RISK MANAGEMENT PLAN (RMP) PUBLIC SUMMARY

ETORICOXIB ORION

(ETORICOXIB)

30 MG, 60 MG, 90 MG & 120 MG FILM-COATED TABLET

DATE: 07-10-2016, VERSION 1.2

VI.2 Elements for a Public Summary

Etoricoxib Orion is indicated in adults and adolescents 16 years of age and older for:

- Reducing the pain and swelling (inflammation) in the joints and muscles associated with OA, rheumatoid arthritis (RA), ankylosing spondylitis and gout.
- Short-term treatment of moderate pain associated with dental surgery.

VI.2.1 Overview of disease epidemiology

Osteoarthritis (OA)

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. Old age, female gender, overweight and obesity, knee injury, repetitive use of joints, bone density, muscle weakness, and joint laxity play roles in the development of joint OA, particularly in the weight-bearing joints.

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. Prevalence ranges from 0.5-1.5% of the population in industrialised countries. The incidence of the condition is low, with around 1.5 men and 3.6 women developing RA per 10 000 people per year. The overall occurrence of RA is two to four times greater in women than in men. The peak age of incidence for both genders is the 70s, but people of all ages can develop the disease.

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. It most often affects middle-aged to elderly men and postmenopausal women.

Ankylosing spondylitis

Ankylosing spondylitis is an inflammatory disease of the spine and large joints. It usually initially presents during the third decade of life, and rarely after the age of 45 years. The prevalence of ankylosing spondylitis is generally believed to be between 0.1% and 1.4% globally.

VI.2.2 Summary of treatment benefits

Etoricoxib belongs to a group of medicines called coxibs which selectively blocks enzyme COX-2 and inhibits the production of prostaglandin that cause pain, inflammation, and fever.

The efficacy of etoricoxib for the treatment for OA was established in a study as compared to placebo.

For the treatment of RA and ankylosing spondylitis, etoricoxib was found to provide significant improvements in pain, swelling, mobility, and function in one study.

For acute gout arthritis, efficacy of etoricoxib in relieving moderate to extreme joint pain and swelling was established in a study compared to indomethacin.

For treatment of dental pain after surgery, etoricoxib was found to have a similar pain relieving effect as compared to ibuprofen, and greater efficacy as compared to paracetamol-codeine combination and placebo.

VI.2.3 Unknowns relating to treatment benefits

Clinical experience is limited particularly in patients with moderate hepatic dysfunction and caution is advised. There is no clinical experience in patients with severe hepatic dysfunction (Child-Pugh score >10); therefore, its use is contraindicated in these patients.

No clinical data on exposed pregnancies are available for etoricoxib. The potential for human risk in pregnancy is unknown. It is also unknown whether etoricoxib is excreted in human milk.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Serious events in stomach and bowel (Serious GI events)	Stomach and upper bowel complications (perforations, ulcers or bleedings), some of them causing death, have occurred in patients taking etoricoxib. There is a further increase in the risk of stomach and upper intestinal side effects with etoricoxib (ulcers or other GI complications), when etoricoxib is taken at the same time as aspirin (even at low doses). Inflammation of the lining of the stomach (gastritis), heartburn, diarrhoea,	Patients with stomach ulcers and risk of bleeding should be informed to avoid taking etoricoxib. Caution is advised in patients who are at risk of developing stomach and intestinal complications like elderly patients, patient already using NSAIDs and aspirin, or patients with prior history of stomach and intestinal ulcers and bleeding.

Risk	What is known	Preventability
	indigestion (dyspepsia)/stomach discomfort, nausea and vomiting, inflammation of the food pipe (oesophagus), stomach or bowel bloating, stomach ulcer, inflammation of the stomach lining that can become serious which may lead to bleeding, and inflammation of pancrease are reported as side effects to etoricoxib therapy.	
Disorders related to heart and blockage of blood vessels (Thrombotic cardiovascular events)	Treatment with etoricoxib is associated with the risk of fast or irregular heartbeat (palpitations), irregular heart rhythm (arrhythmia), feeling of tightness, pressure or heaviness in the chest (angina pectoris), heart attack, heart failure, stroke, flushing, and inflammation of the blood vessels. Clinical trials suggest that the drugs that block COX-2 proteins in the body are found to be associated with blocking of arteries (thrombosis) (especially heart attack [MI] and stroke).	As the cardiovascular risks of etoricoxib may increase with dose and duration of therapy, the lowest effective daily dose should be used for the shortest period of time. Etoricoxib should not be taken if the patient has a diagnosed heart problems including heart failure (moderate or severe types) and chest pain (angina), or if the patient had heart attack, bypass surgery, poor circulation in legs or feet due to narrow or blocked arteries (peripheral arterial disease). Etoricoxib should be used with caution in patients with history of heart failure, other heart problems or high blood pressure. Blood pressure should be regularly monitored during treatment with etoricoxib.
Events related to kidney and blood vessels: Swelling and retention of fluid, increased blood pressure and heart failure (Renovascular events: Oedema, hypertension and CHF)	Prostaglandins help in maintenance of blood flow in kidney. Therefore, under conditions of reduced blood flow in kidneys, etoricoxib by decreasing production of prostaglandins, further limits	Etoricoxib should be used with caution in patients with a medical history of impaired kidney function, heart failure, or cirrhosis. Kidney functions in such patients should be monitored.

Risk	What is known	Preventability
	the blood flow, imparing kidney function. As with other medicinal products known to inhibit prostaglandin production, retention of fluid, swelling (oedema) and raised blood pressure have been observed in patients taking etoricoxib. In patients with impaired kidney functions, co-administration of etoricoxib with diuretics ('water tablets'), and blood pressure-reducing medications like ACE inhibitors and angiotensin II blockers may further deteriorate kidney functions including possible reversible kidney failure. High levels of potassium in blood, changes in blood or urine tests related to kidney, and serious kidney problems are side effects to etoricoxib therapy.	Caution is also advised while prescribing etoricoxib with diuretics, ACE inhibitors and angiotensin II blockers especially in elderly and dehydrated patients. Etoricoxib should be used with caution in patients with history of heart failure, other heart problems or high blood pressure. Blood pressure should be regularly monitored during treatment with etoricoxib.
Allergic and serious skin reactions (Hypersesitivity-related events and serious skin reactions)	Some cases of serious allergic reactions with swelling of the face, lips, tongue and/or throat which may cause difficulty in breathing or swallowing, (angioedema) and anaphylactic or anaphylactoid reactions including shock, which may be serious enough to require immediate medical attention have been reported with etoricoxib. Serious skin reactions like peeling of the skin over large areas of the body (exfoliative dermatitis); painful, extensive peeling and blistering of skin (SJS and TEN), which may result in death have been reported	Etoricoxib should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of allergic reactions.

Risk	What is known	Preventability
	very rarely with the use of etoricoxib.	

Missing information

Risk	What is known
Use in pregnancy and lactating women	There is no data available on pregnancies where etoricoxib has been taken. Studies in animals have shown that etoricoxib interferes with the normal reproductive ability. Etoricoxib should not be used during pregnancy. If a woman becomes pregnant during treatment, etoricoxib must be discontinued. It is not known whether etoricoxib is released in human milk. Etoricoxib has been detected in the milk of female rats. Women who use etoricoxib must not breast feed.
Use in patients less than 16 years of age	Etoricoxib should not be used in children and adolescents under 16 years of age.
Use in patients with reduced kidney function (renal insufficiency)	Etoricoxib should not be administered in patients with impaired kidney function (creatinine clearance <30 ml/min)
Use in patients with liver impairment (hepatic impairment)	In patients with mild liver disease (Child-Pugh score 5-6), a dose of 60 mg once daily should not be exceeded. In patients with moderate liver disease (Child-Pugh score 7-9), the dose of 30 mg once daily should not be exceeded. There is no clinical experience in patients with severe liver function impairment (Child-Pugh score >10), therefore, its use is prohibited in these patients.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) 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. The Summary of Product Characteristics and the Package leaflet for Etoricoxib Orion can be found in the national authority's web page.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan (if applicable)

Not applicable.

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

Not applicable.