הודעה על החמרה (מידע בטיחות) בעלון לרופא

(מעודכן 05.2013)

אושר – 3.16

תאריך _____07.02.2016____

שם תכשיר באנגלית ומספר הרישום:

1. ATOSIBAN- 119 10 29995 01

שם בעל הרישום: _FERRING PHARMACEUTICALS LTD.

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
Patients with renal or hepatic impairment There is no experience with atosiban treatment in patients with impaired function of the liver or kidneys. Renal impairment is not likely to warrant a dose adjustment, since only a small extent of atosiban is excreted in the urine. In patients with impaired hepatic function, atosiban should be used with caution. Paediatric population The safety and efficacy of atosiban in pregnant women aged less than 18 years have not been established. No data are available.	There is no data available regarding the need for dose adjustments in patients with renal or liver insufficiency	**Posology and method of administration**
Atosiban should not be used in the following conditions: - Gestational age below 24 or over 33 completed weeks - Premature rupture of the membranes >30 weeks of gestation -Abnormal Foetal heart rate - - Antepartum uterine haemorrhage requiring immediate delivery - Eclampsia and severe pre-eclampsia requiring	Atosiban should not be used in the following conditions: - Gestational age below 24 or over 33 completed weeks - Premature rupture of the membranes >30 weeks of gestation - Intrauterine growth retardation and abnormal foetal heart rate - Antepartum uterine haemorrhage requiring immediate delivery - Eclampsia and severe pre-eclampsia requiring delivery	**Contraindications**

delivery - Intrauterine foetal death - Suspected intrauterine infection - Placenta praevia - Abruptio placenta - Any other conditions of the mother or foetus, in which continuation of pregnancy is hazardous - Hypersensitivity to the active substance or any of the excipients listed in section 6.1.	- Intrauterine foetal death - Suspected intrauterine infection - Placenta praevia - Abruptio placenta - Any other conditions of the mother or foetus, in which continuation of pregnancy is hasardous - Known hypersensitivity to the active substance or any of the excipients.	
There is no experience with Atosiban treatment in patients with impaired function of the liver or kidneys. Renal impairment is not likely to warrant a dose adjustement, since only a small extent of atosiban is excreted in the urine. In patients with impaired hepatic function atosiban should be used with caution Multiple pregnancy and medicinal products with tocolytic activity like calcium channel blockers and beta-mimetics are known to be associated with increased risk of pulmonary oedema. Therefore, atosiban should be used with caution in case of multiple pregnancy and/or concomitant administration of other medicinal products with tocolytic activity (see section 4.8).	There is no experience with Atosiban treatment in patients with impaired function of the liver or kidneys. -	**Special warnings and precautions for use**
It is unlikely that atosiban is involved on cytochrome P450 mediated drug-drug interactions as in vitro investigations have shown that atosiban is not a substrate for the cytochrome P450 system, and does not inhibit the drug metabolizing cytochrome P450 enzymes. Interaction studies have been performed with labetalol and betamethasone in healthy, female volunteers. No clinically relevant interaction was found between atosiban and bethamethasone or labetalol.	It is unlikely that atosiban is involved on cytochrome P450 mediated drug-drug interactions as in vitro investigations have shown that atosiban is not a sustrate for the cytochrome P450 system, and does not inhibit the drug metabolizing cytochrome P450 enzymes. Interaction studies were performed in healthy, female volunteers with betamethasone and labetalol. No clinically relevant interaction was observed between atosiban and betamethasone. When atosiban and labetalol were co-administered, Cmax of labetalol was decreased by 36% and Tmax increased by 45 minutes. However, the extent of labetalol bioavailability in terms of AUC did not change. The interaction observed has no clinical relevance. Labetalol had no effect on Atosiban pharmacokinetics. No interaction study has been perfomed with antibiotics, ergot alkaloids, and anti-hypertensive agents other than labetalol.	
Fertility, pregnancy and lactation Atosiban should only be used when pre-term labour has been diagnosed between 24 and 33 completed	Atosiban should only be used when pre-term labour has been diagnosed between 24 and 33 completed weeks of gestation. In Atosiban clinical trials, no effects were	**Pregnancy and lactation**

weeks of gestation. If during pregnancy the woman is already breast-feeding an earlier child, then breast-feeding should be discontinued during treatment with Atosiban, since the release of oxytocin during breast-feeding may augment uterine contractility, and may counteract the effect of tocolytic therapy. In Atosiban clinical trials, no effects were observed on lactation. Small amounts of atosiban have been shown to pass from plasma into the breast milk of lactating women. Embryo-fetal toxicity studies have not shown toxic effects of atosiban. No studies were performed that covered fertility and early embryonic development (see section 5.3).	observed on lactation. Small amounts of atosiban have been shown to pass from plasma into the breast milk of lactating women Embryo-fetal toxicity studies have not shown toxic effects of atosiban. No studies were performed that covered fertility and early embryonic development.	
טקסט נוכחי: Possible undesirable effects of atosiban were described for the mother during the use of Atosiban in clinical trials. The observed undesirable effects were generally of a mild severity. In total 48% of the patients treated with Atosiban experienced undesirable effects. For the newborn, the clinical trials did not reveal any specific undesirable effects of atosiban. The infant adverse events were in the range of normal variation and were comparable with both placebo and beta-mimetic group incidences. The undesirable effects in the women were the following: Very common (>10%) — Nausea Common (1-10%) — Central & peripheral nervous system disorders: headache, dizziness Body as a whole – general disorders: hot flushes intestinal system disorders: vomiting Cardiovascular disorders: tachycardia, hypotension Application site disorders: injection site reaction Metabolic and nutritional disorders: hyperglycaemia Uncommon (0.1-1%) — Body as a whole - general disorders: fever disorders: insomnia Skin and disorders: pruritis, rash Rare (<0.1%) — Incidental cases of uterine haemorrhage/uterine atony were reported. The frequency did not exceed that of the control groups in clinical trials.		**Undesirable effects**
טקסט חדש: Possible adverse reactions of atosiban were described for the mother during the use of Atosiban in clinical trials. In total 48% of the patients treated with atosiban experienced adverse reactions during clinical trials. The observed adverse reactions were generally of a mild severity. The most commonly reported adverse reaction in the mother is nausea (14%). For the newborn, the clinical trials did not reveal any specific undesirable effects of atosiban. The infant adverse reactions were in the range of normal variation and were comparable with both placebo and beta-mimetic group incidences. The frequency of adverse reactions listed below is defined using the following convention: Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.		

MedDRA System Organ (SOC)	Very common	Common	Uncommon	Rare
Immune system disorders				Allergic reaction
Metabolism and nutrition		Hyperglycemia		
Psychiatric disorders			Insomnia	
Nervous system disorders		Headache Dizziness		
Cardiac disorders		Tachycardia		
Vascular disoorders		Hypotention Hot flush		
Gastrointestinal disorders	Nausea	Vomiting		
Skin and subcutaneous tissue disorders			Pruritis Rash	
Reproductive system and breast cancer disorder				Uterine haemorrage, Uterine atony
General disorders and administration site conditions		Injection site reaction	pyrexia	

Post-marketing experience

Respiratory events like dyspnoea and pulmonary oedema, particularly in association with concomitant administration of other medicinal products with tocolytic activity, like calcium antagonists and beta-mimetics, and/or in women with multiple pregnancy, have been reported post-marketing.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form

http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

מצ"ב העלון, שבו מסומנות ההחמרות המבוקשות על רקע צהוב.

שינויים שאינם בגדר החמרות סומנו (בעלון) בצבע שונה. יש לסמן רק תוכן מהותי ולא שינויים במיקום הטקסט.

הועבר בדואר אלקטרוני בתאריך...07.02.2016.

.....