Etoricoxib STADA 30 mg, 60 mg, 90 mg and 120 mg film-coated tablets

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PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

VI.2 Elements for a Public Summary

Etoricoxib STADA 30 mg film-coated tablets

Etoricoxib STADA 60 mg film-coated tablets

Etoricoxib STADA 90 mg film-coated tablets

Etoricoxib STADA 120 mg film-coated tablets

VI.2.1 Overview of disease epidemiology

Etoricoxib Stada, containing the active ingredient etoricoxib, is one of a group of medicines called selective COX-2 inhibitors. These belong to a family of medicines called non-steroidal anti-inflammatory drugs (NSAIDs). Etoricoxib Stada may be used for any of the conditions listed below.

Osteoarthritis (OA) and rheumatoid arthritis (RA)

Arthritis is inflammation of one or more joints. The main symptoms include joint pain and stiffness. The most common types of arthritis are osteoarthritis (OA) and rheumatoid arthritis (RA).

OA occurs when the protective cartilage on the ends of bones wears down over time. It most commonly affects joints in hands, knees, hips and spine. In RA, immune system attacks the lining of the joints, causing a painful swelling which, if not treated early enough, can lead to joint deformity. RA usually affects the small joints of the hand. There is symmetry with RA, i.e. same joints on both sides are affected, whilst this is not the case with OA, where a joint on only one side is typically affected. Morning stiffness with RA tends to last longer than with OA.

The prevalence of RA is believed to range from 0.5-1.0% in the general population. In 1995-2007, 41 per 100,000 people were diagnosed with RA each year. RA most commonly starts between the ages of 40 and 50. About three times as many women as men are affected.

Among adults 60 years of age or older the prevalence of symptomatic knee OA is approximately 10% (10 in 100) in men and 13% (13 in 100) in women. OA usually develops in people over 45 years of age.

Acute gouty arthritis

Acute gouty arthritis is another form of arthritis, which develops as a consequence of uric acid accumulation in the joints. It usually starts with a sudden attack of pain and swelling in one joint. The attack may last from a few days to 2 weeks. Men are more likely to get acute gouty arthritis, but women become increasingly susceptible after menopause. The prevalence of gout among USA adults in 2007–2008 was 3.9%. The prevalence of gout among men was 5.9% and the prevalence among women was 2.0%.

Ankylosing spondylitis

Ankylosing spondylitis is an inflammatory disease that leads to fusing of the vertebrae in the spine. Symptoms include pain and stiffness in lower back and hips, especially in the morning and after periods of inactivity. Ankylosing spondylitis affects men more than women. The mean prevalence per 10,000 people is estimated at 23.8 in Europe, 16.7 in Asia, 31.9 in North America, 10.2 in Latin America and 7.4 in Africa.

Pain after dental surgery
Dental surgery (e.g. root canal surgery, crown replacement surgery) is frequently associated with pain, which varies in intensity. Intensity of pain needs to be determined by patient himself / herself, as the perception of pain and pain threshold are different from patient to patient. Various pain scales may be used to establish the pain intensity. Etoricoxib Stada is indicated for the short term treatment of moderate pain after dental surgery.

VI.2.2 Summary of treatment benefits

Etoricoxib Stada helps to reduce the pain and swelling (inflammation) in the joints and muscles of people with osteoarthritis, rheumatoid arthritis, ankylosing spondylitis and gout.

Etoricoxib Stada is also used for the short term treatment of moderate pain after dental surgery.

Etoricoxib Stada is indicated in adults and adolescents at the age of 16 years and older.

VI.2.3 Unknowns relating to treatment benefits

None.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Stomach disorders (e.g. stomach holes, sores, bleeding) (Gastrointestinal disorders (e.g. perforation, ulcer, bleeding))	Stomach disorders (e.g. stomach holes, sores, bleeding), some of them resulting in fatal outcome, have occurred in patients treated with etoricoxib. Patients who are more at risk of developing these stomach problems are the elderly, patients using any other drug form the same group (e.g. ibuprofen, diclofenac) or aspirin concomitantly, or patients with a prior history of stomach disease.	Tell your doctor if you are taking ibuprofen, diclofenac, aspirin or a similar analgesic drug (even if this is over-the counter). Inform your doctor of any previous stomach condition you may have had (e.g. stomach sores). Inform your doctor immediately if you develop any of the following for prolonged periods of time: • Diarrhoea • Vomiting • Stool changes • Indigestion • Heartburn • Loss of appetite

Clot formation in the blood vessels of the heart and brain leading to heart attack and / or stroke (Cardiovascular and cerebrovascular thrombotic disorders (e.g. myocardial infarction, stroke))	Drug class which etoricoxib is part of may be associated with a risk of clot formation in the blood vessels of the heart and brain, potentially leading to heart attack and / or stroke. Patients with significant risk factors for these events are those with high blood pressure (hypertension), high blood lipids, diabetes and those who smoke.	Higher doses taken over long periods of time may increase the risk of these events. Your doctor will aim to prescribe you etoricoxib for the shortest duration and the lowest effective daily dose possible. Tell your doctor if you have family history of these events, if you suffer from high blood pressure, high lipids or diabetes. Inform your doctor immediately if you develop any of the following for prolonged periods of time: • Shortness of breath • Chest pain • Abnormal heartbeat • Pain, numbness, weakness or coldness in your legs or arms • Fatigue • Fainting • Swollen ankles
Reduction in hormone synthesis leading to impaired kidney function and other adverse events such as heart failure, high blood pressure and swelling (Renovascular disorders (e.g. hypertension, edema, congestive heart failure))	Etoricoxib may cause a reduction in kidney hormone called prostaglandin. This leads to reduction in blood flow through the kidney. Patients at greatest risk of this effect are those with pre-existing kidney or liver problems and heart failure. Inhibition of prostaglandin hormone synthesis may also lead to fluid accumulation in the body. Adverse events, such as swelling of ankles, high blood pressure or heart failure, may occur.	Tell your doctor if you have or have ever had kidney or liver problems. Your doctor will perform regular tests to examine your kidney function. It is essential that you turn up for your tests. Inform your doctor immediately if you develop any of the following: • Decreased urine output • Swelling in your legs, ankles or feet • Drowsiness • Shortness of breath • Fatigue • Confusion • Nausea

Severe skin reactions	Serious skin reactions, including: o exfoliative dermatitis (inflammatory skin disease) o Stevens-Johnson syndrome (rare, serious disorder of your skin and mucous membranes) o toxic epidermal necrolysis (rare, life-threatening skin condition) have been reported very rarely in association with the use of NSAIDs and some selective COX-2 inhibitors during post-marketing surveillance. Patients appear to be at highest risk for these reactions early in the course of therapy, with the onset of the reaction occurring in the majority of cases within the first month of treatment. Risk of skin reactions may be higher in patients with a history of any drug allergy.	Tell your doctor if you have or have ever had any long-term skin conditions or any allergies which have primarily manifested on the skin. Inform your doctor immediately if you develop any of the following: • Facial swelling • Tongue swelling • Hives • Skin pain • A red or purple skin rash that spreads within hours to days • Blisters on skin and the mucous membranes of mouth, nose, eyes and genitals • Shedding of the skin
Kidney disorders (Renal disorders (e.g. renal failure))	Etoricoxib may cause a reduction in kidney hormone called prostaglandin. This leads to reduction in blood flow through the kidney and to subsequent kidney failure in extreme cases. Patients at greatest risk of this effect are those with pre-existing kidney or liver problems and heart failure.	Tell your doctor if you have or have ever had kidney or liver problems. Your doctor will perform regular tests to examine your kidney function. It is essential that you turn up for your tests. Inform your doctor immediately if you develop any of the following: • Decreased urine output • Swelling in your legs, ankles or feet • Drowsiness • Shortness of breath • Fatigue • Confusion • Nausea

Liver disorders (Hepatic disorders)	Adnormal liver function tests have been reported in approximately 1% of patients in clinical trials treated for up to one year with etoricoxib 30, 60 and 90 mg daily. Liver inflammation (hepatitis) and liver failure have been reported in up to 1 in a 1000 patients.	Tell your doctor if you have or have ever had liver problems. Your doctor will perform regular tests to examine your liver function. It is essential that you turn up for your tests. If signs of liver problems occur, or if persistently abnormal liver function tests (three times the upper limit of normal) are detected, your doctor will most likely discontinue Etoricoxib Stada. Inform your doctor immediately if you develop any of the following: • Yellowing of your skin and eyeballs • Pain in upper right abdomen • Abdominal swelling • Nausea • Vomiting • A general sense of feeling unwell (malaise) • Disorientation or confusion • Sleepiness

Important potential risks

Risk	**What is known (Including reason why it is considered a potential risk)**
None	NA

Missing information

Risk	**What is known**

Use during pregnancy and lactation	No clinical data on exposed pregnancies are available for etoricoxib. Studies in animals have shown reproductive toxicity. The potential for human risk in pregnancy is unknown. Etoricoxib, as with other medicinal products inhibiting prostaglandin (hormone) synthesis, may cause absence of effective uterine contractions during labor and premature closure of the foetus's blood vessel during the last trimester. Etoricoxib is contraindicated in pregnancy. If a woman becomes pregnant during treatment, etoricoxib must be discontinued. It is not known whether etoricoxib is excreted in human milk. Etoricoxib is excreted in the milk of lactating rats. Women who use etoricoxib must not breastfeed.
Safety and efficacy in children and adolescents < 16 years of age	Etoricoxib is contra-indicated in children and adolescents under 16 years of age as the safety and efficacy in this patient group have not been established.
Safety and efficacy in patients with hepatic impairment	Regardless of indication, in patients with mild liver dysfunction a dose of 60 mg once daily should not be exceeded. In patients with moderate liver dysfunction regardless of indication, the dose of 30 mg ***once daily*** should not be exceeded. Clinical experience is limited particularly in patients with moderate liver dysfunction and caution is advised. There is no clinical experience in patients with severe liver dysfunction; therefore, its use is contra- indicated in these patients.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No post-authorisation studies have been imposed or are planned.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable.