VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Osteoarthritis: Osteoarthritis is a disease of the joints. It results from the gradual breakdown of cartilage that cushions the ends of the bones. This causes swelling (inflammation), pain, tenderness, stiffness and disability.

Rheumatoid arthritis: Rheumatoid arthritis is a long term inflammatory disease of the joints. It causes pain, stiffness, swelling, and increasing loss of movement in the joints it affects. It may also cause inflammation in other areas of the body.

Gout: Gout is a disease of sudden, recurring attacks of very painful inflammation and redness in the joints. It is caused by deposits of mineral crystals in the joint.

Ankylosing spondylitis: Ankylosing spondylitis is an inflammatory disease of the spine and large joints

VI.2.2 Summary of treatment benefits

Etoricoxib is one of a group of medicines called selective cyclooxygenase-2 (COX-2) inhibitors. These belong to a family of medicines called non-steroidal anti-inflammatory drugs (NSAIDs). Two isoforms of cyclooxygenase have been identified: cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). COX-1 is responsible amongst others for stomach protection and platelet aggregation. Inhibition of COX-1 by nonselective NSAIDs (who inhibit both COX-1 and COX-2) has been associated with stomach problems and inhibition of platelet aggregation. COX-2 has been shown to be primarily responsible for the synthesis of mediators of pain, inflammation, and fever. Selective inhibition of COX-2 by Etoricoxib (within the clinical dose range) decreases these clinical signs and symptoms with decreased potential for stomach toxicity and effects on platelet aggregation.

Based on the available data from clinical studies and clinical experience of several years, Etoricoxib represents an effective drug in the treatment of pain and swelling (inflammation) in the joints and muscles of people with osteoarthritis, rheumatoid arthritis, ankylosing spondylitis and gout. It is also used for the short term treatment of moderate pain after dental surgery.

If administered as indicated in the Summary of Product Characteristics and taking into account the contra-indications, the warnings and precautions, Etoricoxib can be considered effective in the approved indications and generally well tolerated.

VI.2.3 Unknowns relating to treatment benefits

Not applicable.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Heart attack (myocardial infarction), stroke (cardiovascular thrombotic events)	Etoricoxib may slightly increase your risk of heart attack and stroke, especially after prolonged treatment with high doses.	Do not take Etoricoxib if your doctor has diagnosed heart problems including angina (chest pain) or if you have had a heart attack, bypass surgery, peripheral arterial disease (poor circulation in legs or feet due to narrow or blocked arteries), or any kind of stroke (including mini-stroke, transient ischaemic attack (TIA)). Talk to your doctor or pharmacist before taking Etoricoxib if you have a history of any form of heart disease or if you have diabetes, high cholesterol, or are a smoker. Do not take more than the recommended dose for your condition. Your doctor will want to discuss your treatment from time to time. It is important that you use the lowest dose that controls your pain and you should not take Etoricoxib for longer than necessary.
Increased blood pressure (hypertension), fluid retention (oedema) and associated heart failure (renovascular adverse effects and associated congestive heart failure)	Etoricoxib can be associated with increased blood pressure, fluid retention (oedema), and associated new onset or recurrent heart failure. Etoricoxib may be associated with more frequently and severely increased blood pressure than some other NSAIDs (non-steroidal anti-inflammatory drugs) and selective COX-2 inhibitors, especially at high doses.	Do not take Etoricoxib if your doctor has diagnosed heart problems including heart failure (moderate or severe types). Do not take Etoricoxib if you have high blood pressure that has not been controlled by treatment (check with your doctor or nurse if you are not sure whether your blood pressure is adequately controlled). Talk to your doctor or pharmacist before taking

Risk	What is known	Preventability
		Etoricoxib if you have a history of heart failure or if you have swelling due to fluid retention or if you have a history of high blood pressure. If you develop any of these signs you should stop Etoricoxib and talk to your doctor immediately: shortness of breath, chest pains, or ankle swelling appear or if they get worse.
Adverse effects affecting the stomach or intestine (gastrointestinal adverse effects) including ulcer, perforation, bleeding	Etoricoxib can be associated with uncommon adverse effects affecting the stomach or intestine like ulcer, perforation, bleeding. The risk of stomach ulcers is greater if you take Etoricoxib with acetylsalicylic acid (aspirin).	Do not take Etoricoxib if you have a current stomach ulcer or bleeding in your stomach or intestines. Talk to your doctor or pharmacist before taking Etoricoxib if you have a history of stomach bleeding or ulcers. Do not take high dose acetylsalicylic acid (aspirin) or other anti-inflammatory medicines while taking Etoricoxib. If you are currently taking low-dose acetylsalicylic acid to prevent heart attacks or stroke, you should not stop taking acetylsalicylic acid until you talk to your doctor. Your doctor may want to monitor you to check that your medicines are working properly. If you develop any of these signs you should stop Etoricoxib and talk to your doctor immediately: severe or continual stomach pain or your stools become black.
Severe adverse effects affecting the skin (Stevens-Johnson syndrome, toxic epidermal necrolysis)	Etoricoxib can be associated rarely with severe adverse effects affecting the skin and/or mucous membranes with blistering, ulcers and skin detachment.	Do not take Etoricoxib if you are allergic to non-steroidal anti-inflammatory drugs (NSAIDs), including acetylsalicylic acid (aspirin) and COX-2 inhibitors. If you develop any of these signs you should stop Etoricoxib and talk to your doctor

Risk	What is known	Preventability
		immediately: an allergic reaction- which can include skin problems such as ulcers or blistering.
Adverse effects affecting the kidney (renal adverse effects) including impaired kidney function (renal insufficiency), kidney failure (renal failure)	Etoricoxib can be associated with uncommon adverse effects affecting the kidney like impaired function and kidney failure. The risk of kidney impairment is greater in patients with pre-existing kidney disease or dehydrated patients. In some patients with impaired kidney function the co-administration of an ACE inhibitor or angiotensin receptor blocker (drugs to control high blood pressure and heart failure, e.g. Enalapril, Ramipril, Losartan, Valsartan) and Etoricoxib may result in further deterioration of kidney function, including possible kidney failure, which is usually reversible.	Do not take Etoricoxib if you have serious kidney disease. Talk to your doctor or pharmacist before taking Etoricoxib if you have any history of kidney disease, or if you are dehydrated, for example by a prolonged bout of vomiting or diarrhoea. If you are taking medicines used to help control high blood pressure and heart failure called ACE inhibitors and angiotensin receptor blockers, examples include Enalapril and Ramipril, and Losartan and Valsartan, your doctor may want to monitor you to check that your medicines are working properly, once you start taking Etoricoxib.

Important potential risks

None

Missing information

Risk	What is known
Use during pregnancy and breastfeeding	There are no data available on Etoricoxib use during pregnancy. Studies in animals have shown reproductive toxicity. The potential for human risk in pregnancy is unknown. Etoricoxib, as other NSAID (non-steroidal anti-inflammatory drugs), may cause absence of effective uterine contractions during labour and premature closure of the ductus arteriosus in the child during the last trimester of pregnancy. It is not known whether Etoricoxib is excreted in human milk. Etoricoxib is excreted in the milk of breastfeeding rats. Due to lack of data, Etoricoxib is contra-indicated during pregnancy and breastfeeding.
Use in children and adolescents under 16 years of age	There are no data available on Etoricoxib use in children and adolescents under 16 years of age; therefore Etoricoxib is contraindicated in children and adolescents less than 16 years of age.

Risk	What is known
Use in patients with renal insufficiency (estimated creatinine clearance ≤30 ml/min)	There is limited data available on Etoricoxib use in patients with kidney disease who have estimated creatinine clearance ≤30 ml/min (a measure used to monitor kidney function). Therefore, etoricoxib should not be used in those patients.
Use in patients with hepatic impairment	There is limited data available on Etoricoxib use in patients with liver disease; therefore Etoricoxib use is limited in this patient group. Talk to your doctor or pharmacist before taking Etoricoxib If you have any history of liver disease. If patients suffer from mild liver disease, they should not take more than 60 mg of etoricoxib a day. If they have moderate liver disease, you should not take more than 30 mg of etoricoxib a day. There is no clinical experience in patients with severe liver disease; therefore, its use is contra-indicated in these patients.

VI.2.5 Summary of risk minimisation measures by safety concern

No additional risk minimisation measures are proposed.

VI.2.6 Planned post authorisation development plan

Not applicable.

VI.2.7 Summary of changes to the risk management plan over time

Version	Date	Safety Concerns	Comment
1.1	15 January 2016	Identified Risks • Cardiovascular thrombotic events (myocardial infarction, stroke) • Renovascular adverse effects (hypertension, oedema) and associated congestive heart failure • Gastrointestinal adverse effects (perforation, ulcer, bleeding) • Serious skin reactions (Stevens-Johnson syndrome, toxic epidermal necrolysis) • Renal adverse effects (renal insufficiency, renal failure) Potential Risks None Missing information • Use during pregnancy and lactation • Use in children and adolescents under 16 years of age • Use in patients with renal insufficiency (estimated creatinine clearance ≤ 30 ml/min) • Use in patients with hepatic impairment	RMP v1.1 was approved in procedures DE/H/5031+5032/001-004/DC
2.0	4 August 2016	No change in the list of safety concerns or PhV and risk minimization activities.	The RMP was updated due to change in posology in the PI.