ספטמבר 2023

רוקח/ת נכבד/ה,רופא/ה נכבד/ה,

חברת פרופארם בע"מ מודיעה על העדכונים הבאים בעלון לרופא של התכשיר:

ATOSIBAN ALTAN

אטוסיבן אלטן

חומר פעיל: ATOSIBAN 7.5 MG/ML

צורת מינון: SOLUTION FOR INJECTION / CONCENTRATE FOR SOLUTION FOR INFUSION

צורת המתן: I.V.

עדכונים בעלון לרופא

התויה כפי שאושרה בתעודת הרישום:

Atosiban Altan is indicated to delay imminent pre-term birth in pregnant women with:
- regular uterine contractions of at least 30 seconds duration at a rate of 4 or more per 30 minutes
- a cervical dilation of 1 to 3 cm (0-3 for nulliparas) and effacement of 50 % or more
- age: 18 years and above - a gestational age from 24 until 33 completed weeks
- a normal foetal heart rate.

ברצונינו להודיע שהעלונים עודכנו, בפירוט שלהלן כלולים העדכונים העיקריים בלבד(תוספות /שינויים מסומנים באדום והחמרות/מידע חדש על רקע צהוב):

עדכונים עיקריים בעלון לרופא:

1. TRADE NAME OF THE MEDICINAL PRODUCT

Atosiban Altan
~~Solution for injection and concentrate for solution for infusion~~

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml solution contains 7.5 mg atosiban base in the form of atosiban acetate.
Solution for injection: each ampoule of 0.9 ml solution contains 6.75 mg atosiban (as acetate).
Concentrate for solution for infusion: each vial of 5 ml solution contains 37.5 mg atosiban (as acetate). ~~Concentrate:~~
After dilution ~~according to the instructions (see section "Pharmaceutical Particulars for instructions for use and handling")~~, the concentration of atosiban is ~~Altan is~~ 0.75 mg/ml.
For a full list of excipients, ~~excipients see "list of excipients"~~see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection/ ~~and~~ concentrate for solution for infusion.
Clear, colourless solution without particles.

4. CLINICAL PARTICULARS

[…]

4.2 Posology and method of administration

Posology

[…]

Atosiban Altan is administered intravenously in three successive stages: an initial bolus dose (6.75 mg), performed with Atosiban Altan 6.75 ml/0.9ml solution for injection, immediately followed by a continuous high dose infusion (loading infusion 300 µg/min) of Atosiban Altan 37.5 mg/5 ml concentrate for solution for infusion during three hours, followed by a lower dose of Atosiban Altan 37.5 mg/5 ml concentrate for solution for infusion (subsequent infusion 100 µg/min) up to 45 hours. The duration of the treatment should not exceed 48 hours. The total dose given during a full course of Atosiban Altan therapy should preferably not exceed 330.75 mg of the active substance.

Propharm Ltd., P.O.B. 4046, Zichron Yaacov 30900, Israel, Tel. +972-4-6294242, Fax. +972-4-6392049
Email: info@propharm.co.il , Web: www.propharm.co.il

[…]

The following table shows the full posology of the bolus injection followed by the infusion:

Step	Regimen	~~Injection~~/infusion rate	Atosiban dose
1	0.9 ml intravenous bolus injections given over 1 minute	Not applicable ~~Over 1 minute~~	6.75 mg
2	3 hours intravenous loading infusion	24 ml/hour (300 µg/min)	54 mg
3	Up to 45 hours subsequent intravenous infusion	8 ml/hour (100 µg/min)	Up to 270 mg

[…]

Method of administration

For ~~4.4~~ instructions on preparation of the medicinal product before administration, see section 6.6.

4.~~3~~4 Contraindications

Atosiban Altan ~~should~~ must 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 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 to any of the excipients listed in section 6.1.

[…]

4.~~6~~7 Fertility, pregnancy and lactation

Atosiban should only be used when pre-term labour has been diagnosed between 24 and 33 completed weeks of gestation.

If during pregnancy the woman is already breast-feeding an earlier child, then breastfeeding should be discontinued during treatment with Atosiban Altan, since the release of oxytocin during ~~lactating~~ breastfeeding may augment uterine contractility, and may counteract the effect of tocolytic therapy.

[…]

4.8 Undesirable effects

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 the 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 affects~~ adverse reactions of atosiban. The infant adverse reactions were in the range of normal variation and were comparable with both placebo and beta-mimetic group incidences.

[…]

MedDRA System Organ (SOC) Class	Very common	Common	Uncommon	Rare
Immune system disorders				Allergic reaction
Metabolism and nutrition disorders		Hyperglycaemia		

[…]

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

[…]

Phase III clinical trials (CAP-001 studies) include data from 742 women who were diagnosed with pre-term labour at 23–33 weeks of gestation and were randomised to receive either atosiban ~~altan (~~according to this labelling) or β-agonist (dose-titrated).

[…]

Of the 361 women who received atosiban ~~altan~~ treatment in the phase III studies, 73 received at least one re-treatment, 8 received at least 2 re-treatments and 2 received 3 re-treatments (see section 4.4).

As the safety and efficacy of atosiban in women with a gestational age of less than 24 completed weeks has not been established in controlled randomised studies, the treatment of this patient group with atosiban is not recommended (see section 4.3 ~~Contraindications~~).

In a placebo-controlled study, foetal/infant deaths were 5/295 (1.7%) in the placebo group and 15/288 (5.2%) in the atosiban group, ~~at~~ of which two occurred at five and eight months of age. Eleven out of the 15 deaths in the atosiban group occurred in pregnancies with a gestational age of 20 to 24 weeks, although in this subgroup patient distribution was unequal (19 women on atosiban, 4 on placebo). For women with a gestational age greater than 24 weeks there was no difference in mortality rate (1.7% in the placebo group and 1.5% in the atosiban group).

5.2 Pharmacokinetic properties

In healthy non-pregnant subjects receiving atosiban ~~altan~~ infusions (10 to 300 micrograms/min over 12 hours), the steady state plasma concentrations increased proportionally to the dose. The clearance, volume of distribution and half-life were found to be independent of the dose.

In women in pre-term labour receiving atosiban ~~altan~~ by infusion (300 micrograms/min for 6 to 12 hours), steady state plasma concentrations were reached within one hour following the start of the infusion (mean 442 ± 73 ng/ml, range 298 to 533 ng/ml).

[…]

There is no experience with atosiban ~~altan~~ 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 (see sections 4.2 and 4.4).

6 PHARMACEUTICAL PARTICULARS

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products, except those mentioned in section 6.6.

6.4 Special precautions for storage

Store at 2°C - 8°C~~, store~~ in the original package in order to protect from light.

Atosiban Altan 5 ml vial after dilution: Chemical and physical stability has been demonstrated for 24 hours at 25°C. From a microbiological point of view, the product should be used immediately. If not used immediately, in use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless dilution has taken place in controlled and validated aseptic conditions.

6.5 Nature and contents of container

One vial of solution for injection contains 0.9 ml solution, corresponding to 6.75 mg atosiban base.

One ampoule of concentrate for solution for infusion contains 5 ml solution, corresponding to 37.5 mg atosiban base.

Transparent type I glass vial/ampoule.

[…]

6.6 Instructions for use and handling

The vials/ampoules should be inspected visually for particulate matter and discoloration prior to administration.

Preparation of the initial intravenous injection:
Withdraw 0.9 ml of a 0.9 ml ampoule of Atosiban Altan ~~6.75 mg/0.9ml~~, solution for injection, and administer slowly as an intravenous bolus dose over one minute, under adequate medical supervision in an obstetric unit. The Atosiban Altan ~~6.75 mg/0.9ml~~ ampoule, solution for injection, should be used immediately.In the absence of incompatibility studies, this medicinal product should not be mixed with other medicinal products (see section "Incompatibilities").

Preparation of intravenous infusion solution:
For intravenous infusion, following the bolus dose, Atosiban ~~37.5mg~~ Altan 5 ml vial, concentrate for solution for infusion, should be diluted in one of the following solutions:

- sodium chloride 9mg/ml (0.9%) solution for injection
- Ringer's lactate solution
- 5% w/v glucose solution

Withdraw 10 ml solution from a 100 ml infusion bag and discard. Replace it by 10 ml Atosiban Altan 37.5 mg/5 ml concentrate for solution for infusion from two 5 ml vials to obtain a concentration of 75 mg atosiban in 100 ml.

העלון לרופא מצורף להודעה זו וכן נשלח לפרסום במאגר התרופות שבאתר האינטרנט של משרד הבריאות.
ניתן לקבל את העלון מודפס ע"י פניה לבעל הרישום, חברת פרופארם בע"מ, טל 04-6294242.

בברכה,

מירי חזן
רוקחת ממונה