VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Pre-term birth

A baby is born 'pre-term' if he or she is born before 37 weeks of pregnancy have been completed. Normally, a pregnancy lasts about 40 weeks.
Pre-term birth happens for many different reasons, like being pregnant with more than one baby, infections and permanent conditions, such as diabetes and high blood pressure. A history of pre-term labour increases the risk, as does not gaining sufficient weight, suffering from anaemia (lack of enough red blood cells) during pregnancy and smoking or drinking alcohol. However, often no reason can be found. There is also a genetic influence [5, 6, 7].

Premature birth can be dangerous for both mother and child because it is a departure from the normal progress of pregnancy. Babies in particular can have many health problems as a result of premature birth, ranging from breathing difficulties or neurological disorders to potential death. Doctors and mothers usually take a number of steps to keep the baby or babies in the womb for as long as possible. If at all possible, labour will be delayed with medications that slow or stop contractions of the womb (so called tocolytic drugs) [7, 8].

VI.2.2 Summary of treatment benefits

A tocolytic agent is a drug given to a pregnant woman to stop labour and delay pre-term birth. The delay allows to give the mother steroid hormones to develop the lungs of the unborn baby and reduce the chance of breathing difficulties and potential death. The delay also gives enough time to transfer the pregnant woman to a health care facility that can handle the care of a pre-term baby [9, 10, 11, 12, 13].

There are several studies that compare the effectiveness of different types of tocolytic drugs:
They show that other tocolytic drugs cause more unwanted side effects than atosiban, like a fast heart beat and an unpleasant sensation of irregular or forceful beating of the heart, as well as uncontrolled trembling or shaking. These effects do not occur during treatment with atosiban.

In a study comparing different tocolytics, atosiban and another type of tocolytic drug (prostaglandin synthesis inhibitor) were the only drugs not associated with serious adverse drug reactions.

Atosiban is the best tolerated tocolytic drug and in general is not associated with serious unwanted drug reactions [3].

VI.2.3 Unknowns relating to treatment benefits

Patients with liver problems

There is no experience with atosiban treatment in patients with liver problems. In patients with liver problems, atosiban should be used with caution.

Patients with kidney problems

There is no experience with atosiban treatment in patients with kidney problems. Adjusting the dose is not likely to be needed, as only a small amount of atosiban is eliminated with the urine.

Women less than 18 years old

Atosiban EVER Pharma has not been studied in pregnant women less than 18 years old. Atosiban EVER Pharma is not intended for use in women less than 18 years of age.

Interaction with other medicines that can delay the birth of the baby , antibiotics and medicines that lower the blood pressure

When used in combination with other medicines that can delay the birth of the baby, adverse reactions like shortness of breath or accumulation of fluid in the lungs are possible.

There is not enough experience with atosiban treatment in patients treated with antibiotics and medicines that lower the blood pressure.

Multiple pregnancies

There is no experience with atosiban treatment in patients with multiple pregnancies.

VI.2.4 Summary of safety concerns

Important identified risk

Risk	What is known	Preventability
Shortness of breath and accumulation of fluid in the lungs (dyspnoea and pulmonary oedema)	Caution is needed if the mother is pregnant with more than one baby and/or is given other medicines that can delay the birth of the baby, such as medicines used for high blood pressure. This may increase the risk of shortness of breath and accumulation of fluid in the lungs.	Yes, by using Atosiban EVER Pharma with care if the mother is pregnant with more than one baby and/or is given other medicines that can delay the birth of the baby, such as medicines used for high blood pressure.

Important potential risk

Risk	What is known	Preventability
Harm to the unborn (fetal harm)	There are no known side effects on the unborn or new-born baby. It is not known if there might be any side effects on the unborn if the drug is administered during the very beginning of the pregnancy.	Yes, by using Atosiban EVER Pharma only when pre-term pregnancy has been diagnosed between 24 and 33 completed weeks of pregnancy.
Use of the drug for an unapproved reason (off label)	Atosiban is sometimes used although pregnancy week 24 is not completed.	Yes, by using Atosiban EVER Pharma only when pre-term pregnancy has been diagnosed between 24 and 33 completed weeks of pregnancy.
Urinary tract infection	There is currently not enough evidence that atosiban might cause urinary tract infection. However, urinary tract infections are known to cause pre-term birth and this might be the reason that urinary tract infections are linked with atosiban.	Unknown
Medication error	EVER Neuro Pharma introduced an additional strength, i.e. Atosiban EVER Pharma 75 mg/10 ml concentrate for solution for infusion, containing the same concentration of atosiban as Atosiban EVER Pharma 37.5 mg/5 ml	Unknown

Risk	What is known	Preventability
	concentrate for solution for infusion - each ml of solution contains 7.5 mg atosiban. As the 75 mg/10 ml strength is not available with the originator product there is a potential risk that, by mistake, two vials of Atosiban EVER Pharma 75 mg/10 ml concentrate for solution for infusion are used to prepare the intravenous infusion solution as it is necessary with the originator product that contains 37.5 mg/5 ml of atosiban.	

Missing information

Risk	What is known
Limited information on use in patients with liver problems.	There is no experience with atosiban treatment in patients with liver problems. In patients with liver problems, atosiban should be used with caution.
Limited information on use in patients with kidney problems.	There is no experience with atosiban treatment in patients with kidney problems. Adjusting the dose is not likely to be needed, as only a small amount of atosiban is eliminated with the urine.
Women less than 18 years old	Atosiban EVER Pharma has not been studied in pregnant women less than 18 years old. Atosiban EVER Pharma is not intended for use in women less than 18 years of age.
Interaction with other medicines that can delay the birth of the baby , antibiotics and medicines that lower the blood pressure	When used in combination with other medicines that can delay the birth of the baby, adverse reactions like shortness of breath or accumulation of fluid in the lungs are possible. There is not enough experience with atosiban treatment in patients treated with antibiotics and medicines that lower the blood pressure.
Multiple pregnancies	There is no experience with atosiban treatment in patients with multiple pregnancies.

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.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

N/A

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

Version	Date	Safety Concerns	Comment
1.2	30. December 2015	Dyspnoea and pulmonary oedema	This safety concern has been added to the important identified risks.
1.2	30. December 2015	Fetal harm	This safety concern has been added to the important potential risks.
1.2	30. December 2015	Off label use	This safety concern has been added to the important potential risks.
1.2	30. December 2015	Urinary tract infection	This safety concern has been added to the important potential risks.
1.2	30. December 2015	Interaction with other tocolytics, antibiotics and anti-hypertensive agents	This safety concern has been added to the missing information.
1.2	30. December 2015	Multiple pregnancies	This safety concern has been added to the missing information.
1.3	21. March 2016	Medication error	This safety concern has been added to the important potential risks.