1. Name of the medicinal product
ARIGESIC GEL

2. Qualitative and quantitative composition
Each gram of gel contains : Diclofena diethylamine, Menthol & Methyle Salicylate..

Excipient(s) with known effect:

Isopropyl alcohol, Diethylamine, Polysorbate-80 & Cetostearyl alcohol.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form
Gel.

White, smooth, homogeneous gel, with a slight characteristic odour.

4. CLINICAL PARTICULARS

4.1.Therapeutic indications

Local treatment of inflammatory and degenerative forms of diseases of musculoskeletal system, which are accompanied by pain and swelling such as rheumatoid arthritis, ankylosing spondylitis (Bechterew's disease), acute podagric (related to gout), psoriatic and post- traumatic arthritis, rheumatic damage of soft tissues (tendovaginitis bursitis, myositis), degeneration diseases of joints (arthrosis of large and small joints), osteochondritis of spinalcolumn, myalgia, neuralgia, lumbosacral radiculitis, trauma pain, ligamentous laxity, sprain of ligaments, muscles, tendons, pain in muscles and joints, induced by hard physical activity.

4.2.Posology and method of administration

Depending on area of painfulness 2-4 g of gel (strip is 4 to8 cm) is applied on skin is rubbedlightly 2-3 times per day. Average daily dose compound 10 g of gel, equivalent to 100 mg ofDiclofenac.

The drug should not be applied on damaged skin. One should be careful to avoid accidentalcontact with the eyes and on mucous tunic.

4.3.Contraindications

Hypersensitivity to Diclofenac and other components of this drug; Aspirin induced

bronchial asthma;

Break in the skin or open wound in area should be avoided

Children below 12 years of age (because there is no data about external usage this medicine in this age group).

4.4.Special warnings and precautions for use

Consult the doctor before using the medicine

The drug is prescribed carefully for patients with hypersensitivity to acetylsalicylic acid, different salicylates and other NSAID (bronchial asthma attacks, skin reactions and acute rhinitis). It is necessary to weigh all factors of usefulness and risk.

Arigesic is used carefully in patients with ulcer of the stomach or intestines, disorders of theliver and kidney, haematological disorders, relapse of nasal polyposis.

It is necessary to wash hands after usage of medicine to avoid the accidental entry of drug ineyes and mucous tunics.

4.5.Interaction with other medicinal products and other forms of interaction

Arigesic Gel can be used along with other medicines, because the components of this drug do not interact systemically with other medicines, including use of Diclofenac sodium by oral route.

But in cases of long usage of Arigesic Gel in large dosage it is necessary to know that Diclofenac can increase effect of anticoagulants, GCS, Lithium and it can decrease action offurosemide, thiazide diuretics. It can increase concentration of digoxin in plasma and decrease tolerance of other NSAID, increasing their ulcerogenic action on mucous coat of GIT.

The concurrent local usage of some medicines, containing NAAA, can irritate the skin locallyin the form of urtricaria, reddening, desquamation.

4.6.Pregnancy and lactation

It is not allowed to apply gel on big areas of body or to use for a long time in last three months of pregnancy and during lactation period, because data about safety of the drug on foetus and neonates is not available.

The matter of administration of the drug during the pregnancy and lactation is to be decidedonly by the doctor.

4.7.Effects on ability to drive and use machines

The drug does not adversely affect the ability to drive vehicles and other potentially dangerous machinery.

4.8.Undesirable effects

Generally, the preparation is tolerated well. The small part of drug (about 5 %) is absorbed into the bloodstream when used locally.

It more or less eliminates possibility of side effects associated with NSAIDs.

Sometimes skin irritation such as, skin rash, oedema, appearance of wheals, papules, scutes, reddening, burning, prickling, skin itch occur at the site of application. If Diclofenac is used on large area for long duration following systemic side effects may occur, in cases of concurrent usage of Diclofenac tablets, suppository and/or ampoules.

Side effects related to GIT, appearance of generalize rash, development of reaction of increased sensibility, such as oedema of face (angioedema), apnoea, photosensitivity is rare. In a case of any unusual reactions it is necessary to consult the doctor immediately and stopthe further usage of the medicine.

4.9.Overdose

The overdose is not possible as a result of local application of Arigesic Gel.

In case of accidental ingestion, the treatment is the same as in case of poisoning by nonsteroidal anti-inflammatory drugs. The patient should seek medical attention.

Symptomatic treatment is performed in case of emergence of signs of complications, such as high blood pressure, renal failure, seizures, respiratory depression, gastrointestinal disorders.

5. PHARMACOLOGICAL PROPERTIES

5.1.Pharmacodynamic properties

Pharmacotherapeutic group: Nonsteroidal anti-inflammatory and anti-rheumatic ATC Code: M02AA65.

Mechanism of Action of each component of Arigesic gel is explained as follows.

Diclofenac inhibits the cyclooxygenase, suppresses synthesis of prostaglandins – Endogenous substances, which play a significant role in the genesis of the inflammation, pain, and fever. Diclofenac reduces pain, eliminates inflammation.

Menthol acts on the temperature receptors. It is gives sensation of coolness, constricts capillaries, and decrease of their permeability. It provides local counter-irritation and gentle analgesic actions.

Methyl salicylate is a derivative of salicylic acid, which has local irritation action. Methyl salicylate decreases the pain because of irritation of skin receptors. Methyl salicylate inhibits synthesis of prostaglandins, decreases swelling and infiltration of inflamed tissues.

Linseed oil contains alfalinoleic acid, which has anti-inflammatory, antioxidant actions, improves blood circulation at place of application.

The action of medicine begins within few minutes after application on skin. During 20-30 min it achieves maximum activity level. It provides relief from the symptoms from day one of beginning of treatment.

5.2.Pharmacokinetic properties Absorption

When Diclofenac gel is applied topically, Diclofenac is absorbed into the epidermis. In patients with compromised skin (mainly atopic dermatitis and other dermatitis conditions)

of the hands, arms or face, approximately 10% of the applied dose of Diclofenac was absorbed systemically in both normal and compromised epidermis. After topical application of 2 g Diclofenac gel three times daily for six days, diclofenac could be detected in plasma. Mean bioavailability parameters were AUC0-t 9±19 ng.hr/mL (mean±SD) with a Cmax of 4±5 ng/mL and a Tmax of 4.5±8 hours. In comparison, a single oral 75 mg dose of diclofenac produced an AUC of 1600 ng.hr/mL. Therefore, the systemic bioavailability after topical application of Diclofenac gel is lower than after oral dosing. No information is available on the absorption of Diclofenac when Diclofenac gel is used under occlusive bandage.

Distribution

Diclofenac binds tightly to serum albumin. The volume of distribution of diclofenac following oral administration is approximately 550 mL/kg.

Metabolism

Biotransformation of Diclofenac following oral administration involves conjugation at the carboxyl group of the side chain or single or multiple hydroxylation's resulting in several phenolic metabolites, most of which are converted to glucuronide conjugates. Two of these phenolic metabolites are biologically active, however to a much smaller extent than Diclofenac. Metabolism of Diclofenac following topical administration is thought to be similar to that after oral administration. The small amounts of Diclofenac and its metabolites appearing in the plasma following topical administration makes the quantification of specificmetabolites imprecise.

Elimination

Diclofenac and its metabolites are excreted mainly in the urine after oral dosing. Systemic clearance of Diclofenac from plasma is 263±56 mL/min (mean±SD). The terminal plasma half-life is 1-2 hours. Four of the metabolites also have short terminal

half-lives of 1-3 hours

5.3.Preclinical safety data

Not stated

6. Pharmaceutical particulars

6.1 List of excipients

Carbomer

Diethylamine

Isopropyl Alcohol

Propylene Glycol

Polysorbate-80

Cetostearyl Alcohol

Purified water

6.2 Incompatibilities

None stated.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

30 gram lami tube.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

The active substance diclofenac occurs frequently in surface water, any unused product or waste should be disposed of in accordance with local requirements.

7. Marketing authorisation holder

Makki Pharmaceutical Limited

55 Commissioner's Quarters, Ifite Awka Anambra State

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8. Marketing authorisation number(s)

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9. Date of first authorisation/renewal of the authorisation

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10. Date of revision of the text
