Part VI: Summary of the risk management plan by product

VI.1 Elements for summary tables in the EPAR

VI.1.1 Summary table of Safety concerns

Summary of safety concerns	
Etoricoxib 30mg/60mg/90mg/120mg Film-Coated Tablets	
Important identified risks	Serious gastrointestinal events Thrombotic cardiovascular events Renovascular events: oedema, hypertension and congestive heart failure Hypersensitivity-related events and serious skin reactions
Important potential risks	None
Missing information	Use in pregnancy and lactating women Use in patients less than 16 years of age Use in patients with renal insufficiency Use in patients with hepatic impairment

VI.1.2 Table of on-going and planned studies in the Post-authorisation Pharmacovigilance Development Plan (if applicable)

Not applicable

VI.1.3 Summary of Post authorisation efficacy development plan (if applicable)

Not applicable

VI.1.4 Summary table of Risk Minimisation Measures

Safety concern Etoricoxib 30mg/60mg/90mg/120mg Film-Coated Tablets	Routine risk minimisation measures	Additional risk minimisation measures
Important Identified Risks		
Serious gastrointestinal events	Upper gastrointestinal complications [perforations, ulcers or bleedings (PUBs)], some of them resulting in fatal outcome , have occurred in patients treated with Etoricoxib. Therefore, Etoricoxib should not be used in patients with active peptic ulceration, active gastro-intestinal (GI) bleeding or inflammatory bowel disease. This information is included with appropriate wording in 4.3 Contraindications of SPC. Caution is advised with treatment of patients most at risk of developing a gastrointestinal complication with NSAIDs; the elderly, patients using any other NSAID or acetylsalicylic acid concomitantly or patients with a prior history of gastrointestinal disease, such as ulceration and GI bleeding. There is a further increase in the risk of gastrointestinal adverse effects (gastrointestinal ulceration or other gastrointestinal complications) when Etoricoxib is taken concomitantly with acetylsalicylic acid (even at low doses). A significant difference in GI safety between selective COX-2 inhibitors + acetylsalicylic acid vs. NSAIDs + acetylsalicylic acid has not been demonstrated in long-term clinical trials (see section 5.1). This information is included with appropriate wording in 4.4 Special warnings and precautions for use / 4.5 Interaction with other medicinal products and other forms of interaction of SPC. Undesirable effects regarding gastrointestinal disorders are listed in SPC section 4.8. In the PIL this information is included with appropriate wording in 2. What you need to know before you take ETORICOXIB – Do not take ETORICOXIB, -Warnings and precautions, - Other medicines and ETORICOXIB and 4. Possible side effects.	None proposed

Thrombotic cardiovascular events	The cardiovascular risks of Etoricoxib may increase with dose and duration of exposure. Therefore, the shortest duration possible and the lowest effective daily dose should be used. This information is included with appropriate wording in 4.2 Posology and method of administration and 4.4 Special warnings and precautions for use of the SPC. Clinical trials suggest that the selective COX-2 inhibitor class of drugs may be associated with a risk of thrombotic events (especially myocardial infarction (MI) and stroke), relative to placebo and some NSAIDs. Therefore, Etoricoxib should not be used in patients with established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease. This information is included with appropriate wording in 4.3 Contraindications of the SPC. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically, especially in patients with osteoarthritis (see sections 4.2, 4.3, 4.8 and 5.1). Patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with Etoricoxib after careful consideration (see section 5.1). COX-2 selective inhibitors are not a substitute for acetylsalicylic acid for prophylaxis of cardiovascular thrombo-embolic diseases because of their lack of antiplatelet effect. Therefore antiplatelet therapies should not be discontinued (see SPC sections above, 4.5 and 5.1). Medically appropriate supervision should be maintained when using Etoricoxib in the elderly and in patients with renal, hepatic, or cardiac dysfunction. This information is included in 4.4 Special warnings and precautions for use of the SPC. Undesirable effects regarding gastrointestinal disorders are listed in SPC section 4.8. Besides, pharmacodynamic properties have been discussed and the results of the studies of the MEDAL Programme are summarized in section 5.1. Etoricoxib should be used at the lowest effective dose and for the shortest duration possible. Since ulcers, bleedings and perforations of the stomach and small intestine can occur without any warning patients should understand the importance of periodic follow-ups. In the PIL this information is included with appropriate wording in 2. What you need to know before you take ETORICOXIB –Do not take ETORICOXIB and –Warnings and precautions; and 4. Possible side effects.	None proposed

Renovascular events: oedema, hypertension and congestive heart failure	As with other medicinal products known to inhibit prostaglandin synthesis, fluid retention, oedema and hypertension have been observed in patients taking Etoricoxib. Therefore, Etoricoxib should not be used in patients with congestive heart failure (NYHA II-IV) and patients with hypertension whose blood pressure is persistently elevated. This information is included in 4.3 Contraindications of the SPC. Caution should be exercised in patients with a history of cardiac failure, left ventricular dysfunction, or hypertension and in patients with pre-existing oedema from any other reason. If there is clinical evidence of deterioration in the condition of these patients, appropriate measures including discontinuation of Etoricoxib should be taken. Hypertension should be controlled before treatment with Etoricoxib (see section 4.3). This information is included with appropriate wording in 4.4 Special warnings and precautions for use. Undesirable effects regarding renovascular events are listed in SPC section 4.8. Besides, pharmacodynamic properties have been discussed and the results of the studies of the MEDAL Programme are summarized in section 5.1. In PIL this information is included with appropriate wording in 2. What you need to know before you take ETORICOXIB –Do not take ETORICOXIB and –Warnings and precautions; and 4. Possible side effects.	None proposed
Hypersensitivity-related events and serious skin reactions	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 NSAIDs and some selective COX-2 inhibitors during post-marketing surveillance (see section 4.8 of SPC). Serious hypersensitivity reactions (such as anaphylaxis and angioedema) have been reported in patients receiving etoricoxib (see section 4.8 of SPC). Therefore, Etoricoxib should not be used in patients with hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Etoricoxib is also contraindicated in patients who, after taking acetylsalicylic or NSAIDs including COX-2 (cyclooxygenase-2) inhibitors, experience bronchospasm, acute rhinitis, nasal polyps, angioneurotic oedema, urticaria, or allergic-type reactions. This information is included in 4.3 Contraindications of the SPC. Some selective COX-2 inhibitors have been associated with an increased risk of skin reactions in patients with a history of any drug allergy. Etoricoxib should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of	None proposed

	hypersensitivity. This information is included in 4.4 Special warnings and precautions for use. Undesirable effects regarding hypersensitivity-related events and serious skin reactions are listed in SPC section 4.8 of the SPC. In the PIL this information is included with appropriate wording in 2. What you need to know before you take ETORICOXIB –Do not take ETORICOXIB and 4. Possible side effects.	
Important Potential Risks		
None	Not applicable	Not applicable
Missing Information		
Use in pregnancy and lactating women	The following information is included in 4.3 Contraindications of SPC: Etoricoxib is contraindicated for pregnancy and lactation (see sections 4.6 and 5.3). The following text is included in SPC section 4.6 Fertility, pregnancy and lactation: No clinical data on exposed pregnancies are available for Etoricoxib. Studies in animals have shown reproductive toxicity (see section 5.3). The potential for human risk in pregnancy is unknown. Etoricoxib, as with other medicinal products inhibiting prostaglandin synthesis, may cause uterine inertia and premature closure of the ductus arteriosus during the last trimester. Etoricoxib is contraindicated in pregnancy (see section 4.3). 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 breast feed (see sections 4.3 and 5.3). The use of Etoricoxib, as with any drug substance known to inhibit COX-2, is not recommended in women attempting to conceive. Preclinical safety data have been summarised in section 5.3 of the SPC. In the PIL this information is included with appropriate wording in–Do not take ETORICOXIB; -Warnings and precautions and –Pregnancy, breast-feeding and fertility.	None proposed
Use in patients less than 16 years of age	There is not much experience with Etoricoxib in patients less than 16 years of age. Therefore, Etoricoxib is indicated in adults and adolescents 16 years of age and older. This information is included with appropriate wording in SPC section 4.1 Therapeutic indications. Etoricoxib is contra-indicated in children and adolescents under 16 years of age (sections 4.2 Posology and method of administration and 4.3 Contraindications). Pharmacokinetics have been discussed in section 5.2.	None proposed

	In the PIL this information is included with appropriate wording in 1. What ETORICOXIB is and what it is used for; -Do not take ETORICOXIB; -Warnings and precautions; 3. How to take ETORICOXIB and 5. How to store ETORICOXIB.	
Use in patients with renal insufficiency	Etoricoxib is contraindicated in patients with estimated renal creatinine clearance <30 ml/min. (SPC section 4.3 Contraindications). The following information is included in SPC section 4.4 Special warnings and precautions for use: Renal prostaglandins may play a compensatory role in the maintenance of renal perfusion. Therefore, under conditions of compromised renal perfusion, administration of Etoricoxib may cause a reduction in prostaglandin formation and, secondarily, in renal blood flow, and thereby impair renal function. Patients at greatest risk of this response are those with pre-existing significantly impaired renal function, uncompensated heart failure, or cirrhosis. Monitoring of renal function in such patients should be considered. Undesirable effects are listed section 4.8. Pharmacodynamics have been discussed in section 5.1. Pharmacokinetics have been discussed in section 5.2. In the PIL this information is included with appropriate wording in 2. What you need to know before you take ETORICOXIB –Do not take ETORICOXIB and –Warnings and precautions; and 4. Possible side effects.	None proposed
Use in patients with hepatic impairment	The following information is included in SPC section 4.2 Posology and method of administration. Regardless of indication, in patients with mild hepatic dysfunction (Child-Pugh score 5-6) a dose of 60 mg once daily should not be exceeded. In patients with moderate hepatic dysfunction (Child-Pugh score 7-9), regardless of indication, the dose of 30 mg once daily should not be exceeded. 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 contra-indicated in these patients (see sections 4.3, 4.4 and 5.2). The following information is included in SPC section 4.4 Special warnings and precautions for use: Elevations of alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) (approximately three or more times the upper limit of normal) have been reported in approximately 1% of patients in clinical trials	None proposed

	treated for up to one year with Etoricoxib 30, 60 and 90 mg daily. Any patients with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver function test has occurred, should be monitored. If signs of hepatic insufficiency occur, or if persistently abnormal liver function tests (three times the upper limit of normal) are detected, Etoricoxib should be discontinued. Undesirable effects are listed in section 4.8. Pharmacodynamics have been discussed in section 5.1. Pharmacokinetics have been discussed in section 5.2. In the PIL this information is included with appropriate wording in 2. What you need to know before you take ETORICOXIB –Do not take ETORICOXIB and –Warnings and precautions, 3. How to take ETORICOXIB and 4. Possible side effects.	

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Etoricoxib is indicated in adults and adolescents 16 years of age and older for the symptomatic relief of osteoarthritis (OA), rheumatoid arthritis (RA), ankylosing spondylitis, and the pain and signs of inflammation associated with acute gouty arthritis.

Etoricoxib is indicated in adults and adolescents 16 years of age and older for the short-term treatment of moderate pain associated with dental surgery.

Osteoarthritis (OA)

Osteoarthritis is the most common type of joint disease. Estimates of its frequency vary across different populations. Primary osteoarthritis is a common disorder of the elderly, and patients are often asymptomatic. Approximately 80-90% of individuals older than 65 years have evidence of radiographic primary osteoarthritis.

In individuals older than 55 years, the prevalence of osteoarthritis is higher among women than among men. Women are especially susceptible to osteoarthritis in the DIP joints of the fingers. Women also have osteoarthritis of the knee joints more frequently than men do. Women are also more prone to erosive osteoarthritis.

Interethnic differences in the prevalence of osteoarthritis have been noted. Symptomatic knee osteoarthritis is extremely common in China. In persons older than 65 years, osteoarthritis is more common in whites than in blacks. Knee osteoarthritis appears to be more common in black women than in other groups.

Rheumatoid arthritis (RA)

RA is a chronic systemic inflammatory disease of unknown cause. The annual incidence of RA is approximately 3 cases per 10,000 population, and the prevalence rate is approximately 1%, increasing with age and peaking between the ages of 35 and 50 years.

First-degree relatives of individuals with RA are at 2- to 3-fold higher risk for the disease. Disease concordance in monozygotic twins is approximately 15-20%, suggesting that nongenetic factors play an important role. Because the worldwide frequency of RA is relatively constant, an ubiquitous infectious agent has been postulated to play an etiologic role.

Women are affected by RA approximately 3 times more often than men are, but sex differences diminish in older age groups.

The main risk factors for the disease include genetic factors, sex, age, smoking, infectious agents, hormonal, dietary, socioeconomic and ethnic factors.

Ankylosing spondylitis (AS)

AS is a chronic, multisystem inflammatory disorder primarily involving the sacroiliac joints and the axial skeleton. AS is the most common of the classic spondyloarthropathies. Prevalence varies with the prevalence of the HLA-B27 gene in a given population, which increases with distance from the equator. It occurs in 0.1-1% of the general population, with the highest prevalence in northern European countries and the lowest in sub-Saharan Africa. In general, AS is more common in whites than in non-whites.

The age of onset of AS is usually from the late teens to age 40 years. Approximately 10%-20% of all patients experience symptom onset before age 16 years; in such patients, the disease is referred to as juvenile-onset AS. Onset of AS in persons older than 50 years is unusual. AS, in general, is diagnosed more frequently in males (3:1).

Pain

Etoricoxib is indicated in adults and adolescents 16 years of age and older for the symptomatic relief of the pain and signs of inflammation associated with acute gouty arthritis and for the short-term treatment of moderate pain associated with dental surgery.

Pain is a common complaint among adults, with almost one-fifth reporting general pain, one-third shoulder pain, and up to one-half reporting lower back pain. Acute pain (pain starting suddenly and for shorter duration of time) is the most common symptom for which patients seek medical care. More than half of cases of long standing pain is related to pain of muscles, bones and joints. Approximately, 10% of the general population in the Western suffers from chronic pain of muscles, bones and joints, and is frequent among women as compared with men.

VI.2.2 Summary of treatment benefits

Across studies, Etoricoxib produced dose-dependent inhibition of COX-2 without inhibition of COX-1 at doses up to 150 mg daily and did not inhibit gastric prostaglandin synthesis and had no effect on platelet function.

In patients with osteoarthritis (OA), Etoricoxib 60 mg provided significant improvements in pain and patient assessments of disease status. These beneficial effects were observed as early as the second day of therapy and maintained for up to 52 weeks. Studies with Etoricoxib 30 mg once daily demonstrated efficacy superior to placebo over a 12 week treatment period. In a dose ranging study, Etoricoxib 60 mg demonstrated significantly greater improvement than 30 mg for all 3 primary endpoints over 6 weeks of treatment.

In patients with rheumatoid arthritis (RA), Etoricoxib 90 mg once daily provided significant improvements in pain, inflammation, and mobility. These beneficial effects were maintained over the 12-week treatment periods.

In patients experiencing attacks of acute gouty arthritis, Etoricoxib 120 mg once daily over an eight day treatment period, relieved moderate to extreme joint pain and inflammation comparable to indomethacin 50 mg three times daily. Pain relief was observed as early as four hours after initiation of treatment.

In patients with ankylosing spondylitis, Etoricoxib 90 mg once daily provided significant improvements in spine pain, inflammation, stiffness and function. The clinical benefit of Etoricoxib was observed as

early as the second day of therapy after initiation of treatment and was maintained throughout the 52-week treatment period.

In a clinical study evaluating postoperative dental pain, in the subgroup of patients with moderate pain at baseline, Etoricoxib 90 mg demonstrated a similar analgesic effect to that of ibuprofen 600 mg and greater than that of paracetamol/codeine 600 mg/60 mg and placebo.

VI.2.3 Unknowns relating to treatment benefits

There is insufficient data on the use of Etoricoxib in children and adolescents under 16 years of age therefore Etoricoxib is not recommended for use in children and adolescents younger than 16.

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 synthesis, may cause uterine inertia and premature closure of the ductus arteriosus during the last trimester. Etoricoxib is therefore contraindicated in pregnancy. If a woman becomes pregnant during treatment, Etoricoxib must be discontinued.

It is also not known whether Etoricoxib is excreted in human milk. Etoricoxib is excreted in the milk of lactating rats. Women who use Etoricoxib are recommended not to breast feed.

Etoricoxib has not been studied in patients who have severe kidney impairment and should not be used in such patients.

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 contra- indicated in these patients.

VI.2.4 Summary of safety concerns

Important identified risks

Etoricoxib 30mg/60mg/90mg/120mg Film-Coated Tablets		
Risk	**What is known**	**Preventability**
Serious gastrointestinal events	Upper gastrointestinal complications [perforations, ulcers or bleedings], some of them causing death, have occurred in patients taking Etoricoxib. Caution is advised with treatment of patients most at risk of developing a gastrointestinal complication with NSAIDs; the elderly, patients using any other NSAID or aspirin at the same time, or patients with a history of gastrointestinal disease, such as ulceration and gastrointestinal bleeding. There is further increase in the risk of gastrointestinal side effects for Etoricoxib (gastrointestinal ulceration or other gastrointestinal complications), when Etoricoxib is taken at the same time as aspirin (even at low doses). In rat, gastrointestinal toxicity of Etoricoxib increased with dose and exposure time. Gastroduodenal ulcer, peptic ulcers	This risk has been minimized by warning physicians and patients by including this risk with appropriate wording in different sections of SPC and PIL. Etoricoxib is advised not to be used in patients with active peptic ulceration or active gut bleeding.

Etoricoxib 30mg/60mg/90mg/120mg Film-Coated Tablets		
Risk	**What is known**	**Preventability**
	including gastrointestinal perforation and bleeding is uncommon and may affect 1 to 10 users in 1000. Signs of bleeding may include passing black or bloodstained stools or vomiting blood.	
Thrombotic cardiovascular events	Studies suggest that the selective COX-2 inhibitor class of drugs may be associated with a risk of thrombotic events (blood clots in de arteries/veins leading to diseases especially myocardial infarction (MI, heart attack) and stroke), relative to placebo and some NSAIDs. The cardiovascular risks of Etoricoxib may increase with dose and duration of exposure. Therefore, the shortest duration possible and the lowest effective daily dose should be used in patients. Cardiovascular disorders such as myocardial infarction (heart attack), cerebrovascular accident (stroke), transient ischaemic attack (mini-stroke), and vasculitis (inflammation of the blood vessels) are uncommon and may affect 1 to 10 users in 1000.	The physicians are advised to treat the risk group of patients at the lowest effective daily dose and the shortest duration possible. The physicians and the patients are advised not to use Etoricoxib if the patients suffer from established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease. Caution is advised when treating patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking). Patients having any signs or symptoms of such events should report them promptly to their physicians.
Renovascular events: oedema, hypertension and congestive heart failure	In patients with impaired blood flow to the kidneys due to any reason, certain mediators maintain the perfusion of the kidneys. Use of non-selective non-steroidal anti-inflammatory agents (NSAIDs that block both COX enzymes, COX-1 and COX-2) in such patients blocks the production of these compensatory mediators and compromises blood flow to the kidneys. This leads to impairment of kidney function. Impairment of blood flow to the kidneys and kidney function may lead to fluid build-up in the legs and feet (oedema), high blood pressure and congestive heart failure. Patients at risk of such events are those with pre-existing impaired kidney function, heart failure or oedema. Also Etoricoxib, which is a selective COX-2 inhibitor, can increase blood pressure in some people especially at high doses. Cardiovascular disorders such as palpitations (fast or irregular heart beat), arrhythmia (irregular heart rhythm), hypertension are common and may affect 1 to 10 users in 100 and atrial fibrillation (abnormal heart rhythm), tachycardia (fast	Etoricoxib should not be used in patients with advanced kidney impairment, persistent uncontrolled high blood pressure (blood pressure is persistently elevated above 140/90mmHg and has not been adequately controlled). and moderate and severe congestive heart failure. (NYHA II-IV), Blood pressure should be monitored frequently in patients on etoricoxib. Patients having any signs or symptoms of oedema, high blood pressure and congestive heart failure should report them promptly to their physicians. The physicians are advised to treat the risk group of patients at the lowest effective daily dose and the shortest duration possible.

Etoricoxib 30mg/60mg/90mg/120mg Film-Coated Tablets		
Risk	**What is known**	**Preventability**
	heart rate), congestive heart failure, nonspecific ECG changes, angina pectoris (pressure or heaviness in the chest), flushing, hypertensive crisis (severe increase in blood pressure) are uncommon and may affect 1 to 10 users in 1000.	
Hypersensitivity-related events and serious skin reactions	Angioedema (an allergic reaction with swelling of the face, lips, tongue and/or throat which may cause difficulty in breathing or swallowing, which may be serious enough to require immediate medical attention), anaphylactic/ anaphylactoid reactions including shock (a serious allergic reaction that requires immediate medical attention) have been reported rarely in patients treated with Etoricoxib and may affect 1 to 10 users in 10,000. Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis (red, itchy and scaly skin and severe ulcerations of the mucous membranes and skin), have been reported very rarely with Etoricoxib. 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. Swelling of the face, skin rash or itchy skin, redness of the skin are uncommon observed side effects and may affect 1 to 10 users in 1,000. Severe skin reactions are observed very rarely and may affect 1 to 10 users in 10,000. Etoricoxib should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.	The patients and the physicians are advised not to use Etoricoxib if the patients are allergic to Etoricoxib or to any of the other ingredients of this medicine. Patients should be alert to the signs and symptoms of allergic reactions and serious skin reactions and visit their doctor immediately, should these occur. The physicians and the patients are warned to discontinue Etoricoxib at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Important potential risks

Etoricoxib 30mg/60mg/90mg/120mg Film-Coated Tablets	
Risk	**What is known**
None	

Missing information

Etoricoxib 30mg/60mg/90mg/120mg Film-Coated Tablets	
Risk	**What is known**
Use in pregnancy and lactating women	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 should not be used in pregnancy. If a woman becomes pregnant during treatment, Etoricoxib must be discontinued. It is also not known whether Etoricoxib is excreted in human milk. Etoricoxib is excreted in the milk of lactating rats. Women who use Etoricoxib must not breast feed. Etoricoxib is not recommended in women attempting to become pregnant.
Use in patients less than 16 years of age	There is not much experience with Etoricoxib in children and adolescents under 16 years of age. Therefore, Etoricoxib is indicated in adults and adolescents 16 years of age and older.
Use in patients with renal insufficiency	Etoricoxib can reduce kidney function and may lead to fluid retention, swelling (oedema) and high blood pressure. Patients at greatest risk of this response are those with pre-existing reduced kidney function, heart failure, or serious liver problems. If there is clinical evidence of deterioration in the condition of these patients, appropriate measures including discontinuation of Etoricoxib should be taken. Monitoring of renal function in such patients is important. Etoricoxib may be associated with more frequent and severe hypertension than some other NSAIDs and selective COX-2 inhibitors, particularly at high doses. Therefore, hypertension should be controlled before treatment with Etoricoxib and special attention should be paid to blood pressure monitoring during treatment with Etoricoxib. Blood pressure should be monitored within two weeks after initiation of treatment and periodically thereafter. If blood pressure rises significantly, alternative treatment should be considered. Swelling of the legs and/or feet due to fluid retention (oedema), increased blood pressure is common and may affect 1 to 10 users in 100. High levels of potassium in blood, change in blood and urine tests related to kidney, serious kidney problems is uncommon and may affect to 1 to 10 users in 1,000. Low blood levels of sodium may affect 1 to 10 users in 10,000 (rare).
Use in patients with hepatic impairment	Clinical experience is limited particularly in patients with moderate hepatic dysfunction and caution is advised. There is no clinical experience in patients with severe liver problems. Therefore, Etoricoxib should not be used in these patients. If the patients have mild liver disease, they should not take Etoricoxib more than 60 mg per day and if they have moderate liver disease, they should not take more than 30 mg Etoricoxib. Changes in blood tests related to liver (approximately three or more times the upper limit of normal) have been reported in approximately 1% of patients in studies treated for up to one year with Etoricoxib 30, 60 and 90 mg daily. Any patients with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver function test has occurred, should be monitored. If signs of liver problems occur, or if persistently abnormal liver function tests (three times the upper limit of normal) are detected, Etoricoxib should be discontinued. Changes in blood tests related to liver are common and may affect 1 to 10 users in 100.

Etoricoxib 30mg/60mg/90mg/120mg Film-Coated Tablets	
Risk	**What is known**
	Liver problems (hepatitis), liver failure, yellowing of the skin and/or eye are rare and may affect 1 to 10 users in 10,000

VI.2.5 Summary of risk minimisation measures by safety concern

Summary of Product Characteristics (SPC) of Etoricoxib 30mg/60mg/90mg/120mg film-coated tablets 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 has been provided in the form of the package leaflet (PIL).

Etoricoxib 30mg/60mg/90mg/120mg film-coated tablets has no additional risk minimisation measures.

Safety concern in lay terms (medical term)

Not applicable.

VI.2.6 Planned post authorisation development plan

Not applicable.

List of studies in post authorisation development plan

Not applicable.

Studies which are a condition of the marketing authorisation

Not applicable.

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

Not applicable, since this is the first version of the RMP.