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RMP section VI.2 Elements for Public Summary

Product: Atosiban Stragen, 6,75mg/0,9ml solution for injection
Atosiban Stragen, 37,5mg/5ml concentrate for solution for infusion

RMP: RMP-PID-ATO-v03

DLP: 13-02-2017

MAH: Stragen Nordic A/S

2. Elements for a public summary

2.1. Overview of disease epidemiology

The target population for use of medicinal products Atosiban <to be completed nationally> are pregnant adult women with risk of preterm birth.

The preterm birth, defined as childbirth occurring at less than 37 completed weeks of gestation, is a major reason of neonatal mortality and morbidity and has long-term adverse consequences for health. The preterm birth occurs in 5-10% of pregnancies in developed countries due to high blood pressure and pre-eclampsia. In developing countries the preterm birth occurs in 25% of pregnancies, mainly due to infection. Other causes of premature birth include multiple pregnancy, intrauterine growth restriction, maternal stress and heavy physical work.

2.2. Summary of treatment benefits

The medicinal products Atosiban <to be completed nationally> are intended to delay the preterm birth in pregnant adult women.

Atosiban <to be completed nationally> works by blocking the effect of a natural hormone called “oxytocin” and making the contractions in womb (*uterus*) less strong. It also makes the contractions happen less often.

2.3. Unknowns relating to treatment benefits

The safety and efficacy of Atosiban <to be completed nationally> have not been established:

- in patients with kidney or liver problems,
- in pregnant women aged less than 18 years,
- in women with multiple pregnancies.

Medicines that can delay the birth of baby, such as medicines used for high blood pressure, particularly in association with concomitant administration of other medicines to delay the preterm birth, may increase the risk of lung oedema (accumulation of fluid in the lungs).

2.4. Summary of safety concerns

The summary of safety concerns is proposed below in table 6.

Table 6: **Summary of safety concerns**

Important identified risks

Risk	What is known	Preventability
• lung oedema (accumulation of fluid in the lungs)	Multiple pregnancy and other medicines products to delay the preterm birth has known to be associated with increased risk of lung oedema in pregnant women..	Yes: Atosiban should be used with caution in case of multiple pregnancy and/or concomitant administration of other medicines products to delay the preterm birth.

Important potential risks

• foetal harm	An abnormal heart rate (tachycardia) could develop for unborn baby (foetus).	Yes: The monitoring of uterine contractions and foetal heart rate during administration of atosiban and in case of persistent uterine contractions should be considered.
• off-label use	There are two medicinal products (Atosiban <to be completed nationally> 6.75 mg/0.9 ml solution for injection and Atosiban <to be completed nationally> 37.5 mg/5 ml concentrate for solution for infusion) available.	Yes: • treatment with atosiban should be initiated and maintained by a physician experienced in the treatment of preterm labour; • Atosiban should be given intravenously in three successive stages; • Atosiban should not be mixed with other medicinal products in the infusion bag.

• urinary tract infection	The increased risk of premature rupture of membranes and intra-amniotic inflammation are possible.	Yes: When atosiban is used in patients in whom premature rupture of membranes cannot be excluded, the benefits of delaying delivery should be balanced against the potential risk of chorioamnionitis

Missing information

Risk	**What is known** (including reason why it is considered a potential risk)
• multiple pregnancy	Multiple pregnancy and medicines to delay the preterm birth has known to be associated with increased risk of lung oedema in pregnant women. Therefore, atosiban should be used with caution in case of multiple pregnancy.
• women less than 18 years	The safety and efficacy of atosiban in pregnant women aged less than 18 years have not been established.
• interaction with other tocolytics, antihypertensive agents and antibiotics	*Antihypertensive agents* The data regarding to interaction between atosiban and antihypertensive agents are not available in the published scientific literature. Respiratory events like dyspnoea and lungy oedema, particularly in association with concomitant administration of other medicines to delay the preterm birth, like calcium antagonists and beta mimetics have been reported. *Antibiotics* The possible interaction between atosiban and antibiotics is not sufficiently investigated.
• use in patients with hepatic or renal impairment	*Hepatic insufficiency* There is no experience with atosiban treatment in patients with impaired function of the liver. Therefore, atosiban should be used with caution in patients with impaired hepatic function. *Renal insufficiency* There is no experience with atosiban treatment in patients with impaired function of the kidneys. Renal impairment is not likely to warrant a dose adjustment, since only a small extent of atosiban is excreted in the urine. However, atosiban should be used with caution

Risk	What is known (including reason why it is considered a potential risk)
	in patients with impaired kidney function.

2.5. Summary of risk minimisation measures by safety concern

Routine risk minimisation measures are proposed in the SPC and PIL excluding the only safety concern in patients of different racial and/or ethnic origin. In accordance with available literature data, ethnic differences can explain only a very small proportion of global preterm births.

This medicine has no additional risk minimisation activities regarding to safety concerns.

The applicant assumes an obligation to keep to the Reference product information, as well as published scientific literature data regarding to any information changes.

2.6. Planned post-authorisation development plan

The PSUR is not required for a product referred to in Article 10(1) of Directive 2001/83/EC. Applicant will monitor, summarise and report AEs in usual pharmacovigilance system, presented in the Marketing Application.