HOVID-CELECOXIB CAPSULE 200 MG

eVICEL01-0 (SIN)

DESCRIPTION

White opaque/white opaque capsule with "CL200" printed on one end and "hovid" printed on the other end
Fill material: white to off white granules
Capsule size: size 0

COMPOSITION

Each capsule contains Celecoxib 200 mg.

Excipients: Lactose monohydrate, dodecyl sulphate sodium, polyethylene glycol, polyvinylpyrrolidone, crospovidone, magnesium stearate.

PHARMACODYNAMICS

Mechanism of action: Celecoxib is an oral, selective, cyclooxygenase-2 (COX-2) inhibitor within the clinical dose range (200-400 mg daily). No statistically significant inhibition of COX-1 (assessed as *ex vivo* inhibition of thromboxane B2 [TxB2] formation) was observed in this dose range in healthy volunteers.

Pharmacodynamic effects: Cyclooxygenase is responsible for generation of prostagladins. Two isoforms, COX-1 and COX-2, have been identified. COX-2 is the isoform of the enzyme that has been shown to be induced by pro-inflammatory stimuli and has been postulated to be primarily responsible for the synthesis of prostanoid mediators of pain, inflammation, and fever. COX-2 is also involved in ovulation, implantation and closure of the ductus arteriosus, regulation of renal function, and central nervous system functions (fever induction, pain perception and cognitive function). It may also play a role in ulcer healing. COX-2 has been identified in tissue around gastric ulcers in human but its relevance to ulcer healing has not been established.

The difference in antiplatelet activity between some COX-1 inhibiting NSAIDs and COX-2 selective inhibitors may be of clinical significance in patients at risk of thrombo-embolic reactions. COX-2 selective inhibitors reduce the formation of systemic (and therefore possibly endothelial) prostacyclin without affecting platelet thromboxane.

Celecoxib is a diaryl-substituted pyrazole, chemically similar to other non-arylamine sulfonamides (e.g. thiazides, furosemide) but differs from arylamine sulfonamides (e.g. sulfamethoxizole and other sulfonamide antibiotics).

A dose dependent effect on TxB2 formation has been observed after high doses of celecoxib. However, in healthy subjects, in small multiple dose studies with 600 mg BID (three times the highest recommended dose) celecoxib had no effect on platelet aggregation and bleeding time compared to placebo.

PHARMACOKINETICS

Absorption: Celecoxib is well absorbed reaching peak plasma concentrations after approximately 2-3 hours when given under fasted conditions. Dosing with food (high fat meal) delays absorption of celecoxib by about 1 hour resulting in a T_{max} of about 4 hours and increases bioavailability by about 20%.

In healthy adult volunteers, the overall systemic exposure (AUC) of celecoxib was equivalent when celecoxib was administered as intact capsule or capsule contents sprinkled on applesauce. There were no significant alterations in C_{max}, T_{max} or $T_{1/2}$ after administration of capsule contents on applesauce.

Distribution: Plasma protein binding is about 97 % at therapeutic plasma concentrations and the drug is not preferentially bound to erythrocytes.

Metabolism: Celecoxib metabolism is primarily mediated via cytochrome P450 2C9. Three metabolites, inactive as COX-1 or COX-2 inhibitors, have been identified in human plasma i.e., a primary alcohol, the corresponding carboxylic acid and its glucuronide conjugate.

Cytochrome P450 2C9 activity is reduced in individuals with genetic polymorphisms that lead to reduced enzyme activity, such as those homozygous for the CYP2C9*3 polymorphism.

In a pharmacokinetic study of celecoxib 200 mg administered once daily in healthy volunteers, genotyped as either CYP2C9*1/*1, CYP2C9*1/*3, or CYP2C9*3/*3, the median Cmax and AUC0-24 of celecoxib on day 7 were approximately 4-fold and 7-fold, respectively, in subjects genotyped as CYP2C9*3/*3 compared to other genotypes, in three separate single-dose studies, involving a total of 5 subjects genotyped as CYP2C9*3/*3, single-dose AUC0-24 increased by approximately 3-fold compared to normal metabolizers. It is estimated that the frequency of the homozygous *3/*3 genotype is 0.3% - 1.0% among different ethnic groups.

Patients who are known, or suspected to be CYP2C9 poor metabolizers based on previous history/experience with other CYP2C9 substrates should be administered celecoxib with caution. Consider starting treatment at half the lowest recommended dose.

Excretion: 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 500 mL/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 500 L/70 kg in young healthy adults indicating wide distribution of celecoxib into the tissues. Pre-clinical studies indicate that the drug crosses the blood/brain barrier.

INDICATIONS

hovid-Celecoxib Capsule 200 mg is indicated for:

- Symptomatic treatment of osteoarthritis (OA) and rheumatoid arthritis (RA).
- Management of acute pain in adults.
- Treatment of primary dysmenorrhoea.
- Relief of signs and symptoms of ankylosing spondylitis (AS).
- Management of chronic low back pain.

The decision to prescribe a selective cyclooxygenase-2 (COX-2) inhibitor should be based on an assessment of the individual patient's overall risks.

Contraindications

Celecoxib is contraindicated in:

- Patients with known hypersensitivity to celecoxib or any other ingredient of the product.
- Patients with known sulfonamide hypersensitivity.
- Patients with active peptic ulceration or gastrointestinal (GI) bleeding.
- Patients who have experienced asthma, urticaria or allergic-type reactions after taking acetylsalicylic acid (ASA [aspirin]) or other non-steroidal anti-inflammatory drugs (NSAIDs), including other cyclo-oxygenase-2 (COX-2) specific inhibitors.
- Treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.
- Congestive heart failure (NYHA II-IV).
- Established ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease.

WARNINGS AND PRECAUTIONS

- **Gastrointestinal (GI) effects:** Upper and lower gastrointestinal complications [perforations, ulcers or bleedings (PUBs)], some of them resulting in fatal outcome, have occurred in patients treated with celecoxib. Caution is advised with treatment of patients most at risk of developing a gastrointestinal complication with NSAIDs; patients with CV disease, the elderly, patients using any other NSAID or acetylsalicylic acid concomitantly, glucocorticoids, patients using alcohol, or patients with a prior history of gastrointestinal disease, such as ulceration and GI bleeding. Most spontaneous reports of fatal GI events have been in elderly or debilitated patients.

  There is further increase in the risk of gastrointestinal adverse effects for celecoxib (gastrointestinal ulceration or other gastrointestinal complications), when celecoxib is taken concomitantly with acetylsalicylic acid (even at low doses).
- **Concomitant NSAID use:** The concomitant use of celecoxib and a non-aspirin NSAID should be avoided.
- **Cardiovascular effects:**
  Cardiovascular Thrombotic Events: Celecoxib may cause an increased risk of serious CV thrombotic events, myocardial infarction (MI), and stroke, which can be fatal. All NSAIDs may have a similar risk. This risk may increase with dose and duration of use. The relative increase of this risk appears to be similar in those with or without known CV disease or CV risk factors. However, patients with CV disease or CV risk factors may be at greater risk in terms of absolute incidence, due to their increased rate at baseline. To minimize the potential risk for an adverse CV event in patients treated with celecoxib, the lowest effective dose should be used for the shortest duration possible. Physicians and patients should remain alert for the development of such events, even in the absence of previous CV symptoms. Patients should be informed about the signs and symptoms of serious CV toxicity and the steps to take if they occur.

  Two large, controlled, clinical trials of a different COX-2 selective NSAID for the treatment of pain in the first 10-14 days following CABG surgery found an increased incidence of myocardial infarction and stroke.

  Celecoxib is not a substitute for acetylsalicylic acid for prophylaxis of CV thromboembolic diseases because of the lack of effect on platelet function. Because celecoxib does not inhibit platelet aggregation, anti-platelet therapies (e.g., acetylsalicylic acid) should not be discontinued.

  Hypertension: As with all NSAIDs, celecoxib can lead to the onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. NSAIDs, including celecoxib, should be used with caution in patients with hypertension. Blood pressure should be monitored closely during the initiation of therapy with celecoxib and throughout the course of therapy.

  Fluid retention and oedema: As with other drugs known to inhibit prostaglandin synthesis, fluid retention and edema have been observed in some patients taking celecoxib. Therefore, patients with pre-existing congestive heart failure (CHF) or hypertension should be closely monitored. Celecoxib should be used with caution in patients with compromised cardiac function, pre-existing edema, or other conditions pre-disposing to, or worsened by, fluid retention including those taking diuretic treatment or otherwise at risk of hypovolemia.
- **Hepatic and renal effects:** Compromised renal or hepatic function and especially cardiac dysfunction are more likely in the elderly and therefore medically appropriate supervision should be maintained.

  NSAIDs, including celecoxib, may cause renal toxicity. Clinical trials with celecoxib have shown renal effects similar to those observed with comparator NSAIDs. Celecoxib is not recommended in patients with severe renal impairment. Patients at greatest risk for renal toxicity are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics, ACE-inhibitors, angiotensin II receptor antagonists, and the elderly. Such patients should be carefully monitored while receiving treatment with celecoxib.

  Caution should be used when initiating treatment in patients with dehydration. It is advisable to rehydrate patients first and then start therapy with celecoxib.

  Renal function should be closely monitored in patients with advanced renal disease who are administered celecoxib.

  Patients with severe hepatic impairment (Child-Pugh Class C) have not been studied. The use of celecoxib in patients with severe hepatic impairment is not recommended. Celecoxib should be used with caution when treating patients with moderate hepatic impairment (Child-Pugh Class B or serum albumin of 25-35 g/L), and initiated at half the recommended dose.

  Some cases of severe hepatic reactions, including fulminant hepatitis (some with fatal outcome), liver necrosis and, hepatic failure (some with fatal outcome or requiring liver transplant), have been reported with celecoxib. Among the cases that reported time to onset, most of the severe adverse hepatic events developed within one month after initiation of celecoxib treatment.

  If during treatment, patients deteriorate in any of the organ system functions described above, appropriate measures should be taken and discontinuation of celecoxib therapy should be considered.
- **CYP2D6 inhibition:** Celecoxib has shown to be a moderately potent CYP2D6 inhibitor. For drugs that are metabolized by CYP2D6, a dose reduction during initiation of celecoxib treatment or a dose increase upon termination of celecoxib treatment may be necessary.
- **CYP2C9 poor metabolisers:** Patients known to be CYP2C9 poor metabolisers should be treated with caution.
- **Skin and systemic hypersensitivity reactions:** Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of celecoxib. Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Serious hypersensitivity reactions (including anaphylaxis, angioedema and drug rash with eosinophilia and systemic symptoms (DRESS), or hypersensitivity syndrome), have been reported in patients receiving celecoxib. Patients with a history of sulphonamide allergy or any drug allergy may be at greater risk of serious skin reactions or hypersensitivity reactions. Celecoxib should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
- **General:** Celecoxib may mask fever and other signs of inflammation.
- **Use with oral anticoagulants:** In patients on concurrent therapy with warfarin, serious bleeding events, some of them fatal, have been reported. Increased prothrombin time (INR) with concurrent therapy has been reported. Therefore, this should be closely monitored in patients receiving warfarin/coumarin-type oral anticoagulants, particularly when therapy with celecoxib is initiated or celecoxib dose is changed. Concomitant use of anticoagulants with NSAIDS may increase the risk of bleeding. Caution should be exercised when combining celecoxib with warfarin or other oral anticoagulants, including novel anticoagulants (e.g. apixaban, dabigatran, and rivaroxaban).

  hovid-Celecoxib Capsule 200 mg contains lactose 148 mg. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- Warning to prescriber when prescribing COX-2 Inhibitors to patients with risk factors of heart disease, hypertension (high blood pressure), hyperlipidemia, diabetes, smoking patient and patient with peripheral arterial disease.
- Patients who experience dizziness, vertigo or somnolence while taking celecoxib should refrain from driving or operating machinery.

FERTILITY, PREGNANCY AND LACTATION

Fertility: Based on the mechanism of action, the use of NSAIDs, including celecoxib, may delay or prevent rupture of ovarian follicles, which has been associated with reversible infertility in some women. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of NSAIDs, including celecoxib, should be considered.
Pregnancy: There are no studies in pregnant women. Studies in animals have shown reproductive toxicity. The relevance of these data for humans is unknown.

Celecoxib, as with other drugs inhibiting prostaglandin synthesis, may cause uterine inertia and premature closure of the ductus arteriosus and should be avoided during the third trimester of pregnancy.

Celecoxib should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

Inhibition of prostaglandin synthesis might adversely affect pregnancy. Data from

epidemiological studies suggest an increased risk of spontaneous abortion after use of prostaglandin synthesis inhibitors in early pregnancy. In animals, administration of prostaglandin synthesis inhibitors has been shown to result in increased pre- and post-implantation loss.

If used during second or third trimester of pregnancy, NSAIDs may cause fetal renal dysfunction which may result in reduction of amniotic fluid volume or oligohydramnios in severe cases. Such effects may occur shortly after treatment initiation and are usually reversible. Pregnant women on celecoxib should be closely monitored for amniotic fluid volume.

Use of NSAIDs at about 20 weeks gestation or later in pregnancy may cause foetal renal dysfunction leading to oligohydramnios and in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Oligohydramnios is often, but not always, reversible with treatment discontinuation.

Lactation: Studies in rats show that celecoxib is excreted in milk at concentrations similar to those in plasma. Administration of celecoxib to lactating women has shown very low transfer of celecoxib into breast milk. Because of the potential for adverse reactions in nursing infants from celecoxib, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the expected benefit of the drug to the mother.

DRUG INTERACTIONS

General

Celecoxib metabolism is predominantly mediated via cytochrome P450 (CYP) 2C9 in the liver. Patients who are known or suspected to be poor CYP2C9 metabolizers based on previous history/experience with other CYP2C9 substrates should be administered celecoxib with caution as they may have abnormally high plasma levels due to reduced metabolic clearance. Consider starting treatment at half the lowest recommended dose.

Concomitant administration of celecoxib with inhibitors of CYP2C9 can lead to increases in plasma concentrations of celecoxib. Therefore, a dose reduction of celecoxib may be necessary when celecoxib is co-administered with CYP2C9 inhibitors.

Concomitant administration of celecoxib with inducers of CYP2C9, such as rifampicin, carbamazepine and barbiturates can lead to decreases in plasma concentrations of celecoxib. Therefore, a dose increase of celecoxib may be necessary when celecoxib is co-administered with CYP2C9 inducers.

Clinical pharmacokinetics study and in vitro studies indicate that celecoxib, although not a substrate, is an inhibitor of CYP2D6. Therefore, there is a potential for an in vivo drug interaction with drugs that are metabolized by CYP2D6.

Drug-specific

Interaction of celecoxib with warfarin or similar agents: (see Warnings and Precautions - Use with oral anticoagulants)

Fluconazole and Ketoconazole: Concomitant administration of fluconazole at 200 mg once daily resulted in a 2-fold increase in celecoxib plasma concentration. This increase is due to the inhibition of celecoxib metabolism via CYPP450 2C9 by fluconazole. Celecoxib should be introduced at half the recommended dose in patients receiving the CYP2C9 inhibitor fluconazole. Ketoconazole, a CYP3A4 inhibitor, showed no clinically relevant inhibition in the metabolism of celecoxib.

Anti-hypertensives including *Angiotensin-converting Enzyme Inhibitors (ACEIs), Angiotensin II Antagonists (also known as angiotensin receptor blockers, ARBs), Diuretics and Beta-blockers:* Inhibition of prostaglandins may diminish the effect of anti-hypertensives including ACEIs, and/or ARBs, diuretics and beta-blockers. This interaction should be given consideration in patients taking celecoxib concomitantly with ACEIs and/or ARBs diuretics and beta-blockers.

In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function, co-administration of NSAIDs including selective COX-2 inhibitors with ACE inhibitors, angiotensin II antagonists or diuretics, may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible. Therefore, the concomitant administration of these drugs should be done with caution. Patients should be adequately hydrated and the clinical need to monitor the renal function should be assessed at the beginning of the concomitant treatment and periodically thereafter.

Results from Lisinopril Study: In a 28-day clinical study in patients with lisinopril-controlled Stage I and II hypertension, administration of celecoxib 200 mg BID resulted in no clinically significant increases, when compared to placebo treatment, in mean daily systolic or diastolic blood pressure as determined using 24-hour ambulatory blood pressure monitoring. Among patients co-administered with celecoxib 200 mg BID, 48% were considered unresponsive to lisinopril at the final clinic visit (defined as either cuff diastolic blood pressure >90 mmHg or cuff diastolic blood pressure increased >10% compared to baseline), compared to 27% of patients co-administered with placebo; this difference was statistically significant.

Cyclosporine: Because of their effect on renal prostaglandins, NSAIDs may increase the risk of nephrotoxicity with cyclosporine.

Dextromethorphan and Metoprolol: Concomitant administration of celecoxib 200 mg twice daily resulted in a 2.6-fold and a 1.5-fold increases in plasma concentrations of dextromethorphan and metoprolol (CYP2D6 substrates), respectively. These increases are due to celecoxib inhibition to the CYP2D6 substrate metabolism via CYP2D6. Therefore, the dose of drugs as CYP2D6 substrate may need to be reduced when treatment with celecoxib is initiated or increased when treatment with celecoxib is terminated.

Diuretics: Clinical studies have shown that NSAIDs, in some patients, can reduce the natriuretic effect of furosemide and thiazides by inhibition of renal prostaglandin synthesis.

Methotrexate: No pharmacokinetic and clinically important interactions have been observed in a clinical study between celecoxib and methotrexate.

Oral Contraceptives: In an interaction study, celecoxib had no clinically relevant effects on the pharmacokinetics of a prototype combination oral contraceptive (1 mg norethindrone/0.035 mg ethinyl estradiol).

Lithium: In healthy subjects, lithium plasma levels increased approximately 17% in subjects receiving lithium together with celecoxib. Patients on lithium treatment should be closely monitored when celecoxib is introduced or withdrawn.

Aspirin: Celecoxib does not interfere with the anti-platelet effect of low-dose aspirin. Because of its lack of platelet effects, celecoxib is not a substitute for aspirin in the prophylactic treatment of CV disease.

Other Drugs: No clinically important interactions have been observed with celecoxib and antacids (aluminum and magnesium), omeprazole, glibenclamide (glyburide), phenytoin, or tolbutamide.

MAIN SIDE / ADVERSE EFFECTS

Adverse reactions are listed by system organ class and ranked by frequency: Very Common, Common, Uncommon, Rare, Very Rare and Not Known.

Infections and infestations
Common: Bronchitis, sinusitis, upper respiratory tract infection, urinary tract infection
Uncommon: Pharyngitis, rhinitis

Blood and lymphatic system disorders
Uncommon: Anaemia
Rare: Thrombocytopenia

Immune system disorders
Uncommon: Hypersensitivity
Very rare: Anaphylactic reaction

Psychiatric disorders
Common: Insomnia
Uncommon: Anxiety
Rare: Confusional state, hallucination (includes hallucination and hallucination, visual)

Nervous system disorders
Common: Dizziness
Uncommon: Hypertonia, somnolence
Very rare: Cerebral hemorrhage, meningitis aseptic, ageusia, anosmia

Eye disorders
Uncommon: Vision blurred, conjunctivitis

Ear and labyrinth disorders
Uncommon: Tinnitus

Cardiac disorders
Uncommon: Palpitation
Rare: Cardiac failure congestive, arrhythmia, tachycardia

Vascular disorders
Common: Hypertension (including aggravated hypertension)
Rare: Flushing
Very rare: Vasculitis

Respiratory, thoracic, and mediastinal disorders
Common: Cough
Rare: Pulmonary embolism, pneumonitis

Gastrointestinal disorders
Common: Vomiting, abdominal pain, diarrhea, dyspepsia, flatulence
Uncommon: Gastric ulcer, tooth disorder
Rare: Duodenal ulcer, oesophageal ulcer, gastrointestinal haemorrhage
Very rare: Intestinal perforation, pancreatitis

Hepatobiliary disorders
Uncommon: Hepatic enzyme increased (includes alanine aminotransferase increased and aspartate aminotransferase increased)
Rare: Hepatitis
Very rare: Hepatic failure, hepatitis fulminant, hepatic necrosis, cholestasis, hepatitis cholestatic, jaundice

Skin and subcutaneous tissue disorders
Common: Pruritus (includes pruritus generalized), rash
Uncommon: Urticaria, ecchymosis
Rare: Angioedema, alopecia, photosensitivity reaction
Very Rare: Dermatitis bullous, Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalised exanthematous pustulosis (AGEP), dermatitis exfoliative

Renal and urinary disorders
Rare: Renal failure acute, hyponatraemia
Very rare: Tubulointerstitial nephritis, nephrotic syndrome, glomerulonephritis minimal lesion

Reproductive system and breast disorders
Rare: Menstrual disorder
Frequency unknown: infertility female (female fertility decreased)
General disorders and administrative site conditions
Common: Oedema peripheral
Uncommon: Face edema, influenza-like illness, chest pain

Injury, poisoning and procedural conditions
Uncommon: Injury

OVERDOSE AND TREATMENT

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 drug removal due to high protein binding.

DOSAGE AND ADMINISTRATION

Oral use.

For patients who have difficulty swallowing capsules, the contents of a celecoxib capsule can be added to applesauce, rice gruel, yogurt or mashed banana. To do so, the entire capsule contents must be carefully emptied onto a level teaspoon of cool or room temperature applesauce, rice gruel, yogurt or mashed banana and should be ingested immediately with 240 ml of water. The sprinkled capsule contents on applesauce, rice gruel or yogurt are stable for up to 6 hours under refrigerated conditions (2-8°C). The sprinkled capsule contents on mashed banana should not be stored under refrigerated conditions and should be ingested immediately.

As the cardiovascular risks of celecoxib may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically, especially in patients with osteoarthritis.

Given the association between cardiovascular risk and exposure to COX-2 Inhibitors, doctors are advised to use the lowest effective dose for the shortest possible duration of treatment.

Osteoarthritis (OA): The recommended dose of celecoxib is 200 mg administered as a single dose or as 100 mg twice per day.

Rheumatoid arthritis (RA): The recommended daily dose of celecoxib is 100 mg or 200 mg twice per day.

Ankylosing spondylitis (AS): The recommended dose of celecoxib is 200 mg administered as a single dose or as 100 mg twice per day.

The maximum recommended daily dose is 400 mg for above indications.

Management of acute pain in adults: The recommended dose of celecoxib is 400 mg, initially, followed by an additional 200 mg dose, if needed on the first day. On subsequent days, the recommended dose is 200 mg twice daily, as needed.

Management of Chronic Low Back Pain in Adults: The recommended dose of celecoxib is 200 or 400 mg daily, administered as a 200 mg single dose, or as 100 or 200 mg twice per day. Some patients may benefit from a total daily dose of 400 mg.

Treatment of Primary Dysmenorrhea: The recommended dose of celecoxib is 400 mg, initially, followed by an additional 200 mg dose, if needed on the first day. On subsequent days, the recommended dose is 200 mg twice daily, as needed.

Special populations

Elderly: No dosage adjustment is generally necessary. However, for elderly patients weighing less than 50 kg, it is advisable to initiate therapy at the lowest recommended dose.

Pediatric patients: Celecoxib has not been studied in subjects under 18 years of age.

CYP2C9 poor metabolisers: Patients who are known, or suspected to be CYP2C9 poor metabolisers based on genotyping or previous history/experience with other CYP2C9 substrates should be administered celecoxib with caution. Consider starting treatment at half the lowest recommended dose.

Patients with hepatic impairment: No dosage adjustment is necessary in patients with mild hepatic impairment (Child-Pugh Class A). Treatment should be initiated at half the recommended dose in patients with moderate liver impairment (with serum albumin 25-35 g/L or Child-Pugh Class B.

Patients with severe hepatic impairment (Child-Pugh Class C) have not been studied. The use of celecoxib in this patient population is not recommended.

Patients with renal impairment: No dosage adjustment is necessary in patients with mild or moderate renal impairment. There is no clinical experience in patients with severe renal impairment. The use of celecoxib in this patient population is not recommended.

Co-administration with Fluconazole: Celecoxib should be introduced at half the recommended dose in patients receiving fluconazole, a CYP2C9 inhibitor. Caution is advised when co-administering celecoxib with other CYP2C9 inhibitors.

Note: The information given here is limited. For further information, consult your doctor or pharmacist.

Storage: Store below 30°C.

Presentation/ Packing: Blister pack of 10's, 30's and 100's.
(Not all presentations may be available locally)

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