Summary of Product Characteristics

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1. NAME OF THE MEDICINAL PRODUCT

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Didlyn -50 (Gastro Resistant Diclofenac Tablets BP 50 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Enteric coated tablet contains

Diclofenac Sodium BP 50 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablets [Enteric Coated]

Brown coloured , round , biconvex enteric coated tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

- For the short-term treatment of acute, mild to moderately severe pain that may be accompanied by inflammation.
- For treatment of primary dysmenorrhea
- For relief of the signs and symptoms of osteoarthritis
- For relief of the signs and symptoms of rheumatoid arthritis
- For relief of the signs and symptoms ankylosing spondylitis
- For relief of the signs and symptoms musculoskeletal and/or soft tissue trauma including sprains, postoperative pain following dental extraction, & episiotomy

4.2 Posology and Method of administration

Diclofenac sodium may be administered as 25 mg, 50 mg, or 75 mg tablets.

Regardless of the indication, the dosage of diclofenac should be individualized to the lowest effective dose to minimize adverse effects. The recommended daily dose for diclofenac sodium is 50 mg every 6 to 8 hours as required for a total daily maximum amount of 150 mg.

Primary dysmenorrhea

Treatment may be initiated with a loading dose of 100 mg, followed by 50 mg every 6 to 8 hours, when required. When a loading dose is necessary, the first-day maximum total amount is 200 mg.

Osteoarthritis:

The recommended dosage is 100 to 150 mg/day in divided doses, 50 mg b.i.d. or t.i.d. or 75 mg b.i.d. Dosages above 150 mg/day have not been studied in patients

with osteoarthritis.

Rheumatoid Arthritis:

The recommended dosage is 150 to 200 mg/day in divided doses, 50 mg t.i.d. or q.i.d., or 75 mg b.i.d. Dosages above 225 mg/day are not recommended in patients with rheumatoid arthritis.

Ankylosing Spondylitis:

The recommended dosage is 100 to 125 mg/day, administered as 25 mg q.i.d., with an extra 25 mg dose at bedtime if necessary. Dosages above 125 mg/day have not been studied in patients with ankylosing spondylitis.

Route of administration: oral.

4.3 Contraindications

In patients with a history of recurrent ulceration, active or recent history of inflammatory diseases of the gastrointestinal tract, such as: peptic ulcer, regional enteritis, gastritis, ulcerative colitis.

Known or suspected hypersensitivity to diclofenac or other NSAIDs. Since cross-sensitivity has been demonstrated, diclofenac potassium should not be given to patients with the complete or partial syndrome of nasal polyps or in whom ASA or other NSAIDs have induced asthma, anaphylaxis, rhinitis, urticaria or other allergic manifestations. Fatal anaphylactoid reactions have occurred in such individuals. As well, individuals with the above medical problems are at risk of a severe reaction even if they have taken NSAIDS in the past without any adverse effects.

Significant hepatic impairment or active liver disease.

Severely impaired or deteriorating renal function (creatinine· clearance <30 mL/min [0.5 mL/s]). Individuals with lesser degrees of renal impairment are at risk of deterioration of their renal function when prescribed NSAIDs and must be monitored.

4.4 Special warnings and precautions for use

Diclofenac sodium carmot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to disease exacerbation. Patients on prolonged corticosteroid therapy should have their therapy tapered

slowly if a decision is made to discontinue corticosteroids.

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

When diclofenac sodium tablets are administered with aspirin, its protein binding is reduced. The clinical significance of this interaction is not known; however, as with other NSAIDs, concomitant administration of diclofenac and aspirin is not generally recommended because of the potential of increased adverse effects.

Methotrexate

NSAIDs have been reported to competitively inhibit methotrexate accumulation in rabbit kidney slices. This may indicate that they could enhance the toxicity of methotrexate. Caution should be used when NSAIDs are administered concomitantly with methotrexate.

Cyclosporine

Diclofenac sodium tablets, like other NSAIDs, may affect renal prostaglandins and increase the toxicity of certain drugs. Therefore, concomitant therapy with diclofenac sodium tablets may increase cyclosporine's nephrotoxicity. Caution should be used when diclofenac sodium tablets are administered concomitantly with cyclosporine.

ACE-inhibitors

Reports suggest that NSAIDs may diminish the antihypertensive effect of ACE inhibitors. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE inhibitors.

Furosemide

Clinical studies, as well as posl-markeling observations, have shown that diclofenac
sodium tablets can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy with NSAIDs, lhe palienl should be observed closely for signs ofrenal failure, as well as to assure diuretic efficacy.

Lithium

NSAIDs have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. The mean minimum lithium concentration increased 15% and the renal clearance was decreased by approximately 20%. These effects have been attributed to inhibition of renal prostaglandin synthesis by the NS AID. Thus, when NSAIDs and lithium are administered concurrently, subjects should be observed carefully for signs oflithium toxicity.

4.6 Fertility, Pregnancy and Lactation

Pregnancy:

The use of diclofenac in pregnant women has not been studied. Therefore, diclofenac sodium should not be used during the first two trimesters of pregnancy unless the potential benefit to the mother outweights the risk to the foetus. As with other NSAIDs, use during the third trimester of pregnancy is contraindicated owing to the possibility of uterine inertia and/or premature closure of the ductus arteriosus.

Lactation:

Like other NSAIDs, diclofenac passes into the breast milk in small amounts. Therefore, diclofenac sodium should not be administered during breast feeding in order to avoid adverse effects in the infant.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

Gastrointestinal experiences including: abdominal pain, constipation, diarrhea, dyspepsia, flatulence, gross bleeding/perforation, heartburn, nausea, GI ulcers (gastric/duodenal) and vomiting.

Abnormal renal function, anemia, dizziness, edema, elevated liver enzymes, headaches, increased bleeding time, pruritus, rashes and tinnitus.

Additional adverse experiences reported occasionally include:

Body as a Whole

fever, infection, sepsis

Cardiovascular System

congestive heart failure, hypertension, tachycardia, syncope

Digestive System

dry mouth, esophagitis, gastric/peptic ulcers, gastritis, gastrointestinal bleeding, glossitis, hematemesis, hepatitis, jaundice

Hemic and Lymphatic System

ecchymosis, eosinophilia, leukopenia, melena, purpura, rectal bleeding, stomatitis, thrombocytopenia

Metabolic and Nutritional

weight changes

Nervous System

anxiety, asthenia, confusion, depression, dream abnormalities, drowsiness, insomnia, malaise, nervousness, paresthesia, somnolence, tremors, vertigo

Respiratory System

asthma, dyspnea

Skin and Appendages

alopecia, photosensitivity, sweating increased

Special Senses

blurred vision

Urogenital System

cystitis, dysuria, hematuria, interstitial nephritis, oliguria/polyuria, proteinuria, renal failure

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 via EFDA yellow Card Scheme, online at https://primaryreporting.who-umc.org/ET or toll free call 8482 to Ethiopian food and drug authority (EFDA).

4.9 Overdose

Symptoms: vomiting, gastrointestinal haemorrhage, diarrhoea, dizziness, tinnitus or convulsions. In the event of significant poisoning, acute renal failure and liver damage are possible.

Treatment

•Special measures such as forced diuresis,

•dialysis or haemoperfusion are probably of no help in eliminating NSAIDs due to the high protein binding and extensive metabolism.

•Activated charcoal may be considered after ingestion of a potentially toxic overdose, and

•gastric decontamination (e.g. vomiting, gastric lavagf) after ingestion of a potentially life-threatening overdose.

5.0 Pharmacological Properties

5.1 Pharmacodynamic Properties

Diclofenac sodium, a non-steroidal compound with pronounced antirheumatic, anti-inflammatory, analgesic and antipyretic properties. Inhibition of prostaglandin biosynthesis, which has been demonstrated in experiments, is considered fundamental to its mechanism of action. Prostaglandins play a major role in causing inflammation, pain and fever.

Diclofenac sodium in vitro does not suppress proteoglycan biosynthesis in cartilage at concentrations equivalent to those reached in humans.

In post-traumatic and post-operative inflammatory conditions, diclofenac sodium rapidly relieves both spontaneous pain and pain on movement and reduces inflammatory swelling and wound oedema.

5.2 Pharmacokinetic properties

Absorption

Diclofenac is 100% absorbed after oral administration compared to IVadministration as measured by urine recovery. However, due to first-pass metabolism, only about 50% of the absorbed dose is systemically available (see Table 1). Food has no significant effect on the extent of diclofenac absorption. However, there is usually a delay in the onset of absorption of 1 to 4.5 hours and a reduction in peak plasma levels of <20%.

Distribution

The apparent volume of distribution (V/F) of diclofenac sodium is 1.4 L/kg.

Diclofenac is more than 99% bound to human serum proteins, primarily to albumin. Serum protein binding is constant over the concentration range (0.15-105 µg/mL) achieved with recommended doses.

Diclofenac diffuses into and out of the synovial fluid. Diffusion into the joint occurs when plasma levels are higher than those in the synovial fluid, after which the process reverses and synovial fluid levels are higher than plasma levels. It is not known whether diffusion into the joint plays a role in the effectiveness of diclofenac.

Metabolism

Five diclofenac metabolites have been identified in human plasma and urine. The metabolites include 4'-hydroxy-, 5-hydroxy-, 3'-hydroxy-, 4',5-dihydroxy- and 3'-hydroxy-4' -methoxy diclofenac. In patients

with renal dysfunction, peak concentrations of metabolites 4' -hydroxy- and 5-hydroxy-diclofenac were approximately 50% and 4% of the parent compound after single oral dosing compared to 27% and 1 % in normal healthy subjects. However, diclofenac metabolites . undergo further glucuronidation and sulfation followed by biliary excretion.

One diclofenac metabojite 4'-hydroxy-diclofenac has very weak pharmacologic activity.

Excretion

Diclofenac is eliminated through metabolism and subsequent urinary and biliary excretion of the glucuronide and the sulfate conjugates of the metabolites. Little or no free unchanged diclofenac is excreted in the urine. Approximately 65% of the dose is excreted in the urine and approximately 35% in the bile as conjugates of unchanged diclofenac plus metabolites. Because renal elimination is not a significant pathway of elimination for unchanged diclofenac, dosing adjustment in patients with mild to moderate renal dysfunction is not necessary. The terminal half.life of unchanged diclofenac is approximately 2 hours.

5.3 Preclinical safety data

Not applicable.

6.0 Pharmaceutical particulars

6.1 List of excipients

Magnesium Stearate , Sodium Starch Glycolate (Type A) ,Colloidal Anhydrous Silica, Microcrystalline Cellulose (PH-102), Isopropyl Alcohol*, Purified Water*, Cellulose Acetate Phthalate , Titanium Dioxide , Diethyl Phthalate , Ethyl Cellulose , Colour Ferric Oxide, Colour Ferric Oxide, Dichloromethane*.

*Lost during processing

6.2 Incompatibilities

None stated

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C in a dry place. Protect from light.

6.5 Nature and contents of container

10 Tablets packed in Blister Aluminium Foil and Amber PVC film and such 10 blisters are packed in a unit carton along with package insert.

6.6 Special precautions for disposal and other handling

Return any leftover medicine to your pharmacist.

7. Marketing Authorisation Holder

MEDICAMEN BIOTECH LIMITED

SP-1192 A & B, Phase-IV,
Industrial Area, Bhiwadi-301019,
Distt Alwar, Rajasthan India

8. Number(s) in the national register of finished pharmaceutical products

Registration No 07836/08607/NMR/2020

9. Date of first authorisation/renewal of the authorisation

Approval date 30-09-2022

10. Date of revision of the text

July 2023