KINBREX

ROENTGEN IMPEX

Module 1: - Administrative information and prescribing information:

1.3.1Summary of Product Characteristics (SmPC):

Summary Product Characteristics (SPC)

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

KINBREX (CELECOXIB CAPSULES BP 200 MG)
Composition
Each hard gelatin capsule contains
Celecoxib BP 200 mg
Excipients Q.S.
Colour: Approved colours used in empty capsule shell

QUALITATIVE AND QUANTITATIVE COMPOSITION

Ingredients	Qty./ Cap In mg	Use/Function
$Celecoxib BP	200.00 mg	Active material
#Talcum BP	6.0 mg	Glidant / Diluent
Dummy Granules	339.0 mg	Diluent
Sodium Lauryl sulfate BP	6.0 mg	Binder/ Lubricant
Colloidal silicon dioxide BP	6.00 mg	Disintegrant
Magnesium Stearate BP	3.0 mg	Lubricant

BP = British Pharmacopoeia
$ Quantity to be changed based on potency of API.
# Quantity of Talcum is to be adjusted to keep the total mass.

3. PHARMACEUTICAL FORM
Oral capsule

4. CLINICAL PARTICULARS
4.1 Therapeutic indications

Symptomatic treatment of inflammation and pain in osteoarthritis and rheumatoid arthritis.
Treatment of pain post dental surgery.

4.2 Posology and method of administration

Osteoarthritis and Rheumatoid arthritis: The recommended daily dose is 200-400 mg taken in two divided doses. 200 mg once a day can also be used in osteoarthritis.
Pain post dental surgery: The recommended dose is 100 mg to 200 mg up to a maximum daily dose of 400 mg. Dosing intervals should not be less than 4 hours.

4.3 Contraindications

- Hypersensitivity to any ingredient of the product; known sulphonamide hypersensitivity. Severe impairment of hepatic function.
- Severe impairment of renal function.
- Asthma, urticaria or allergic-type reactions precipitated by aspirin or non-steroidal anti-inflammatory agents.
- Pregnancy and lactation, as safety has not been demonstrated.

4.4 Special warnings and precautions for use

Hepatic Impairment
In patients with moderate hepatic impairment (Child-Pugh Class B), reduce the dose by 50%. The use of CELEBREX in patients with severe hepatic impairment is not recommended
Poor Metabolizers of CYP2C9 Substrates
In adult patients who are known or suspected to be poor CYP2C9 metabolizers based on genotype or previous history/experience with other CYP2C9 substrates (such as warfarin, phenytoin), initiate treatment with half of the lowest recommended dose.

4.5 Interaction with other medicinal products and other forms of interaction
Celecoxib interact with the following drugs:
Anticoagulants, Anti-hypertensives, Ciclosporin and Tacrolimus, Acetylsalicylic acid

4.6 Fertility, pregnancy and lactation

For pregnant women:
Use of NSAIDs, including CELEBREX, can cause premature closure of the fetal ductus arteriosus and fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Because of these risks, limit dose and duration of CELEBREX use between about 20 and 30 weeks of gestation and avoid CELEBREX use at about 30 weeks of gestation and later in pregnancy

For women who are breastfeeding:
Caution should be exercised when CELEBREX is administered to a nursing woman. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for CELEBREX and any potential adverse effects on the breastfed infant from the CELEBREX or from the underlying maternal condition

4.7 Effects on ability to drive and use machines
Patients who experience dizziness, vertigo or somnolence while taking celecoxib should

refrain from driving or operating machinery.

4.8 Undesirable effects
Adverse events reported in controlled clinical trials:
Central Nervous System: Headache, dizziness
Gastrointestinal: Constipation, nausea, abdominal pain, diarrhoea, dyspepsia, flatulence, vomiting. Serious clinically significant upper gastro-intestinal bleeding has been observed in patients receiving CELECOXIB, although infrequently.
Respiratory: Bronchitis, coughing, pharyngitis, rhinitis, sinusitis, upper respiratory tract infection
Other: Arthralgia, back pain, insomnia, myalgia, pain, peripheral pain, pruritus, tooth disorder, accidental injury, allergy aggravated, 'flu-like symptoms, peripheral oedema, rash, urinary tract infection

4.9 Overdose

In cases of suspected overdosage, symptomatic and supportive therapy, which would include ECG and blood electrolyte monitoring, should be given as appropriate.

In the event of an acute overdose, the stomach should be emptied. The patient should be observed and appropriate hydration maintained.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Non-steroidal anti-inflammatory and anti-rheumatic drugs, NSAIDs; Coxibs. **ATC code:** M01AH01.
Celecoxib is a specific cyclooxygenase-2 inhibitor (SCI). Cyclooxygenase-2 (COX-2) is induced in response to inflammatory stimuli. This leads to the synthesis and accumulation of inflammatory prostanoids, in particular prostaglandin E2, causing inflammation, oedema and pain. Celecoxib acts as an anti-inflammatory, analgesic and anti-pyretic agent by blocking the production of inflammatory prostanoids via COX-2 inhibition.

5.2 Pharmacokinetic properties

When given under fasting conditions celecoxib is absorbed reaching peak plasma concentrations after approximately 2-3 hours. Celecoxib exhibits linear and dose proportional pharmacokinetics over the therapeutic dose range. Plasma protein binding, which is concentration independent, is about 97% at therapeutic plasma concentrations and the drug is not preferentially bound to erythrocytes in the blood. Dosing with food (high fat meal) delays absorption resulting in a Tmax of about 4 hours and increases bioavailability by about 20%.

Celecoxib is metabolised in the liver by hydroxylation, oxidation and some glucuronidation and in vitro and in vivo studies indicate that metabolism is mainly by cytochrome P450 CYP2C9. Pharmacological activity resides in the parent drug. The main metabolites found in

the circulation have no detectable COX-1 or COX-2 inhibitory activity.
Elimination of celecoxib is mostly by hepatic metabolism with less than 1 % of the dose excreted unchanged in urine. After multiple dosing elimination half life is 8-12 hours and the rate of clearance is about 500ml/min. With multiple dosing steady state plasma concentrations are reached before day 5. The intersubject variability on the main pharmacokinetic parameters (AUC, Cmax, elimination half-life) is about 30%. The mean steady state volume of distribution is about 500L/70kg in young healthy adults after a single 200mg dose indicating wide distribution of celecoxib into the tissues. Pre-clinical studies indicate that the drug crosses the blood/brain barrier.

5.3 Preclinical safety data

- Non-clinical safety data revealed no special hazard for humans based on conventional studies of repeated dose toxicity, mutagenicity or carcinogenicity.
- Celecoxib at oral doses ≥150 mg/kg/day (approximately 2-fold human exposure at 200 mg twice daily as measured by AUC0-24), caused an increased incidence of ventricular septal defects, a rare event, and fetal alterations, such as ribs fused, sternebrae fused and sternebrae misshapen when rabbits were treated throughout organogenesis. A dose-dependent increase in diaphragmatic hernias was observed when rats were given celecoxib at oral doses ≥30 mg/kg/day (approximately 6-fold human exposure based on the AUC0-24 at 200 mg twice daily) throughout organogenesis. These effects are expected following inhibition of prostaglandin synthesis. In rats, exposure to celecoxib during early embryonic development resulted in pre-implantation and post-implantation losses, and reduced embryo/fetal survival.
- Celecoxib was excreted in rat milk. In a peri-post natal study in rats, pup toxicity was observed.
- In a two-year toxicity study an increase in nonadrenal thrombosis was observed in male rat at high doses.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

#Talcum	BP
Dummy Granules	BP
Sodium Lauryl sulfate	BP
Colloidal silicon dioxide	BP
Magnesium Stearate	BP

6.2 Incompatibilities
None

6.3 Shelf life
36 months

6.4 Special precautions for storage
Keep in cool & Dry place, below 30°C. Protect from light.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container
1 X 10 capsules in one monopack.

6.6 Special precautions for disposal and other handling
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.

7. APPLICANT/MANUFACTURER

APPLICANT
KINGZY PHARMACEUTICALS LTD.,
142, OKPORO ROAD, PORT HARCOURT,
RIVERS STATE, NIGERIA

Exported by:
ROENTGEN IMPEX
NO. 2063/A, RABARI VAS, KHORAJ VILLAGE,
DIST. GANDHINAGAR-382735, GUJARAT, INDIA

Manufactured by:
Naxcure Healthcare Pvt. Ltd.
SURVEY NO.-889/1,B/H CHADASANA ONGC,
CHADASANA-JHULASAN ROAD, AT & POST.- JHULASAN,
TA.- KADI, DIST.- MEHSANA-382705
GUJARAT, INDIA