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A review on use in the management of arthritis and acute pain of Celecoxib

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ABSTRACT selective COX-2 inhibitor administered orally as analgesic and anti-inflammatory drug in the treatment of osteoarthritis, rheumatoid arthritis, acute pain, painful menstruation and menstrual symptoms, and to reduce numbers of colon and rectum polyps in patients with familial adenomatous polyposis. The poor aqueous solubility of the drug leads to variable dissolution rates. The present work has been an attempt to prepare orodispersible tablets of celecoxib with a combination of superdisintegrants, amino acids, and sweeteners. Camphor was used as a sublimating agent. Tablets are prepared by direct compression and mannitol is used as bulking agent. The tablets were evaluated for weight variation, hardness, thickness, friability, disintegrating time, and drug release .

Fast dissolving tablets are one of the FDT have benefits such as accurate dosing, easy portability and manufacturing, good physical and chemical stability and an ideal alternative for pediatric and geriatric patients. Some tablets are designed to dissolve fastly in saliva, within a few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity and are more appropriately termed fast-disintegrating tablets, as they may take up to a minute to completely disintegrate.

Keywords Fast dissolving tablet, Celecoxib, Orodispersible tablet, Solid dispersion , formulation excipients .

Introduction Fast dissolving dosage forms can be disintegrated, dissolved, or suspended by saliva in the mouth. This fast dissolving tablet disintegrates instantaneously when placed on tongue and releases the drug dissolves or disperses in the saliva. Fast dissolving tablets are useful in patients, like pediatric, geriatric, bedridden, or mentally disabled, who may face difficulty in swallowing conventional tablets or capsules leading

to ineffective therapy, with persistent nausea, sudden episodes of allergic attacks, or coughing for those who have an active life style. Fast dissolving tablets are also applicable when local action in the mouth is desirable such as local anesthetic for toothaches, oral ulcers, cold sores, or teething, and to those who cannot swallow intact sustained action tablets/capsules .

Mouth dissolving drug delivery systems (MDDDS) are a new generation of formulations which combine the advantages of both liquid and conventional tablet formulations, and at the same time, offer added advantages over both the traditional dosage forms. They provide the convenience of a tablet formulation and also allow the ease of swallowing provided by a liquid formulation. MDDDS offer the luxury of much more accurate dosing than the primary alternative, oral liquids. This segment of formulation is especially designed for dysphagic, geriatric, pediatric, bed-ridden, travelling and psychotic patients who are unable to swallow or refuse to swallow conventional oral formulations. 1-3 As they dissolve/disintegrate very fast when placed in the mouth, MDDDS are the most convenient dosage forms for dysphagic, pediatric and geriatric patients with swallowing .

They do not require water for administration, thus are good alternative for travelers and for bed ridden patients.4 They simply vanish when placed in the mouth, so cannot be hidden in mouth by psychotic patients. These products not only increase the patient's compliance but also fetch large revenues to manufacturers due to line extension of the existing formulation. In the recent past, several new advanced technologies have been introduced for the formulation of mouth dissolving tablets (MDTs) with very interesting features, like extremely low disintegration time, exceptional taste masking ability, pleasant mouth feel and sugar free tablets for diabetic patients.5-8 The technologies utilized for fabrication of MDDDS include lyophilization, moulding, direct compression and cotton candy process, spray drying sublimation, mass extrusion, nanonization and quick dissolve film formation. These techniques are based on the principles of increasing porosity and/or addition of superdisintegrants and water soluble excipients in the tablets. The formulations prepared from these techniques differ from each other on the basis of the factors like mechanical strength of final product, drug and dosage form stability, mouth feel, taste, rate of dissolution of the formulation in saliva, rate of absorption from saliva and overall drug bioavailability. Dosage forms in last two decades, but so far no standardized technique has been designed or mentioned in pharmacopoeias for their evaluation except in European Pharmacopoeia (EP), which defines orodispersible tablets as uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed. EP also specifies that dispersible tablets should disintegrate within 3 minutes when subjected to conventional disintegration test used for tablets and capsules. This article presents a detailed review regarding the evaluation measures available in literature to characterize the MDTs, which have been .

Drinking water plays an important role in the swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition And bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Orodispersible tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people.4 Fast dissolving tablets are also called as mouthdissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapimelts, porous tablets, quick dissolving etc. Fast dissolving tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolves or disperses in the saliva. 5 The faster the drug into solution, quicker the absorption and onset of clinical effect. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form. The advantage of mouth dissolving dosage forms are increasingly being recognized in both, industry and academics.7 According to European pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes. The basic approach in development of FDT is the use of superdisintegrants like cross linked carboxymethyl cellulose (Croscarmellose), sodium starch glycolate (Primogel, Explotab), polyvinylpyrollidone

(Polyplasdone) etc, which provide instantaneous disintegration of tablet after putting on tongue, their by release the drug in saliva. The bioavailability of some drugs may be increased due to absorption of drug in oral cavity .

Requirements of Fast Dissolving Tablets

- Have an acceptable taste masking property.
- Be harder and less friable
- Leave minimal or no residue in mouth after administration.
- Exhibit low sensitivity to environmental conditions (temperature and humidity).
- Allow the manufacture of tablet using conventional processing and packaging equipment

Benefits of Fast Dissolving Tablets

I. Ease of Administration to the patient who cannot swallow, such as the elderly, stroke victims, bedridden patients, patient affected by renal failure and patient who refuse to swallow such as pediatric, geriatric and psychiatric patients.

II. No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water.

III. Rapid dissolution and absorption of the drug, which will produce quick onset of action.

IV. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases bioavailability of drug is increased.

V. Pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage; improve clinical performance through a reduction of unwanted effects

VI. Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patient.

VII. The risk of chocking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.

VIII. New business opportunity like product differentiation, product promotion, patent extensions and life cycle management .

Mechanism of action

Celecoxib prevents the synthesis of a chemical called prostaglandin by inhibiting an enzyme called cyclooxygenase 2 (COX-2). Prostaglandins are important mediators of pain and inflammation in the bodyMost NSAIDS inhibit the two forms of cyclooxygenase (COX -1 and COX-2) but celecoxib is a selective inhibitor of COX-2. Both COX-1 and COX-2 are involved in converting arachidonic acid to prostaglandin H2, a precursor for prostaglandin and thromboxane.

Celecoxib has a sulfonamide side chain that binds to a hydrophilic region near to the active binding site of COX-2. The accumulation of prostaglandins, particularly prostaglandin E2, causes inflammation, pain and swelling as part of the healing process. Inhibiting the production of these prostaglandins through COX-2 inhibition therefore alleviates this pain and swelling .

Platelet In clinical trials using normal volunteers, CELEBREX at single doses up to 800 mg and multiple doses of 600 mg twice daily for up to 7 days duration (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, CELEBREX is not a substitute for aspirin for cardiovascular prophylaxis. It is not known if there are any effects of CELEBREX on platelets that may contribute to the increased risk of serious cardiovascular thrombotic adverse events associated with the use of CELEBREX.

Fluid 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 .

Pharmacokinetics the movement of the drug within the body

When taken as a 200 mg oral dose celecoxib reaches a peak plasma concentration of 705 ng/mL after 3 hours. If the drug is taken with a high fat meal, the peak concentration is achieved around an hour or two later than this and if the drug is taken with antacids containing aluminium and magnesium salts, the plasma concentration falls by around 37% Once absorbed from the gut, 97% of the drug binds to proteins in the blood and is transported to the liver where it is broken down and excreted in the feces and urine .

AbsorptionPeak plasma levels of celecoxib occur approximately 3 hrs after an oral dose. Under fasting conditions, both peak plasma levels and area under the curve (AUC) are roughly dose proportional up to 200 mg BID; at higher doses there are less than proportional increases in Cmax and AUC .

Food Effects When CELEBREX capsules were taken with a high fat meal, peak plasma levels were delayed for about 1 to 2 hours with an increase in total absorption (AUC) of 10% to 20%. Under fasting conditions, at doses above 200 mg, there is less than a proportional increase in Cmax and AUC, which is thought to be due to the low solubility of the drug in aqueous media. Coadministration of CELEBREX with an aluminum- and magnesium containing antacid resulted in a reduction in plasma celecoxib concentrations with a decrease of 37% in Cmax and 10% in AUC. CELEBREX, at doses up to 200 mg BID can be administered without regard to timing of meals. Higher doses (400 mg BID) should be administered with food to improve absorption. 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 Cmax , Tmax or T1/2 after administration of capsule contents .

Distribution celecoxib is highly protein bound (~97%) within the clinical dose range. In vitro studies indicate that celecoxib binds primarily to albumin and, to a lesser extent, α1-acid glycoprotein. The apparent volume of distribution at steady state (Vss/F) is approximately 400 L, suggesting extensive distribution into the tissues. Celecoxib is not preferentially bound to red blood cells

Metabolism Celecoxib metabolism is primarily mediated via cytochrome P450 2C9 and the age 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. Patients who are known or suspected to be P450 2C9 poor metabolizers based on a previous history should be administered celecoxib with caution as they may have abnormally high plasma levels due to reduced metabolic clearance .

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 .

Hepatic Insufficiency A pharmacokinetic study in subjects with mild (Child-Pugh Class A) and moderate (Child-Pugh Class B) hepatic impairment has shown that steadystate celecoxib AUC is increased about 40% and 180%, respectively, above that seen in healthy control subjects. Therefore, the daily recommended dose of CELEBREX capsules should be reduced by approximately 50% in patients with moderate (Child-Pugh Class B) hepatic impairment. Patients with severe hepatic impairment (Child-Pugh Class C) have not been studied. The use of CELEBREX in patients with severe hepatic impairment is not recommended (see DOSAGE AND ADMINISTRATION).

Renal Insufficiency In a cross-study comparison, celecoxib AUC was approximately 40% lower in patients with chronic renal insufficiency (GFR 35-60 mL/min) than that seen in subjects with normal renal function. No significant relationship was found between GFR and celecoxib clearance. Patients with severe renal insufficiency have not 5 been studied. Similar to other NSAIDs, CELEBREX is not recommended in patients with severe renal insufficiency (see WARNINGS – Advanced Renal Disease)

Uses

Celecoxib is recommended for the relief of pain and inflammation in osteoarthritis, rheumatoid arthritis and a condition called ankylosing spondylitis. The drug is also used to manage pain after surgery or injury or due to menstrual cramps.

contraindications for the drug include the following factors .

- Age under 18 years
- Pregnant and breastfeeding mothers
- Allergy to NSAIDs
- Unstable ischemic heart disease
- Peripheral arterial disease
- Heart failure
- Stroke or cerebrovascular disease
- Peptic ulcer

- Gastrointestinal bleeding
- Liver or kidney damage

Contradiction

Contraindicated in patient with known hypersensitivity to celecoxib in patient who have demonstrated allergic type reaction to sulfonamide in patient who have experienced asthma ,articaria , or allergic type reaction after taking aspirin or other nsaids severe rarely fatal anaphylactic like reaction tonsaids have been reported in such patient , contraindicted in the treatment of perioperative pain in setting of coronary artery bypass surgery .

Studies

Osteoarthritis CELEBREX has demonstrated significant reduction in joint pain compared to placebo. CELEBREX was evaluated for treatment of the signs and the symptoms of OA of the knee and hip in placebo- and active-controlled clinical trials of up to 12 weeks duration. In patients with OA, treatment with CELEBREX 100 mg BID or 200 mg QD resulted in improvement in WOMAC (Western Ontario and McMaster Universities) osteoarthritis index, a composite of pain, stiffness, and functional measures in OA. In three 12-week studies of pain accompanying OA flare, CELEBREX doses of 100 mg BID and 200 mg BID provided significant reduction of pain within 24-48 hours of initiation of dosing. At doses of 100 mg BID or 200 mg BID the effectiveness of CELEBREX was shown to be similar to that of naproxen 500 mg BID. Doses of 200 mg BID provided no additional benefit above that seen with 100 mg BID. A total daily dose of 200 mg has been shown to be equally effective whether administered as 100 mg BID or 200 mg QD .

Rheumatoid Arthritis CELEBREX has demonstrated significant reduction in joint tenderness/pain and joint swelling compared to placebo. CELEBREX was evaluated for treatment of the signs and symptoms of RA in placebo- and active-controlled clinical trials of up to 24 weeks in duration. CELEBREX was shown to be superior to placebo in these studies, using the ACR20 Responder Index, a composite of clinical, laboratory, and functional measures in RA. CELEBREX doses of 100 mg BID and 200 mg BID were similar in effectiveness and both were comparable to naproxen 500 mg BID. Although CELEBREX 100 mg BID and 200 mg BID provided similar overall effectiveness, some patients derived additional benefit from the 200 mg BID dose. Doses of 400 mg BID provided no additional benefit above that seen with 100-200 mg BID .

Juvenile Rheumatoid Arthritis In a 12-week, randomized, double-blind active controlled, parallel-group, multicenter, non-inferiority study, patients from 2 years to 17 6 years of age with particular, polyarticular course JRA or systemic onset JRA (with currently inactive systemic features), received one of the following treatments: celecoxib 3 mg/kg (to a maximum of 150 mg) twice daily; celecoxib 6 mg/kg (to a maximum of 300 mg) twice daily; or naproxen 7.5 mg/kg (to a maximum of 500 mg) twice daily. The response rates were based upon the JRA Definition of Improvement greater than or equal to 30% (JRA DOI 30) criterion, which is a composite of clinical, laboratory, and functional measures of JRA. The JRA DOI 30 response rates at

week 12 were 69%, 80% and 67% in the celecoxib 3 mg/kg BID, celecoxib 6 mg/kg BID, and naproxen 7.5 mg/kg BID treatment groups, respectively .

Ankylosing SpondylitisCELEBREX was evaluated in AS patients in two placeboand active-controlled clinical trials of 6 and 12 weeks duration. CELEBREX at doses of 100 mg BID, 200 mg QD and 400 mg QD was shown to be statistically superior to placebo in these studies for all three co-primary efficacy measures assessing global pain intensity (Visual Analogue Scale), global disease activity (Visual Analogue Scale) and functional impairment (Bath Ankylosing Spondylitis Functional Index). In the 12-week study, there was no difference in the extent of improvement between the 200 mg and 400 mg celecoxib doses in a comparison of mean change from baseline, but there was a greater percentage of patients who responded to celecoxib 400 mg, 53%, than to celecoxib 200 mg, 44%, using the Assessment in Ankylosing Spondylitis response criteria (ASAS 20). The ASAS 20 defines a responder as improvement from baseline of at least 20% and an absolute improvement of at least 10 mm, on a 0 to 100 mm scale, in at least three of the four following domains: patient global, pain, Bath Ankylosing Spondylitis Functional Index, and inflammation. The responder analysis also demonstrated no change in the responder rates beyond 6 weeks .

Familial Adenomatous Polyposis CELEBREX was evaluated to reduce the number of adenomatous colorectal polyps. A randomized double-blind placebo controlled study was conducted in patients with FAP. The study population included 58 patients with a prior subtotal or total colectomy and 25 patients with an intact colon. Thirteen patients had the attenuated FAP phenotype. One area in the rectum and up to four areas in the colon were identified at baseline for specific follow-up, and polyps were counted at baseline and following six months .

Warnings

Cardiovascular Effects Cardiovascular Thrombotic Events Chronic use of CELEBREX may cause an increased risk of serious adverse cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. In the APC trial, the relative risk for the composite endpoint of cardiovascular death, MI, or stroke was 3.4 (95% CI 1.4 – 8.5) for CELEBREX 400 mg twice daily and 2.5 (95% CI 1.0 – 6.4) for the CELEBREX 200 mg twice daily compared to placebo (see Special Studies – Adenomatous Polyp Studies). All NSAIDs, both COX-2 selective and nonselective, may have a similar risk. Patients with known CV disease or risk factors for CV disease may be at greater risk. To minimize the potential risk for an adverse CV event in patients treated with CELEBREX, 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/or symptoms of serious CV toxicity and the steps to take if they occur. There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious CV thrombotic events associated with NSAID use. The concurrent use of aspirin and CELEBREX does increase the risk of serious GI events (see GI WARNINGS - Risk of GI Ulceration, Bleeding, and Perforation)

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Hypertension All NSAIDS, CELEBREX 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. Patients taking thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDs, including CELEBREX, should be used with caution in patients with hypertension. Blood pressure should be monitored closely during the initiation of therapy with CELEBREX and throughout the course of therapy. The rates of hypertension from the CLASS trial in the CELEBREX, ibuprofen and diclofenac treated patients were 2.4%, 4.2% and 2.5%, respectively(see Special Studies - CLASS)

Congestive Heart Failure and Edema Fluid retention And edema have been observed in some patients taking NSAIDs, including CELEBREX (see ADVERSE REACTIONS). In the CLASS study (see Special Studies – CLASS), the Kaplan-Meier cumulative rates at 9 months of peripheral edema in patients on CELEBREX 400 mg twice daily (4-fold and 2-fold the recommended OA and RA doses, respectively, and the approved dose for FAP), ibuprofen 800 mg three times daily and diclofenac 75 mg twice daily were 4.5%, 6.9% and 4.7%, respectively. CELEBREX should be used with caution in patients with fluid retention or heart failure .

Gastrointestinal (GI) Effects Risk of GI Ulceration, Bleeding, and Perforation NSAIDs, including CELEBREX, can cause serious gastrointestinal events including bleeding, ulceration, and perforation of the 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 NSAIDs. Only one in five patients who develop a serious upper GI adverse event on NSAID therapy is symptomatic. Complicated and symptomatic ulcer rates were 0.78% at nine months for all patients in the CLASS trial, and 2.19% for the subgroup on low dose ASA. Patients 65 years of age and older had an incidence of 1.40% at nine months, 3.06% when also taking ASA (see Special Studies - CLASS). With longer duration of use of NSAIDs, there is a trend for increasing the likelihood of developing a serious GI event at some time during the course of therapy. However, even short-term therapy is not without risk.

Renal Effects 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, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors, angiotensin II receptor antagonists, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state. Clinical trials with CELEBREX have shown renal effects similar to those observed with comparator NSAIDs .

Skin ReactionsCELEBREX is a sulfonamide and can cause serious skin adverse events such as exfoliative dermatitis, Stevens Johnson syndrome (SJS), and toxic epidermal necrolysis (TENS), which can be fatal. These serious events can occur without warning and in patients without prior known sulfa allergy. Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Drug interaction

Furosemid Clinical studies, as well as post marketing observations, have shown that NSAIDs can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis.

Lithium In a study conducted in healthy subjects, mean steady-state lithium plasma levels increased approximately 17% in subjects receiving lithium 450 mg BID with CELEBREX 200 mg BID as compared to subjects receiving lithium alone. Patients on lithium treatment should be closely monitored when CELEBREX is introduced or withdrawn .

MethotrexatIn an interaction study of rheumatoid arthritis patients taking methotrexate, CELEBREX did not have a significant effect on the pharmacokinetics of methotrexate .

Dosage and administration

Carefully consider the potential benefits and risks of CELEBREX and other treatment options before deciding to use CELEBREX. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals .

Osteoarthritis For relief of the signs and symptoms of osteoarthritis the recommended oral dose is 200 mg per day administered as a single dose or as 100 mg twice per day.

Rheumatoid arthritis For relief of the signs and symptoms of rheumatoid arthritis the recommended oral dose is 100 to 200 mg twice per day.

Method of Administration

For patients who have difficulty swallowing capsules, the contents of a CELEBREX 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 .

Ankylosing Spondylitis For the management of the signs and symptoms of AS, the recommended dose of CELEBREX is 200 mg daily 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 .

Acute Pain and Treatment of Primary Dysmenorrhea The recommended dose of CELEBREX 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 .

Conclusion

Celecoxib remains an effective and useful altenative to nonselective NSAIDs in the treatment of acute or chronic musculoskeletal pain. In the latter setting, it offers the prospect of improved GI tolerability and, in patients not taking aspirin for cardioprophylaxis, a GI safety advantage. Currently available evidence of an increase in CV risk with celecoxib is inconsistent; any increase in risk is likely to be small and similar to that with nonselective NSAIDs. As with all NSAIDs, the potential GI, CV and renal risks of celecoxib must be weighed against the potential benefits in each individual; it is a rational choice for patients at low CV risk who require NSAID therapy, especially those at increased risk of NSAID-induced GI toxicity, but also those unresponsive to, or intolerant of, other NSAIDs. If selected, celecoxib, like all NSAIDs, should be used at the lowest effective dose for the shortest possible duration .

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