Bosch

For Medical Professional only

NUZiB® CAPSULES
(Celecoxib)

نیوزب کیپسولز
(سیلیکوکسب)

DESCRIPTION:
NUZIB (celecoxib) capsule is a nonsteroidal anti-inflammatory drug for oral administration. The chemical name is 4-[5-(4-methylphenyl)- 3-(trifluoromethyl)-1H-pyrazol-1-yl] benzenesulfonamide and is a diaryl-substituted pyrazole. The molecular weight is 381.38. Its molecular formula is $C_{17}H_{14}F_3N_3O_2S$. Celecoxib is a white to off-white powder and is practically insoluble in aqueous media at physiological pH range.

COMPOSITION:
Each Nuzib 100mg capsule contains:
Celecoxib U.S.P. 100mg
(Product Specs.: B.P.)

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CLINICAL PHARMACOLOGY:
Pharmacodynamic Properties:
Pharmacotherapeutic group: Non-steroidal anti-inflammatory and antirheumatic drugs, NSAIDs, Coxibs, ATC code: M01AH01.

Platelets
NUZIB at single doses (higher than recommended therapeutic doses) had no effect on reduction of platelet aggregation or increase in bleeding time. Because of its lack of platelet effects, NUZIB is not a substitute for aspirin for cardiovascular prophylaxis. It is not known if there are any effects of NUZIB on platelets that may contribute to the increased risk of serious cardiovascular thrombotic adverse events associated with the use of NUZIB.

Fluid Retention
Inhibition of PGE2 synthesis may lead to sodium and water retention through increased reabsorption in the renal medullary thick ascending loop of Henle and perhaps other segments of the distal nephron. In the collecting ducts, PGE2 appears to inhibit water reabsorption by counteracting the action of antidiuretic hormone.

Mechanism of Action:
Celecoxib has analgesic, anti-inflammatory, and antipyretic properties. The mechanism of action of NUZIB is believed to be due to inhibition of prostaglandin synthesis, primarily via inhibition of COX-2. Celecoxib is a potent inhibitor of prostaglandin synthesis in vitro. Celecoxib concentrations reached during therapy have produced in vivo effects. Prostaglandins sensitize afferent nerves and potentiate the action of bradykinin in inducing pain in animal models. Prostaglandins are mediators of inflammation. Since celecoxib is an inhibitor of prostaglandin synthesis, its mode of action may be due to a decrease of prostaglandins in peripheral tissues.

Pharmacokinetic Properties
Absorption:
Celecoxib is well absorbed reaching peak plasma concentrations after approximately 2-3 hours. Dosing with food (high fat meal) delays absorption of celecoxib by about 1 hour resulting in a Tmax of about 4 hours and increases bioavailability by about 20%.
Coadministration of NUZIB with an aluminum- and magnesium-containing antacids resulted in a reduction in plasma celecoxib concentrations with a decrease of 37% in Cmax and 10% in AUC. NUZIB, at doses up to 200 mg twice daily, can be administered without regard to timing of meals. Higher doses (400 mg twice daily) should be administered with food to improve absorption.

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

Metabolism:
Celecoxib metabolism is primarily mediated via CYP2C9. Three metabolites, a primary alcohol, the corresponding carboxylic acid, and its glucuronide conjugate, have been identified in human plasma. These metabolites are inactive as COX-1 or COX-2 inhibitors

Excretion:
Celecoxib is eliminated predominantly by hepatic metabolism with little (<3%) unchanged drug recovered in the urine and feces. Following a single oral dose of radiolabeled drug, approximately 57% of the dose was excreted in the feces and 27% was excreted into the urine. The primary metabolite in both urine and feces was the carboxylic acid metabolite (73% of dose) with low amounts of the glucuronide also appearing in the urine. It appears that the low solubility of the drug prolongs the absorption process making terminal half-life (t1/2) determinations more variable. The effective half-life is approximately 11 hours under fasted conditions. The apparent plasma clearance (CL/F) is about 500 mL/min.

SPECIFIC POPULATIONS
Renal Impairment
Celecoxib AUC was approximately 40% lower in patients with chronic renal insufficiency (GFR 35-60 mL/min) than that with normal renal function. No significant relationship was found between GFR and celecoxib clearance. Patients with severe renal insufficiency have not been studied. Similar to other NSAIDs, NUZIB is not recommended in patients with severe renal insufficiency.

Hepatic Impairment
Steady-state celecoxib AUC is increased about 40% and 180%, in mild and moderate hepatic impairment respectively. Therefore, the daily recommended dose of NUZIB capsules should be reduced by approximately 50% in patients with moderate hepatic impairment. Patients with severe hepatic impairment have not been studied. The use of NUZIB in patients with severe hepatic impairment is not recommended.

Elderly:
In elderly females, celecoxib Cmax and AUC are higher than those for elderly males due to lower body weight in elderly females. Dose adjustment in the elderly is not generally necessary. However, for patients of less than 50 kg in body weight, initiate therapy at the lowest recommended dose.

THERAPEUTIC INDICATIONS:
Nuzib is indicated in adults for the symptomatic relief in the treatment of osteoarthritis, rheumatoid arthritis, Juvenile Rheumatoid Arthritis, ankylosing spondylitis, Acute Pain and Primary Dysmenorrhea.
The decision to prescribe a selective cyclooxygenase-2 (COX-2) inhibitor should be based on an assessment of the individual patient's overall risks.

DOSAGE AND ADMINISTRATION:

General Dosing Instructions

Carefully consider the potential benefits and risks of NUZIB and other treatment options before deciding to use NUZIB. Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals. These doses can be given without regard to timing of meals.

Osteoarthritis

For OA, the dosage is 200 mg per day administered as a single dose or as 100 mg twice daily.

Rheumatoid Arthritis

For RA, the dosage is 100 mg to 200 mg twice daily.

Ankylosing Spondylitis

For AS, the dosage of NUZIB is 200 mg daily in single (once per day) or divided (twice per day) doses. If no effect is observed after 6 weeks, a trial of 400 mg daily may be worthwhile. If no effect is observed after 6 weeks on 400 mg daily, a response is not likely, and consideration should be given to alternate treatment options.

Management of Acute Pain and Treatment of Primary Dysmenorrhea

For management of Acute Pain and Treatment of Primary Dysmenorrhea, the dosage 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.

Juvenile Rheumatoid Arthritis

For JRA, the dosage for pediatric patients (age 2 years and older) is based on weight. For patients ≥10 kg to ≤ 25 kg the recommended dose is 50 mg twice daily. For patients >25 kg the recommended dose is 100 mg twice daily.

For patients who have difficulty swallowing capsules, the contents of a NUZIB capsule can be added to applesauce. The entire capsule contents are carefully emptied onto a level teaspoon of cool or room temperature applesauce and ingested immediately with water. The sprinkled capsule contents on applesauce are stable for up to 6 hours under refrigerated conditions (2°C to 8°C).

Paediatric population

Celecoxib is not indicated for use in children.

Elderly:

As in younger adults, 200 mg per day should be used initially. The dose may, if needed, later be increased to 200 mg twice daily. Caution should be exercised in elderly with a body weight less than 50 kg.

Patients with Renal Impairment

NUZIB is not recommended in patients with severe renal insufficiency.

Patients with Hepatic Impairment:

In patients with moderate hepatic impairment reduce the dose by 50%. The use of NUZIB in patients with severe hepatic impairment is not recommended.

CYP2C9 poor metabolizers

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 as the risk of dose-dependent adverse effects is increased. Consider reducing the dose to half the lowest recommended dose.

CONTRAINDICATIONS:

NUZIB is contraindicated in the following patients:

- Known hypersensitivity (e.g., anaphylactic reactions and serious skin reactions) to celecoxib, any components of the drug product.
- History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Severe, sometimes fatal, anaphylactic reactions to NSAIDs, have been reported in such patients.
- In the setting of CABG surgery.
- In patients who have demonstrated allergic-type reactions to sulfonamides.

WARNINGS AND PRECAUTIONS:

Lactose:

Product contains lactose.

Possibility of untoward reaction for patient with celiac disease relating to the use of such excipients. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Cardiovascular Events

Several cyclooxygenase-2 (COX-2) selective and nonselective NSAIDs of up to three years duration have shown an increased risk of serious cardiovascular (CV) thrombotic events, including myocardial infarction (MI) and stroke, which can be fatal. To minimize the potential risk for an adverse CV event in NSAID-treated patients, use the lowest effective dose for the shortest duration possible. Physicians and patients should remain alert for the development of such events, throughout the entire treatment course, even in the absence of previous CV symptoms. Patients should be informed about the symptoms of serious CV events and the steps to take if they occur. The concurrent use of aspirin and an NSAID, such as celecoxib, increases the risk of serious gastrointestinal (GI) events.

NSAIDs are contraindicated in the setting of Coronary Artery Bypass Graft (CABG) surgery. Avoid the use of NUZIB in patients with a recent MI unless the benefits are expected to outweigh the risk of recurrent CV thrombotic events. If NUZIB is used in patients with a recent MI, monitor patients for signs of cardiac ischemia.

Gastrointestinal Bleeding, Ulceration, and Perforation

NSAIDs, including celecoxib cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the esophagus, stomach, small intestine, or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NUZIB. Only one in five patients who develop a serious upper GI adverse event on NSAID therapy is symptomatic. Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs occurred in approximately 1% of patients treated for 3 to 6 months, and in about 2% to 4% of patients treated for one year. However, even short-term NSAID therapy is not without risk.

Patients with a prior history of peptic ulcer disease and/or GI bleeding who used NSAIDs had a greater than 10-fold increased risk for developing a GI bleed compared to patients without these risk factors. Other factors that increase the risk of GI bleeding in patients treated with NSAIDs include longer duration of NSAID therapy; concomitant use of oral corticosteroids, antiplatelet drugs (such as aspirin), anticoagulants; or selective serotonin reuptake inhibitors (SSRIs); smoking; use of alcohol; older age; and poor general health status. Most postmarketing reports of fatal GI events occurred in elderly or debilitated patients. Additionally, patients with advanced liver disease and/or coagulopathy are at increased risk for GI bleeding.

Use the lowest effective dosage for the shortest possible duration. And avoid administration of more than one NSAID at a time. Avoid use in patients at higher risk unless benefits are expected to outweigh the increased risk of bleeding. Remain alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy. If a serious GI adverse event is suspected, promptly initiate evaluation and treatment, and discontinue NUZIB until a serious GI adverse event is ruled out. In the setting of concomitant use of low-dose aspirin for cardiac prophylaxis, monitor patients more closely for evidence of GI bleeding.

Hepatotoxicity

Elevations of ALT or AST (three or more times the upper limit of normal [ULN]) have been reported in approximately 1% of NSAID-treated patients. In addition, rare, sometimes fatal, cases of severe hepatic injury, including fulminant hepatitis, liver necrosis, and hepatic failure have been reported. Elevations of ALT or AST (three or more times the upper limit of normal [ULN]) may occur in up to 15% of patients treated with NSAIDs including celecoxib. Inform patients of the warning signs and symptoms of hepatotoxicity (e.g., nausea, fatigue, lethargy, diarrhea, pruritus, jaundice, right upper quadrant tenderness, and "flu-like" symptoms). If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash), discontinue NUZIB immediately, and perform a clinical evaluation of the patient.

Hypertension

NSAIDs, including NUZIB, can lead to new onset of hypertension or worsening of preexisting hypertension, either of which may contribute to the increased incidence of CV events. Patients taking angiotensin converting enzyme (ACE) inhibitors, thiazide diuretics or loop diuretics may have impaired response to these therapies when taking NSAIDs. Monitor blood pressure (BP) during the initiation of NSAID treatment and throughout the course of therapy.

Heart Failure and Edema

NSAID use increased the risk of MI, hospitalization for heart failure, and death. Additionally,

fluid retention and edema have been observed in some patients treated with NSAIDs. Use of celecoxib may blunt the CV effects of several therapeutic agents used to treat these medical conditions (e.g., diuretics, ACE inhibitors, or angiotensin receptor blockers [ARBs]). Avoid the use of NUZIB in patients with severe heart failure unless the benefits are expected to outweigh the risk of worsening heart failure. If NUZIB is used in patients with severe heart failure, monitor patients for signs of worsening heart failure.

Renal Toxicity and Hyperkalemia

Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of an NSAID may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, dehydration, hypovolemia, heart failure, liver dysfunction, those taking diuretics, ACE inhibitors or the ARBs, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state. The renal effects of NUZIB may hasten the progression of renal dysfunction in patients with preexisting renal disease. Monitor renal function in patients with renal or hepatic impairment, heart failure, dehydration, or hypovolemia during use of NUZIB. Avoid the use of NUZIB in patients with advanced renal disease unless the benefits are expected to outweigh the risk of worsening renal function. If NUZIB is used in patients with advanced renal disease, monitor patients for signs of worsening renal function.

Increases in serum potassium concentration, including hyperkalemia, have been reported with use of NSAIDs, even in some patients without renal impairment. In patients with normal renal function, these effects have been attributed to a hyporeninemic-hypoaldosteronism state.

Anaphylactic Reactions

Celecoxib has been associated with anaphylactic reactions in patients with and without known hypersensitivity to celecoxib and in patients with aspirin sensitive asthma. Nuzib is a sulfonamide and both NSAIDs and sulfonamides may cause allergic type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. Seek emergency help if any anaphylactic reaction occurs.

Exacerbation of Asthma Related to Aspirin Sensitivity

Patients with asthma may have aspirin-sensitive asthma which may include chronic rhinosinusitis complicated by nasal polyps; severe, potentially fatal bronchospasm; and/or intolerance to aspirin and other NSAIDs. Because cross-reactivity between aspirin and other NSAIDs has been reported in such aspirin-sensitive patients, NUZIB is contraindicated in patients with this form of aspirin sensitivity. When NUZIB is used in patients with preexisting asthma (without known aspirin sensitivity), monitor patients for changes in the signs and symptoms of asthma.

Serious Skin Reactions

Serious skin reactions have occurred following treatment with Nuzib, including erythema multiforme, exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP). These serious events may occur without warning and can be fatal. Inform patients about the signs and symptoms of serious skin reactions, and to discontinue the use of NUZIB at the first appearance of skin rash or any other sign of hypersensitivity. NUZIB is contraindicated in patients with previous serious skin reactions to NSAIDs.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

DRESS has been reported in patients taking NSAIDs such as NUZIB. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue NUZIB and evaluate the patient immediately.

Fetal Toxicity

Avoid use of NSAIDs, including NUZIB, in pregnant women at about 30 weeks gestation and later. NSAIDs, including NUZIB, increase the risk of premature closure of the fetal ductus arteriosus at approximately this gestational age. Use of NSAIDs, including NUZIB, at about 20 weeks gestation or later in pregnancy may cause fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. If NSAID treatment is necessary between about 20 weeks and 30 weeks gestation, limit NUZIB use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if NUZIB treatment extends beyond 48 hours. Discontinue NUZIB if oligohydramnios occurs and follow up according to clinical practice.

Hematological Toxicity

Anemia has occurred in NSAID-treated patients. This may be due to occult or gross blood loss, fluid retention, or an incompletely described effect on erythropoiesis. If a patient treated with NUZIB has any signs or symptoms of anemia, monitor hemoglobin or hematocrit. Patients on long-term treatment with NUZIB should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia or blood loss. NSAIDs, including NUZIB, may increase the risk of bleeding events. Co-morbid conditions such as coagulation disorders or concomitant use of warfarin, other anticoagulants, antiplatelet drugs (e.g., aspirin), SSRIs and serotonin norepinephrine reuptake inhibitors (SNRIs) may increase this risk. Monitor these patients for signs of bleeding.

Masking of Inflammation and Fever

The pharmacological activity of NUZIB in reducing inflammation, and possibly fever, may diminish the utility of diagnostic signs in detecting infections.

Disseminated Intravascular Coagulation (DIC)

Because of the risk of disseminated intravascular coagulation with use of NUZIB in pediatric patients with systemic onset JRA, monitor patients for signs and symptoms of abnormal clotting or bleeding, and inform patients and their caregivers to report symptoms as soon as possible.

DRUG INTERACTIONS:

Anticoagulants

Anticoagulant activity should be monitored particularly in the first few days after initiating or changing the dose of celecoxib in patients receiving warfarin or other anticoagulants since these patients have an increased risk of bleeding complications. Therefore, patients receiving oral anticoagulants should be closely monitored for their prothrombin time INR, particularly in the first few days when therapy with celecoxib is initiated or the dose of celecoxib is changed. Bleeding events in association with increases in prothrombin time have been reported, predominantly in the elderly, in patients receiving celecoxib concurrently with warfarin, some of them fatal.

Anti-hypertensives

NSAIDs may reduce the effect of anti-hypertensive medicinal products including ACE-inhibitors, angiotensin II receptor antagonists, diuretics, and beta-blockers. As for NSAIDs, the risk of acute renal insufficiency, which is usually reversible, may be increased in some patients with compromised renal function (e.g., dehydrated patients, patients on diuretics, or elderly patients) when ACE-inhibitors, angiotensin II receptor antagonists, and/or diuretics are combined with NSAIDs, including celecoxib. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated, and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

Ciclosporin and tacrolimus

Co-administration of NSAIDs and ciclosporin or tacrolimus may increase the nephrotoxic effect of ciclosporin or tacrolimus, respectively. Renal function should be monitored when celecoxib and any of these medicinal products are combined.

Acetylsalicylic acid

Celecoxib can be used with low-dose acetylsalicylic acid but is not a substitute for acetylsalicylic acid for CV prophylaxis. In the submitted studies, as with other NSAIDs, an increased risk of gastrointestinal ulceration or other gastrointestinal complications compared to use of celecoxib alone was shown for concomitant administration of low-dose acetylsalicylic acid.

CYP2D6 inhibition

Celecoxib is an inhibitor of CYP2D6. The plasma concentrations of medicinal products that are substrates of this enzyme may be increased when celecoxib is used concomitantly. Examples of medicinal products which are metabolised by CYP2D6 are antidepressants (tricyclics and SSRIs), neuroleptics, anti-arrhythmic medicinal products, etc. The dose of individually dose-titrated CYP2D6 substrates may need to be reduced when treatment

with celecoxib is initiated or increased if treatment with celecoxib is terminated. Concomitant administration of celecoxib 200 mg twice daily resulted in 2.6-fold and 1.5-fold increases in plasma concentrations of dextromethorphan and metoprolol (CYP2D6 substrates), respectively. These increases are due to celecoxib inhibition of the CYP2D6 substrate metabolism.

Methotrexate
In patients with rheumatoid arthritis celecoxib had no statistically significant effect on the pharmacokinetics (plasma or renal clearance) of methotrexate (in rheumatologic doses). However, adequate monitoring for methotrexate-related toxicity should be considered when combining these two medicinal products.

Lithium
Co-administration of celecoxib 200 mg twice daily with 450 mg twice daily of lithium resulted in a mean increase in Cmax of 16 % and in area under the curve (AUC) of 18 % of lithium. Therefore, patients on lithium treatment should be closely monitored when celecoxib is introduced or withdrawn.

Oral contraceptives
Celecoxib had no clinically relevant effects on the pharmacokinetics of oral contraceptives (1 mg norethisterone /35 micrograms ethinylestradiol).

Glibenclamide/tolbutamide
Celecoxib does not affect the pharmacokinetics of tolbutamide (CYP2C9 substrate), or glibenclamide to a clinically relevant extent.

CYP2C9 poor metabolisers
In individuals who are CYP2C9 poor metabolisers and demonstrate increased systemic exposure to celecoxib, concomitant treatment with CYP2C9 inhibitors such as fluconazole could result in further increases in celecoxib exposure. Such combinations should be avoided in known CYP2C9 poor metabolisers.

CYP2C9 inhibitors and inducers
Since celecoxib is predominantly metabolised by CYP2C9 it should be used at half the recommended dose in patients receiving fluconazole. Concomitant use of 200 mg single-dose of celecoxib and 200 mg once daily of fluconazole, a potent CYP2C9 inhibitor, resulted in a mean increase in celecoxib Cmax of 60% and in AUC of 130%. Concomitant use of inducers of CYP2C9 such as rifampicin, carbamazepine and barbiturates may reduce plasma concentrations of celecoxib.

Ketoconazole and antacids
Ketoconazole or antacids have not been observed to affect the pharmacokinetics of celecoxib.

ADVERSE EFFECTS:
Very Common: Hyper-tension (including aggravated hyper-tension).
Common: Sinusitis, upper respiratory tract infection, pharyngitis, urinary tract infection, Hyper-sensitivity, Insomnia, Dizziness, hypertonia, headache, Myocardial infarction, Rhinitis, cough, dyspnoea, Nausea, abdominal pain, diarrhoea, dyspepsia, flatulence, vomiting, dysphagia, Rash, pruritus (includes pruritus generalised), Arthralgia, Influenza-like illness, oedema peripheral/ fluid retention, Injury (accidental injury).
Uncommon: Anaemia, Hyperkalaemia, Anxiety, depression, fatigue, Cerebral infarction, paraesthesia, somnolence, Vision blurred, conjunctivitis, Tinnitus, hypoacusis, Cardiac failure, palpitations, tachycardia, Bronchospasm, Constipation, gastritis, stomatitis, gastrointestinal inflammation (including aggravation of gastrointestinal inflammation), eructation, Hepatic function abnormal, hepatic enzyme increased (including increased SGOT and SGPT), Urticaria, ecchymosis, Muscle spasms (leg cramps), Blood creatinine increased, blood urea increased, Face oedema, chest pain.
Rare: Leukopenia, thrombo-cytopenia, Confusional state, hallucinations, Ataxia, dysgeusia, Eye haemorrhage, Arrhythmia, Pulmonary embolism, flushing, Pneumonitis, Gastro-intestinal haemorrhage, duodenal ulcer, gastric ulcer, oesophageal ulcer, intestinal ulcer, large intestinal ulcer, intestinal perforation, oesophagitis, melaena, pancreatitis, colitis, Hepatitis, Angioedema, alopecia, photo-sensitivity, Renal failure acute, hyponatraemia, Menstrual disorder.
Very Rare: Pancytopenia, Anaphylactic shock, anaphylactic reaction, Haemorrhage intracranial (including fatal intracranial haemorrhage), meningitis aseptic, epilepsy (including aggravated epilepsy), ageusia, anosmia, Retinal artery occlusion, retinal vein occlusion, Vasculitis, Hepatic failure, (sometimes fatal or requiring liver transplant), hepatitis fulminant, (some with fatal outcome), hepatic necrosis, cholestasis, hepatitis cholestatic, jaundice, Dermatitis exfoliative, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalised exanthematous pustulosis (AGEP), dermatitis bullous, Myositis, Tubulointerstitial nephritis, nephrotic syndrome, glomerulonephritis minimal lesion.
Not Known: Infertility female (female fertility decreased.

USE IN PREGNANCY AND LACTATION:
Pregnancy:
The potential for human risk in pregnancy is unknown, but cannot be excluded. Celecoxib, as with other medicinal products inhibiting prostaglandin synthesis, may cause uterine inertia and premature closure of the ductus arteriosus during the last trimester. During the second or third trimester of pregnancy, NSAIDs including celecoxib 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. Celecoxib is contraindicated in pregnancy and in women who can become pregnant. If a woman becomes pregnant during treatment, celecoxib should be discontinued.

Lactation:
Administration of celecoxib to a limited number of lactating women has shown a very low transfer of celecoxib into breast milk. Women who take Nuzib should not breastfeed.

OVERDOSE:
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 product removal due to high protein binding.

SHELF LIFE:
3 years

INSTRUCTION & STORAGE:
Protect from heat, sunlight & moisture, store below 30°C.
The expiration date refer to the product correctly stored at the required condition.
Keep out of the reach of children.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com.
To be sold on prescription of a registered medical practitioner only.
"Product contains lactose"

PRESENTATION:
Nuzib (Celecoxib) 100mg Capsules: 1x10's in blister pack
Nuzib (Celecoxib) 200mg Capsules: 1x10's in blister pack

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
دھوپ، گرمی اور نمی سے محفوظ ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
بچوں کی پہنچ سے دُور رکھیں۔ صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

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