European Medicines Agency
Press office

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Key elements for the summaries of product characteristics of non-selective NSAIDs adopted by the CHMP during its meeting in October 2005

GASTROINTESTINAL SAFETY OF NSAIDS

Section 4.3 Contraindications
History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.
Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

Section 4.4 Special warnings and precautions for use
The use of <Invented name> with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided.

Undesirable effects may be minimised by using the minimum effective dose for the shortest duration necessary to control symptoms.

Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (See section 4.2).

Gastrointestinal bleeding, ulceration and perforation: GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at anytime during treatment, with or without warning symptoms or a previous history of serious GI events.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (See section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (See below and 4.5).

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.
Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin (See section 4.5).

When GI bleeding or ulceration occurs in patients receiving <Invented name>, the treatment should be withdrawn.

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as their condition may be exacerbated (See section 4.8 – undesirable effects).

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Section 4.5 Interactions with other medicaments and other forms of interaction
Corticosteroids: increased risk of gastrointestinal ulceration or bleeding (See section 4.4)
Anti-coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin (See section 4.4).
Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (See section 4.4).

Section 4.8 Undesirable effects
Gastrointestinal: The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (See section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (See section 4.4 - Special warnings and precautions for use) have been reported following administration. Less frequently, gastritis has been observed.

CARDIOVASCULAR SAFETY OF NSAIDS

Section 4.3 Contraindications
Severe heart failure

Section 4.4 Special warnings and precautions for use
Caution is required in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Section 4.8 Undesirable effects
Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.

SKIN REACTIONS OF NSAIDS

Section 4.4 Special warnings and precautions for use
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 NSAIDSs (see 4.8). Patients appear to be at highest risk of 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. <Invented name> should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Section 4.8 Undesirable effects
Bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (very rare).

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