1. Name of the Medicinal Product

Zeropain Tablet 10 mg

2. **Qualitative and quantitative composition**

Each tablet contains Ketorolac Tromethamine USP 10 mg as active substance.

3. **Pharmaceutical Form**

Oral Solid Tablet

Zeropain Tablet 10 mg is white, round, biconvex, film coated tablets with one side plain and other side breakline which is packed in a Blister.

4. **Clinical Particulars**

4.1 Therapeutic Indications

Short-term management of moderate to severe acute pain that requires analgesia at the opioid level.

4.2 Posology and method of Administration

Usual dose:

Adult: 10mg 4-6 hourly, maximum 7 days.

Descriptive doses:

Patient Population	Dosage
< 17 years of age	Not established
< 65 years	10 mg 4-6 hourly. Maximum daily dose 40mg. Maximum 7 days
>_ 65 years of age or renally impaired or body mass <50 kg	10 mg 4-6 hourly. Maximum daily dose 40mg. Maximum 7 days

Note: When converting from parenteral to oral administration, total combined dose on the day of conversion should not exceed 120 mg (60 mg for >_ 65 years of age or renally impaired or body mass <50 kg) of which the oral should not exceed 40 mg.

4.3 Contraindication

Zeropain® is contraindicated in patients with active or a history of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy. It is also contraindicated in severe heart failure, moderate to severe renal impairment (serum creatinine > 442mmol/L), dehydration, hypovolemia, in labour and delivery, patients with suspected or confirmed cerebrovascular bleeding, in patients with currently receiving ASA or other NSAIDs and hypersensitivity to NSAIDs.

4.4 Special warnings and precautions for use

Concomitant use of ketorolac with other NSAIDs should be avoided. It should be used at the lowest effective dose with shortest duration. Zeropain® should administer with caution in patients with previous history of inflammatory bowel syndrome, coagulation disorder, hypertension, mild to moderate congestive

heart failure, impaired renal function, asthma, liver dysfunction and elderly patients as they are at high risk of adverse reactions to NSAIDs. Zeropain® should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity. During the use of Ketorolac tromethamine, caution should be advised in patients receiving concomitant medications of oral corticosteroids, anticoagulants like warfarin, SSRIs, or antiplatelets.

4.5 Interaction with other medicinal products and other forms of interaction

Concurrent treatment with probenecid is contraindicated because of increases in ketorolac tromethamine plasma level and half-life. Concurrent treatment with lithium is contraindicated because there is a possible inhibition of renal lithium clearance, increased plasma lithium concentration, and potential lithium toxicity. Zeropain® should not be used with other NSAIDs because of the potential for additive side effects. There is an increased risk of renal impairment when ketorolac tromethamine is administered concurrently with ACE inhibitors, particularly in volume-depleted patients.

4.6 Pregnancy, nursing mothers

The safety of Ketorolac tromethamine in human pregnancy has not been established. Pregnancy Category C, Contraindicated in nursing mother.

4.7 Effects on ability to drive and use machines

None

4.8 Undesirable effects

Gastro-intestinal: Nausea, dyspepsia, gastro-intestinal pain, gastro-intestinal bleeding, abdominal discomfort, haematemesis, gastritis, diarrhoea, eructation, constipation, flatulence, fullness, melaena, peptic ulcer, rectal bleeding, stomatitis, vomiting, haemorrhage, perforation.

Central nervous/musculoskeletalsystems: Anxiety, drowsiness, dizziness, headache, sweating, dry mouth, nervousness, paraesthesia, functional disorders, depression, euphoria, convulsions, excessive thirst, insomnia, vertigo, myalgia, hallucinations, hearing loss, tinnitus, aseptic meningitis, psychotic reactions.

Renal: increased urinary frequency, oliguria, acute renal failure, hyponatraemia, hyperkalaemia, haemolytic uraemic syndrome, flank pain (with or without haematuria), interstitial nephritis, and urinary retention. *Cardiovascular/haematological:* Flushing, bradycardia, pallor, purpura, thrombocytopenia, and hypertension.

Respiratory: Dyspnoea, asthma, pulmonary oedema. *Skin & Subcutaneous tissue Disorders:* Pruritus, urticaria, Lyell's syndrome, Stevens-Johnson syndrome. *Hypersensitivity reactions:* Anaphylaxis, bronchospasm, laryngeal oedema, hypotension, rash. Such reactions may occur in patients with or without known sensitivity to Zeropain¨ or other non-steroidal anti-inflammatory drugs.

Bleeding: Postoperative wound haemorrhage, haematomata, and epistaxis.

Other: Asthenia, oedema, weight gain, abnormalities of liver function tests.

Reporting of suspected adverse reactions
Healthcare professionals are requested to report any suspected adverse reactions via national Pharmacovigilance Electronic Reporting Systems to the respective national regulatory authorities.

4.9 Overdose

Abdominal pain and peptic ulcers which have healed after discontinuation of dosing. Two patients recovered from unsuccessful suicide attempts. One patient experienced nausea after 210mg ketorolac, and the other hyperventilation after 300 mg ketorolac.

5.0 Pharmacological Properties

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Analgesic agent of NSAID class.
ATC Code: S01BC05
Ketorolac is a non-selective NSAID and acts by inhibiting both COX-1 and COX-2 enzymes which are normally responsible for converting arachidonic acid to prostaglandins. The COX-1 enzyme is constitutively active and can be found in platelets, gastric mucosa, and vascular endothelium. On the other hand, the COX-2 enzyme is inducible and mediates inflammation, pain and fever. As a result, inhibition of the COX-1 enzyme is linked to an increased risk of bleeding and risk of gastric ulceration, while the desired anti-inflammatory and analgesic properties are linked to inhibition of the COX-2 enzyme. Therefore, despite it's effectiveness in pain management, ketorolac should not be used long-term since this increases the risk of serious adverse effects such as gastrointestinal bleeding, peptic ulcers, and perforations.

5.2 Pharmacokinetic properties

The terminal plasma half-life is on average 5.3 hours in young adults and 7 hours in elderly patients (mean age 72). Steady-state plasma levels are achieved after dosing every 6 hours for one day. The primary route of excretion of ketorolac tromethamine and its

metabolites is renal: 92% (mean) of a given dose being found in the urine and 6% (mean) in the feces. More than 99% of the ketorolac tromethamine in plasma is protein-bound over a wide concentration range.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the Summary of Product Characteristics.

6.0 Pharmaceutical Particulars

6.1. List of excipients

-Microcrystalline Cellulose (Type 102)
-Lactose Monohydrate (Spray Dried)
-Magnesium Stearate
-Opadry White YS-1-7002
-Talc
-Purified Water

6.2. Incompatibilities

None

6.3 Shelf life

3 years (36 months)

6.4 Special Precaution for storage

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

6.5 Nature and contents of container

Zeropain Tablet 10 mg is white, round, biconvex, film coated tablets with one side plain and other side breakline which is packed in a blister. Each blister contains 10 Tablets and each inner carton contains 3 blister of Zeropain Tablet 10 mg- i.e. 3 X 10's.

6.6 Special precautions for disposal and other handling

No special requirements

7.0 Marketing Authorization Holder

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8.0 Marketing Authorization Number

H2025/CTD11067/24467

9.0 Date of first authorisation/date of last renewal

10. Date of revision of the text