Prescribing information (Summary of products characteristics)

1. **Name of the finished pharmaceutical product**

International Non–Proprietary Name(INN)	Diclofenac Potassium, Paracetamol and Chlorzoxazone Tablets
Trade mark name	**Nac MR**
Generic Name	Diclofenac Potassium, Paracetamol and Chlorzoxazone Tablets

1.1 Strength

Diclofenac Potassium BP 50 mg / Tablet

Chlorzoxazone USP 250 mg / Tablet

Paracetamol BP 325 mg / Tablet

1.2 Pharmaceutical form

Pharmaceutical Dosage form: Oral Tablets

Visual and Physical Characteristics of the product: White coloured, elongated shaped, film coated tablets having break line on one side and other side plain.

2. Qualitative and quantitative composition

Standard batch Size: 100,000 Tablets

Sr. No.	Material Name	Spc.	Function	Theo. Qty per tablet (mg)	OA %	Actual qty per tablet (mg)	Qty. req per batch (Kg)
Mixing							
01	Diclofenac Potassium	BP	Active	50.00	2	51.00	2.550
02	Chlorzoxazone	USP	Active	250.00	2	255.00	12.750
03	Paracetamol	BP	Active	325.00	2	331.50	16.575
04	Maize starch	BP	Diluents	240.00	10	264.00	13.200
05	Dibasic calcium phosphate	BP	Diluents	80.00	4	83.20	4.160
Wet Granulation							
06	Maize starch	BP	Binder	40.00	-	40.00	2.00
07	Povidone	BP	Binder	5.00	-	5.00	0.25
08	Purified water	BP	Solvent	0.15	-	0.15	0.75
09	Sodium Benzoate	BP	Preservative	2.00	-	2.00	0.100
Lubrication							
10	Magnesium Stearate	BP	Anti-adherent	10.00	-	10.00	0.50
11	Purified talc	BP	Anti-adherent	10.00	-	10.00	0.50
12	Sodium starch Glycolate Type C)	BP	Disintegrating agent	15.00	-	15.00	0.75
13	Sodium Lauryl sulphate	BP	Disintegrating agent	5.00	-	5.00	0.25
14	Colloidal anhydrous silica	BP	Anti-adherent	3.00	-	3.00	0.15
Compression Tablet						**1074.70 mg**	**53.735 Kg**
Film Coating							
15	Cotab RFC (White)	IH	Coating agent	15.00	-	15.00	0.75
16	Titanium Dioxide	BP	Coating agent	2.00	-	2.00	0.10
17	Purified water	BP	Solvent	0.15	-	0.15	7.50
Total weight						**1091.70 mg**	**54.585 Kg**

2.3 Salts and hydrates

Not Applicable

2.4 Esters and pro-drugs

Not Applicable

2.5 Oral powders for solution or suspension

Not Applicable

2.6 Parenterals excluding powders for reconstitution

Not Applicable

2.5 Oral powders for solution or suspension

Not Applicable

2.6 Parenterals excluding powders for reconstitution

Not Applicable

4. Clinical Particulars

4.1 Therapeutic indications

• Soft tissue injuries with spasm and inflammation,

• Neck / shoulder / back pain,

• Tendonitis / tenosynovitis / bursitis

• Musculoskeletal disorders

4.2 Posology and method of administration

Adults: One tablet two to three times daily

4.3 Method of administration

Oral Route

4.4 Contraindications

Contraindicated in patients with known hypersensitivity to any of the

ingredients.

4.5 Special warnings and precautions for use

Not Stated.

4.6 Paediatric population

Not Stated.

4.7 Interaction with other medicinal products and other forms of interaction

• Diclofenac may increase the plasma concentrations of lithium, digoxin and methotrexate. It may increase the activity of anticoagulants, inhibit the activity of diuretics, enhance cyclosporine nephrotoxicity and precipitate convulsions when co-administered with quinolone antibiotics.

• The risk of paracetamol toxicity may be increased in patients receiving other potentially hepatotoxic drugs or drugs that induce hepatic microsomal enzymes.

Co-administration of paracetamol with rifampicin, isoniazid, chloramphenicol, antiepileptic drugs and antiviral drugs is to be avoided.

Metoclopromide may increase the absorption of paracetamol whereas excretion and plasma concentration may be altered when coadministered with probenecid. Cholestyramine also reduces the absorption of paracetamol.

• The concomitant use of chlorzoxazone with alcohol or other CNS depressants may have an additive effect

4.8 Additional information on special populations

Not stated.

4.9 Paediatric population

Not stated.

4.10 Fertility, pregnancy and lactation

4.10.1 General principles

Not stated.

4.10.2 Women of childbearing potential / Contraception in males and females

Not stated.

4.10.3 Pregnancy

Diclofenac Potassium: Congenital abnormalities have been reported in association with NSAID administration in man; however, these are low in frequency and do not appear to follow any discernible pattern. In view of the known effects of NSAIDs on the foetal cardiovascular system (risk of closure of the ductus arteriosus), use in the last trimester of pregnancy is contraindicated.

The onset of labour may be delayed and the duration increased with an increased bleeding tendency in both mother and child. NSAIDs should not be used during the first two trimesters of pregnancy or labour unless the potential benefit to the patient outweighs the potential risk to foetus.

Paracetamol: Epidemiological studies in human pregnancy have shown no effects due to paracetamol used in the recommended dosage. However, paracetamol should be avoided in pregnancy unless considered essential by the physician.

Chlorzoaxzone: Chlorzoaxzone is not recommended during pregnancy or lactation since safety in pregnant women or nursing mothers has not been established.

4.10.4 Breastfeeding

Diclofenac Potassium: In limited studies so far available, NSAlDs can appear in breast milk in very low concentrations. NSAlDs should, if possible, be avoided when breastfeeding.

Paracetamol: Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding.

Chlorzoaxzone: Chlorzoaxzone is not recommended during pregnancy or lactation since safety in pregnant women or nursing mothers has not been established.

4.10.5 Fertility

Not stated.

4.11 Effects on ability to drive and use machines

Not stated.

4.12 Undesirable effects

Drowsiness, dizziness, light- headedness, malaise, or overstimulation may be noted by an occasional patient.

Rarely, a patient may note discoloration of the urine resulting from a phenolic metabolite of chlorzoxazone.

Pregnancy & Lactation - Not recommended in pregnant and lactating women.

4.13 Overdose

Over dosage may cause nausea, vomiting, pain abdomen, dizziness, somnolence, headache, sweating, pancreatitis, hepatic failure and acute renal failure.

Treatment, if required, includes gastric lavage, activated charcoal and other symptomatic measures as per medical advice.

Pharmacological Properties

5.1 Pharmacodynamics properties

Diclofenac is a NSAID with anti-inflammatory, analgesic and antipyretic properties. It is rapidly and almost completely absorbed when administered as an oral dose. Food does not have a significant effect on the extent of oral absorption. At therapeutic concentrations it is more than 99% bound to plasma proteins. Diclofenac and/or its metabolites are rapidly and preferentially taken up and retained in inflamed tissues. It penetrates synovial fluid where concentrations may persist even when plasma concentrations fall. The terminal half-life is about 1 to 2 hours. Diclofenac acts by inhibiting cyclooxygenase, thus prevents the formation of prostaglandins, the mediators of inflammation. It also inhibits lipoxygenase thus preventing the synthesis of leukotrienes. Thus it acts on both the pathways and is a very potent anti-inflammatory drug/ medicine.

Paracetamol is an effective analgesic-antipyretic (relieves mild to moderate pain) and a weak anti-inflammatory agent. Paracetamol reduces fever by a direct action on the heat regulating centres to increase the dissipation of heat. It is readily absorbed from the g.i. tract with peak plasma concentrations occurring about 10 to 60 min. after oral administration. It is distributed into most body tissues.

Chlorzoxazone is a centrally-acting agent for painful musculoskeletal conditions. It acts primarily at the level of the spinal cord and subcortical areas of the brain where it inhibits multisynaptic reflex arcs involved in producing and maintaining skeletal muscle spasm of varied etiology. The clinical result is a reduction of the skeletal muscle spasm with relief of pain and increased mobility of the involved muscles.

Pharmacokinetic properties

Diclofenac Potassium

Absorption: Diclofenac is rapidly and completely absorbed from sugar-coated tablets. Food intake does not affect absorption. Peak plasma concentration after one 50 mg sugar-coated tablet was 3.9 μmol/l after 20-60 minutes. The plasma concentrations show a linear relationship to the size of the dose. Diclofenac undergoes first-pass metabolism and is extensively metabolised.

Distribution: Diclofenac is highly bound to plasma proteins (99.7%), chiefly albumin (99.4%)

Elimination: The total systemic clearance of diclofenac in plasma is 263 ± 56 ml/min (mean ± SD).

The terminal half-life in plasma is 1 – 2 hours. Repeated oral administration of Diclofenac Potassium tablets for 8 days in daily doses of 50 mg t.d.s does not lead to accumulation of diclofenac in the plasma.

Approx. 60% of the dose administered is excreted in the urine in the form of metabolites, and less than 1% as unchanged substance. The remainder of the dose is eliminated as metabolites through the bile in the faeces.

Biotransformation: The biotransformation of diclofenac involves partly glucuronidation of the intact molecule but mainly single and multiple hydroxylation followed by glucuronidation.

Metabolism: It is metabolised in the liver. A minor hydroxylated metabolite which is usually produced in very small amounts by mixed-function oxidase in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol Overdosage and cause tissue damage.

Elimination: It is excreted in the urine, mainly as the glucuronide and sulphate conjugates. The elimination half-life varies from about 1 to 4 hours.

Chlorzoxazone

Blood levels of Chlorzoxazone can be detected in people during the first 30 min and peak levels may be reached, in about 1 to 2 hours after oral administration.

5.3 Preclinical safety data

No additional data of relevance.

Paracetamol

Absorption: Paracetamol is readily absorbed from the gastrointestinal tract.

Distribution: Peak plasma concentrations occur about 10 to 60 minutes after oral doses. Paracetamol is distributed into most body tissues. It crosses the placenta and is present in breast milk. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

Pharmaceutical Particulars

6.1 List of excipients

Maize starch
Dibasic calcium phosphate
Povidone
Purified water
Sodium Benzoate
Magnesium Stearate
Purified talc
Sodium starch Glycolate (Type C)
Sodium Lauryl sulphate
Colloidal anhydrous silica
Cotab RFC (White)
Titanium Dioxide

6.2 Incompatibilities

None reported.

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store below 30 °C. Protect from light and moisture.
Keep the medicine out of reach of children.

6.5 Nature and contents of container

Alu/Alu blisters of 10 Tablets in a printed carton with a package insert.

6.6 Special precautions for disposal and other handling

None

Marketing authorisation holder and manufacturing site addresses

Marketing authorisation holder

I-CARE PHARMA LIMITED
9-Blackwater, Surrey,
United Kingdom, GU170AU
E-mail: info@i-carepharma.com

Manufacturing site addresses

Corona Remedies Pvt Ltd
Village Jatoli,
Post Office - Oachghat,
Tehsil Solan, Dist. Solan
Himachal Pradesh – 173223.
India
Tele No.: +91-1792-252770
Fax No.: +91-1792-252770
E-mail: info@coronaremedies.com
Web site: www.coronaremedies.com

8. Marketing Authorisation Number

To be included after obtaining first registration.

9. Date of first registration/renewal of the registration

To be included after obtaining first registration or renewal of registration.

10. Date of revision of the text

10/10/2015 (DD/MM/YYYY)

11.Dosimetry (if applicable)

Not Applicable

12. Instructions for preparation of radiopharmaceuticals (If Applicable)

Not Applicable