 2.5 g Diclofenac sodium gel per 500 cm^2, as determined by reference to total renal elimination compared with diclofenac sodium tablets. Absorption of diclofenac increases threefold if an occlusive dressing is applied for 10 hours.

Capsaicin

The absorption of capsaicin after topical application is unknown.

Methyl salicylate

Methyl salicylate is speedily absorbed when applied cutaneously. Percutaneous absorption of methyl salicylate is enhanced by exercise, heat occlusion, or disruption of integrity of the skin. Both the rate and extent of absorption increase after repeated application.

Menthol

Menthol is known to be well absorbed after topical application.

Distribution

Diclofenac

Diclofenac can be detected in plasma, synovial tissue, and synovial fluid after topical application of diclofenac sodium gel to the wrists and knees. Peak plasma concentrations of diclofenac are about 100 times lower after topical application of diclofenac sodium gel than after oral administration of diclofenac sodium tablets. 99.7% of diclofenac binds to serum proteins, mainly to albumin (99.4%).

Capsaicin

The distribution of capsaicin after topical application is unknown.

Methyl salicylate

50-80% of salicylic acid binds to serum proteins.

Menthol

The distribution of menthol after topical application is unknown.

Metabolism

Diclofenac

Biotransformation of diclofenac takes place partly by glucuronidation of the intact molecule, but mainly by single or multiple hydroxylation resulting in several phenolic metabolites, most of which are converted to glucuronide conjugates. Two of these phenolic metabolites are biologically active, but to a much lesser extent than diclofenac.

Capsaicin

Capsaicin seems to be metabolized by cytochrome P450

Methyl salicylate

Methyl salicylate is extensively metabolized to salicylic acid in the dermal and subcutaneous tissues following topical administration.

Menthol

The metabolism of menthol after topical application is unknown.

Elimination

Diclofenac

Total systemic clearance of diclofenac from the plasma is 263 ± 56 mL/min (mean value ± standard deviation). The terminal plasma half-life is 1-2 hours. Four of the metabolites, including the two active metabolites, also have a short plasma half-life (1-3 hours). One metabolite, 3'-hydroxyl-4-methoxy-diclofenac, has a much longer half-life, but the metabolite is virtually inactive. Diclofenac and its metabolites are excreted mainly in the urine.

Capsaicin

The elimination of capsaicin after topical application is unknown.

Methyl salicylate

Salicylic acid and its principal metabolites are excreted in the urine.

Menthol

After absorption, menthol is excreted in the urine and bile as a glucuronide.

Kinetics in special clinical situations

No accumulation of diclofenac and its metabolites is expected in patients with renal impairment.In patients with chronic hepatitis or non-decompensated liver cirrhosis, the kinetics and metabolism of diclofenac are the same as in patients without liver disease.

INDICATIONS

Treatment of:

- Localized forms of soft-tissue rheumatism, e.g. tendovaginitis, shoulder-hand syndrome, bursitis and periarthropathy.
- Localized rheumatic diseases, e.g., osteoarthritis of the peripheral joints and vertebral column.
- Post –traumatic inflammation of the tendons, ligaments, muscles, and joints e.g., due to sprains, strains, or bruises.

DOSAGE/ADMINISTRATION

Diclogesic Gel is applied locally 3-4 times daily to the skin and rubbed in gently. Depending on the size of the painful area to be treated, 2-4 g Diclogesic Gel is sufficient to treat an area of about 400-800 cm^2. An occlusive dressing should not be used. The hands should be washed after application of the gel, unless the hands are the treated areas, in which case, they should be washed 30 minutes after application. Heating pads should not be used with Diclogesic Gel, and patients should avoid taking a hot bath or shower immediately before or after application as the burning sensation may be exacerbated. The duration of treatment should not be longer than one week (7 days).

Children

Diclogesic Gel should not be used in children.

Skin Tolerability testing

The skin tolerability of diclofenac diethylamine gel with capsaicin, methyl salicylate and menthol has been tested in healthy human volunteers. Generally the topical application is well tolerated without major untoward effects.

Restrictions on use

Contraindications

Hypersensitivity to diclofenac, acetylsalicylic acid, and other non-steroidal anti-inflammatory agents, to capsaicin, menthol, benzyl alcohol and to isopropanol or propylene glycol.

Precautions

Diclogesic Gel should be applied only to intact skin, and not be broken or irritated skin or open wounds. The preparation should not come into contact with the eyes or mucous membranes. It should be used with care on the extremities of patients with impaired peripheral circulation or diabetes. The gel should not be used before phototherapy or phototesting procedures.

Pregnancy and lactation

Use in pregnancy

For Diclogesic Gel no clinical data on exposed pregnancies are available. Animal studies are insufficient with respect to effects on pregnancy/and - or /embryonal / foetal development /and-or /parturition/and-or /postnatal development. The potential risk for humans is unknown.
Diclogesic Gel should not be used during pregnancy unless clearly necessary.

Use during lactation

Measurable quantities of the active substance should not be seen in the breast milk. However no experience is available with Diclogesic Gel in breast-feeding women.

UNDESIRABLE EFFECTS

Local reactions

Very common: a warm, stinging, or burning sensation may be experienced at the site of application. Allergic or nonallergic nonallergic contact dermatitis (with symptoms and signs such as itching, reddening of the skin or scaling).

Common: Moderate allergic and non-allergic contact dermatitis such as erythema, oedema, papules, vesicles and bullae.

Systemic reactions
Isolated cases: generalized rash; hypersensitivity reactions (e.g. asthma attack, angioedema); photosensitivity reactions.

Although likelihood of systemic reactions occurring during topical treatment with diclofenac is small compared with the frequency of side effects seen during oral administration, the possibility of developing other diclofenac adverse reactions cannot be completed ruled out. Since methyl salicylate is absorbed through the skin, symptoms of salicylate intoxication can occur following topical application of methyl salicylate.

INTERACTIONS
No interactions have been reported to date with topical diclofenac diethylamine. Potentiation of warfarin anticoagulation has been reported with topical application of methyl salicylate preparations.

OVER DOSAGE
Significant systemic reactions resulting from improper use or accidental over dosage should be treated with the usual measure employed to manage poisoning with non-steroidal anti-inflammatory drugs.

For external use only

WARNING: "NOT FOR VETERINARY USE"

Replace cap tightly, after use.

Keep all Medicines out of reach of children

EXPIRY
Do not use later than the date of expiry.

STORAGE
STORE IN A COOL PLACE, DO NOT FREEZE.

PRESENTATION
Diclogesic® Gel is available in Tube of 30 gm

MARKETED BY

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