1. NAME OF THE MEDICINAL PRODUCT:
KINBREX (Celecoxib Capsules BP 200 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITIONS:

NAME AND QUANTITY OF EACH INGREDIENT:

UNIT DOSE

Batch size: 1,00,000 Capsules

Ingredients	Qty./ Cap In mg	Batch Formula (kg)	Use/Function
Active Ingredient			
Celecoxib BP	200.00 mg	20.4 $	Active
In Active Ingredients			
Colloidal silicon dioxide BP	0.8 mg	0.08	Disintegrant
Di calcium phosphate BP	100 mg	10.0	Diluent
Microcrystalline cellulose BP	11.2 mg	1.12	Disintegrant / Diluent
Sodium Lauryl sulfate BP	2.0 mg	0.2	Lubricant
Starch BP	100 mg	10.0	Diluent
Talcum BP	1.0 mg	0.10	Glidant / Diluent
White / White colour Size "0" hard gelatin capsules	---	1,00,000 No.	Protective shell

***** Including 2 % Overages

Reference:
BP = British Pharmacopoeia
IHS = In-house specification

3. PHARMACEUTICAL FORMS:
Oral capsule
Description: White / white coloured size "0" hard gelatin capsule containing white color powder

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 Drug Interactions
Celecoxib interact with the following drugs:
Anticoagulants, Anti-hypertensives, Ciclosporin and Tacrolimus, Acetylsalicylic acid

4.6 Pregnancy and Lactation
Pregnancy
Use of NSAIDs, including CELECOXIB, 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 CELECOXIB use between about 20 and 30 weeks of gestation and avoid CELECOXIB use at about 30 weeks of gestation and later in pregnancy
Nursing Mother
Caution should be exercised when CELECOXIB is administered to a nursing woman. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for CELECOXIB and any potential adverse effects on the breastfed infant from the CELECOXIB 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 Overdosages

There is no clinical experience of overdose. Single doses up to 1200 mg and multiple doses up to 1200 mg twice daily have been administered to healthy subjects for nine days without clinically significant adverse effects. In the event of suspected overdose, appropriate supportive medical care should be provided e.g. by eliminating the gastric contents, clinical supervision and, if necessary, the institution of symptomatic treatment. Dialysis is unlikely to be an efficient method of medicinal products removal due to high protein binding.

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 Pre-clinical safety data

Not applicable.

6. Pharmaceutical Particulars

6.1. List of excipients

Raw Materials	Pharmacopoeia Reference
Colloidal silicon dioxide	BP
Di calcium phosphate	BP
Microcrystalline cellulose	BP
Sodium Lauryl sulfate	BP
Starch	BP
Talcum	BP
White / White colour Size "0" hard gelatin capsules	--

6.2. Incompatibilities

None

6.3. Shelf life

36 Months

6.4 Special precautions for storage

Keep in cool & Dry place, below 25°C. Protect from light.
Keep out of reach of children.

6.5 Nature and contents of container

1 X 10 capsules in a monopack and 10 such monopacks in a outer box

6.6 Special precautions for disposal

No special requirement

7. APPLICANT/MANUFACTURER

BRUSSELS LABORATORIES PVT. LTD

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