QUALITATIVE AND QUANTITATIVE COMPOSITION
Solution for injection
Each vial 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).
Each ml of solution contains 7.5 mg atosiban.
After dilution, the concentration of atosiban is 0.75 mg/ml.

Excipients: Mannitol, hydrochloric acid 1M and water for injections.

PHARMACEUTICAL FORM
Solution for injection
Solution for injection (injection).
Clear, colourless solution without particles.

Concentrate for solution for infusion
Concentrate for solution for infusion (sterile concentrate).
Clear, colourless solution without particles.

THERAPEUTIC INDICATIONS
Tractocile 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 per 30 minutes
• a cervical dilation of 1 to 3 cm (0-3 for nulliparas) and effacement of ≥ 50%
• age ≥ 18 years
• a gestational age from 24 until 33 completed weeks
• a normal foetal heart rate

POSOLOGY AND METHOD OF ADMINISTRATION
Posology
Treatment with Tractocile should be initiated and maintained by a physician experienced in the treatment of pre-term labour.

Tractocile is administered intravenously in three successive stages: an initial bolus dose (6.75 mg), performed with Tractocile 6.75 mg/0.9 ml solution for injection, immediately followed by a continuous high dose infusion (loading infusion 300 micrograms/min) of Tractocile 37.5 mg/5 ml concentrate for solution for infusion during three hours, followed by a lower dose of Tractocile 37.5 mg/5 ml concentrate for solution for infusion (subsequent infusion 100 micrograms/min) up to 45 hours. The duration of the treatment should not exceed 48 hours. The total dose given during a full course of Tractocile therapy should preferably not exceed 330.75 mg of atosiban.
Intravenous therapy using the initial bolus injection should be started as soon as possible after diagnosis of pre-term labour. Once the bolus has been injected, proceed with the infusion (See Summary of Product Characteristics of Tractocile 37.5 mg/5 ml, concentrate for solution for infusion). In the case of persistence of uterine contractions during treatment with Tractocile, alternative therapy should be considered.

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

<table>
<thead>
<tr>
<th>Step</th>
<th>Regimen</th>
<th>Infusion rate</th>
<th>Atosiban dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.9 ml intravenous bolus injection given over 1 minute</td>
<td>Not applicable</td>
<td>6.75 mg</td>
</tr>
<tr>
<td>2</td>
<td>3 hours intravenous loading infusion</td>
<td>24 ml/hour (300 µg/min)</td>
<td>54 mg</td>
</tr>
<tr>
<td>3</td>
<td>Up to 45 hours subsequent intravenous infusion</td>
<td>8 ml/hour (100 µg/min)</td>
<td>Up to 270 mg</td>
</tr>
</tbody>
</table>

Re-treatment:
In case a re-treatment with atosiban is needed, it should also commence with a bolus injection of Tractocile 6.75 mg/0.9 ml, solution for injection followed by infusion with Tractocile 37.5 mg/5 ml, concentrate for solution for infusion.

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 Tractocile in pregnant women aged less than 18 years have not been established.
No data are available.

Method of administration
For instructions on preparation of the medicinal product before administration, see section INSTRUCTIONS FOR USE AND HANDLING.

CONTRAINDICATIONS
Tractocile 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(s) or to any of the excipients
SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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.

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 (see sections POSOLOGY AND METHOD OF ADMINISTRATION and PHARMACOKINETIC PROPERTIES).

There is only limited clinical experience in the use of atosiban in multiple pregnancies or the gestational age group between 24 and 27 weeks, because of the small number of patients treated. The benefit of atosiban in these subgroups is therefore uncertain.

Re-treatment with Tractocile is possible, but there is only limited clinical experience available with multiple re-treatments, up to 3 re-treatments (see section POSOLOGY AND METHOD OF ADMINISTRATION). In case of intrauterine growth retardation, the decision to continue or reinitiate the administration of atosiban depends on the assessment of fetal maturity.

Monitoring of uterine contractions and fetal heart rate during administration of atosiban and in case of persistent uterine contractions should be considered. As an antagonist of oxytocin, atosiban may theoretically facilitate uterine relaxation and postpartum bleeding therefore blood loss after delivery should be monitored. However, inadequate uterus contraction postpartum was not observed during the clinical trials.

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 UNDESIRABLE EFFECTS).

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

It is unlikely that atosiban is involved in 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 metabolising 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 betamethasone or labetalol.

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 breast-feeding should be discontinued during treatment with Tractocile, 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 breast-feeding. Small amounts of atosiban have been shown to pass from plasma into the breast milk of breast-feeding 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 PRECLINICAL SAFETY DATA).

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

DISETUJUI OLEH BPOM : 16/08/2019

EREG10034611800015

EREG10034611800016
**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 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.

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.

<table>
<thead>
<tr>
<th>MedDRA System Organ Class (SOC)</th>
<th>Very common</th>
<th>Common</th>
<th>Uncommon</th>
<th>Rare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune system disorders</td>
<td></td>
<td></td>
<td></td>
<td>Allergic reaction</td>
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<tr>
<td>Metabolism and nutrition disorders</td>
<td></td>
<td>Hyperglycaemia</td>
<td></td>
<td></td>
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<tr>
<td>Psychiatric disorder</td>
<td></td>
<td></td>
<td></td>
<td>Insomnia</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
<td>Headache,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td></td>
<td>Dizziness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular disorders</td>
<td></td>
<td>Tachycardia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Nausea</td>
<td></td>
<td></td>
<td>Vomiting</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td></td>
<td></td>
<td>Pruritis, Rash</td>
</tr>
<tr>
<td>Reproductive system and breast disorder</td>
<td></td>
<td></td>
<td></td>
<td>Uterine haemorrhage, uterine atony</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Injection site reaction</td>
<td></td>
<td></td>
<td>Pyrexia</td>
</tr>
</tbody>
</table>

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.

**OVERDOSE**
Few cases of atosiban overdosing were reported, they occurred without any specific signs or symptoms. There is no known specific treatment in case of an overdose.

**PHARMACODYNAMIC PROPERTIES**
Pharmacotherapeutic group: Other gynecologicals, ATC code: G02CX01
Proposed packaging material

<table>
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<td>☐ CCDS version: ☐ Core PIL version: ☒ SPC country/version/date: EMA approved SmPC. Date of approval: 13-Jan-2016</td>
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<tr>
<td>LAC no.</td>
<td>LAC 764 ID</td>
</tr>
<tr>
<td>Name &amp; Date</td>
<td>INS, 25-Jan-2019</td>
</tr>
</tbody>
</table>

Tractocile contains atosiban (INN), a synthetic peptide ([Mpa¹,D-Tyr(Et)²,Thr⁴,Orn⁸]-oxytocin) which is a competitive antagonist of human oxytocin at receptor level. In rats and guinea pigs, atosiban was shown to bind to oxytocin receptors, to decrease the frequency of contractions and the tone of the uterine musculature, resulting in a suppression of uterine contractions. Atosiban was also shown to bind to the vasopressin receptor, thus inhibiting the effect of vasopressin. In animals atosiban did not exhibit cardiovascular effects.

In human pre-term labour, atosiban at the recommended dosage antagonises uterine contractions and induces uterine quiescence. The onset of uterus relaxation following atosiban is rapid, uterine contractions being significantly reduced within 10 minutes to achieve stable uterine quiescence ($\leq$ 4 contractions/hour) for 12 hours.

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 (according to this labelling) or $\beta$-agonist (dose-titrated).

**Primary endpoint:** the primary efficacy outcome was the proportion of women remaining undelivered and not requiring alternative tocolysis within 7 days of treatment initiation. The data show that 59.6% (n=201) and 47.7% (n=163) of atosiban- and $\beta$-agonist-treated women (p=0.0004), respectively, were undelivered and did not require alternative tocolysis within 7 days of starting treatment. Most of the treatment failures in CAP-001 were caused by poor tolerability. Treatment failures caused by insufficient efficacy were significantly (p=0.0003) more frequent in atosiban (n=48, 14.2%) than in the $\beta$-agonist-treated women (n=20, 5.8%).

In the CAP-001 studies the probability of remaining undelivered and not requiring alternative tocolytics within 7 days of treatment initiation was similar for atosiban and beta-mimetics treated women at gestational age of 24-28 weeks. However, this finding is based on a very small sample (n=129 patients).

**Secondary endpoints:** secondary efficacy parameters included the proportion of women remaining undelivered within 48 h of treatment initiation. There was no difference between the atosiban and beta-mimetic groups with regard to this parameter.

Mean (SD) gestational age at delivery was the same in the two groups: 35.6 (3.9) and 35.3 (4.2) weeks for the atosiban and $\beta$-agonist groups, respectively (p=0.37). Admission to a neonatal intensive care unit (NICU) was similar for both treatment groups (approximately 30%), as was length of stay and ventilation therapy. Mean (SD) birth weight was 2491 (813) grams in the atosiban group and 2461 (831) grams in the $\beta$-agonist group (p=0.58).

Fetal and maternal outcome did apparently not differ between the atosiban and the $\beta$-agonist group, but the clinical studies were not powered enough to rule out a possible difference.

Of the 361 women who received atosiban 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 Special warnings and precautions for use).

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 CONTRAINDICATIONS).

In a placebo-controlled study, fetal/infant deaths were 5/295 (1.7%) in the placebo group and 15/288 (5.2%) in the atosiban group, 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).

PHARMACOKINETIC PROPERTIES
In healthy non-pregnant subjects receiving atosiban 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 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).

Following completion of the infusion, plasma concentration rapidly declined with an initial ($t_\alpha$) and terminal ($t_\beta$) half-life of 0.21 ± 0.01 and 1.7 ± 0.3 hours, respectively. Mean value for clearance was 41.8 ± 8.2 litres/h. Mean value of volume of distribution was 18.3 ± 6.8 litres.

Plasma protein binding of atosiban is 46 to 48% in pregnant women. It is not known whether the free fraction in the maternal and fetal compartments differs substantially. Atosiban does not partition into red blood cells.

Atosiban passes the placenta. Following an infusion of 300 micrograms/min in healthy pregnant women at term, the fetal/maternal atosiban concentration ratio was 0.12.

Two metabolites were identified in the plasma and urine from human subjects. The ratios of the main metabolite M1 (des-(Orn$^8$, Gly-NH$_2$$^9$)-[Mpa$^1$, D-Tyr(Et)$^2$, Thr$^4$]-oxytocin) to atosiban concentrations in plasma were 1.4 and 2.8 at the second hour and at the end of the infusion respectively. It is not known whether M1 accumulates in tissues. Atosiban is found in only small quantities in urine, its urinary concentration is about 50 times lower than that of M1. The proportion of atosiban eliminated in faeces is not known. The main metabolite M1 is approximately 10 times less potent than atosiban in inhibiting oxytocin-induced uterine contractions in vitro. Metabolite M1 is excreted in milk (see section FERTILITY, PREGNANCY AND LACTATION).

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 (see sections POSOLOGY AND METHOD OF ADMINISTRATION and SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

It is unlikely that atosiban inhibits hepatic cytochrome P450 isoforms in humans (see section INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION).

PRECLINICAL SAFETY DATA
No systemic toxic effects were observed during the two-week intravenous toxicity studies (in rats and dogs) at doses which are approximately 10 times higher than the human therapeutic dose, and during the three-months toxicity studies in rats and dogs (up to 20 mg/kg/day s.c.). The highest atosiban subcutaneous dose not producing any adverse effects was approximately two times the therapeutic human dose.

No studies were performed that covered fertility and early embryonic development. Reproduction toxicity studies, with dosing from implantation up to late stage pregnancy, showed no effects on mothers and fetuses. The exposure of the rat fetus was approximately four times that received by the
human fetus during intravenous infusions in women. Animal studies have shown inhibition of lactation as expected from the inhibition of action of oxytocin.

Atosiban was neither oncogenic nor mutagenic in in vitro and in vivo tests.

INCOMPATIBILITIES
In the absence of incompatibility studies, this medicinal product should not be mixed with other medicinal products.

SHELF LIFE
4 years

Solution for injection
Once the vial has been opened, the product must be used immediately.

Concentrate for solution for infusion
Once the vial has been opened, the dilution must be performed immediately. Diluted solution for intravenous administration should be used within 24 hours after preparation.

SPECIAL PRECAUTIONS FOR STORAGE
Store in a refrigerator (2°C - 8°C).
Store in the original package in order to protect from light.

PACK SIZES
Solution for injection
Box, 1 vial of solution for injection contains 0.9 ml. (Reg. No.: DKI XXXXXXXXXXX)

Concentrate for solution for infusion
Box, 1 vial of concentrate for solution for infusion contains 5 ml. (Reg. No.: DKI XXXXXXXXXXX)

INSTRUCTIONS FOR USE AND HANDLING
The vials 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 labelled vial of Tractocile 6.75 mg/0.9 ml, solution for injection and administer slowly as an intravenous bolus dose over one minute, under adequate medical supervision in an obstetric unit. The Tractocile 6.75 mg/0.9 ml, solution for injection should be used immediately.

Preparation of the intravenous infusion solution:
For intravenous infusion, following the bolus dose, Tractocile 37.5 mg/5 ml, concentrate for solution for infusion should be diluted in one of the following solutions:
- sodium chloride 9 mg/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 Tractocile 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.

The reconstituted product is a clear, colourless solution without particles.
The loading infusion is given by infusing 24 ml/hour (i.e. 18 mg/h) of the above prepared solution over the 3 hour period under adequate medical supervision in an obstetric unit. After three hours the infusion rate is reduced to 8 ml/hour.

Prepare new 100 ml bags in the same way as described to allow the infusion to be continued.

If an infusion bag with a different volume is used, a proportional calculation should be made for the preparation.

To achieve accurate dosing, a controlled infusion device is recommended to adjust the rate of flow in drops/min. An intravenous microdrip chamber can provide a convenient range of infusion rates within the recommended dose levels for Tractocile.

If other medicinal products need to be given intravenously at the same time, the intravenous cannula can be shared or another site of intravenous administration can be used. This permits the continued independent control of the rate of infusion.

MANUFACTURED BY
Ferring GmbH
Kiel, Germany

IMPORTED BY
PT. Abbott Indonesia
Jakarta – Indonesia

HARUS DENGAN RESEP DOKTER

Date of revision: January 2019
Informasi untuk pasien
Tractocile 6,75 mg/0,9 ml larutan untuk injeksi
Tractocile 37,5 mg/5 ml larutan untuk infus
Atosiban

Bacalah seluruh isi leaflet ini dengan seksama sebelum Anda diberikan suntikan TRACTOCILE karena leaflet ini berisi informasi penting untuk Anda.

- Simpanlah leaflet ini, sebab Anda mungkin perlu membacanya lagi dikemudian hari.
- Apabila Anda memiliki pertanyaan lebih lanjut, tanyakan pada dokter, bidan atau perawat Anda.
- Jika Anda mengalami efek samping, beritahukan dokter, bidan atau perawat Anda. Termasuk efek samping yang mungkin tidak tercantum dalam leaflet ini. Lihat bagian 4.

Apa yang ada di leaflet ini?

1. Apa itu TRACTOCILE dan digunakan untuk apa
2. Apa yang perlu Anda ketahui sebelum Anda diberi TRACTOCILE
3. Bagaimana cara pemberian TRACTOCILE
4. Efek samping yang mungkin terjadi
5. Bagaimana cara menyimpan TRACTOCILE
6. Isi kemasan dan informasi lainnya

1. Apa itu TRACTOCILE dan digunakan untuk apa


2. Apa yang perlu Anda ketahui sebelum Anda diberi TRACTOCILE

Jangan menggunakan TRACTOCILE:

- Jika kehamilan Anda kurang dari 24 minggu.
- Jika kehamilan Anda lebih dari 33 minggu.
- Jika air ketuban Anda telah pecah (pecah ketuban secara dini) dan dan usia kehamilan Anda telah genap 30 minggu atau lebih.
- Jika bayi yang belum lahir (janin) memiliki detak jantung yang tidak normal.
- Jika Anda mengalami pendarahan dari vagina Anda dan dokter Anda menginginkan bayi Anda dilahirkan dengan segera waktu itu juga.
- Jika Anda memiliki sesuatu yang disebut "pre-eklampsia berat" dan dokter Anda menginginkan agar bayi Anda dilahirkan dengan segera waktu itu juga. Pre-eklampsia berat adalah ketika Anda memiliki tekanan darah tinggi, retensi cairan dan/atau protein dalam urin Anda.
- Jika Anda memiliki sesuatu yang disebut "eklampsia" yang serupa dengan "pre-eklampsia berat" tetapi Anda juga mengalami kejang-kejang (konvulsi). Ini berarti bayi Anda yang masih dalam kandungan harus segera dilahirkan waktu itu juga.
- Jika bayi Anda yang masih dalam kandungan telah meninggal
- Jika Anda mengalami atau mungkin akan mengalami infeksi di rahim (uterus) Anda.
- Jika plasenta Anda menutupi jalan lahir bayi.
Proposed packaging material

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</thead>
<tbody>
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</tr>
</tbody>
</table>

- Jika plasenta Anda terlepas dari dinding rahim Anda.
- Jika Anda atau calon bayi Anda mengalami kondisi lain di mana akan berbahaya untuk melanjutkan kehamilan Anda.
- Jika Anda alergi terhadap atosiban atau bahan lain dari obat ini (tercantum di bagian 6).

Jangan gunakan TRACTOCILE jika salah satu hal di atas berlaku untuk Anda. Jika Anda tidak yakin, bicarakan dengan dokter Anda, bidan atau, apoteker sebelum Anda disuntik TRACTOCILE.

Peringatan dan tindakan pencegahan

Bicaralah dengan dokter, bidan atau apoteker sebelum Anda diberikan TRACTOCILE:
- Jika Anda pikir air ketuban Anda mungkin telah pecah (pecah ketuban secara dini).
- Jika Anda mengalami masalah ginjal atau liver.
- Jika usia kehamilan Anda antara 24 sampai 27 minggu.
- Jika Anda mengandung lebih dari satu bayi.
- Jika kontraksi Anda mulai lagi, pengobatan dengan TRACTOCILE dapat diulang sampai tiga kali lagi.
- Jika bayi yang dikandung terlalu kecil untuk masa kehamilan Anda saat ini.
- Rahim Anda mungkin kurang dapat berkontraksi setelah bayi Anda lahir. Hal ini dapat menyebabkan pendarahan.
- Jika Anda mengandung lebih dari satu bayi dan/atau diberi obat yang dapat menunda kelahiran bayi Anda, seperti obat-obatan yang digunakan untuk tekanan darah tinggi. Hal ini dapat meningkatkan risiko udema paru (akumulasi cairan di paru-paru).

Jika salah satu di atas berlaku untuk Anda (atau Anda tidak yakin), bicaralah dengan dokter, bidan atau apoteker Anda sebelum Anda diberikan TRACTOCILE.

Anak-anak dan remaja

TRACTOCILE belum pernah diteliti pada wanita hamil yang berusia kurang dari 18 tahun.

Obat-obat lain dan TRACTOCILE

Beritahu dokter, bidan atau apoteker Anda jika Anda sedang minum, baru saja minum atau mungkin akan minum obat-obat lain.

Kehamilan dan menyusui

Jika Anda hamil dan masih menyusui anak yang sebelumnya, Anda harus berhenti menyusui jika Anda diberikan TRACTOCILE.

3. Bagaimana cara pemberian TRACTOCILE

TRACTOCILE diberikan kepada Anda di rumah sakit oleh dokter, perawat atau bidan. Mereka akan memutuskan berapa banyak yang Anda perlukan. Mereka juga memastikan bahwa larutannya jernih dan bebas dari partikel.

TRACTOCILE diberikan ke dalam pembuluh darah (intravena) dalam tiga tahap:
- Injeksi pertama 6,75 mg dalam 0,9 ml disuntikkan perlahan-lahan ke dalam vena Anda lebih dari satu menit.
- Kemudian diberikan infus yang berkelanjutan (menetes) pada dosis 18 mg per jam selama 3 jam.
- Kemudian diberikan infus lain yang juga berkelanjutan (menetes) pada dosis 6 mg per jam selama maksimal 45 jam atau sampai kontraksi Anda berhenti.

Pengobatan harus berlangsung tidak lebih dari 48 jam secara keseluruhan.
Pengobatan lebih lanjut dengan TRACTOCILE dapat dilakukan jika kontraksi Anda mulai lagi. Pengobatan dengan TRACTOCILE dapat dilakukan hingga tiga kali lagi.
Selama pengobatan dengan TRACTOCILE, kontraksi dan detak jantung bayi Anda yang dalam kandungan mungkin akan dipantau.
Dianjurkan agar tidak lebih dari tiga kali pengobatan ulang yang digunakan selama kehamilan.

4. Efek samping yang mungkin terjadi

Seperti semua obat lainnya, obat ini bisa menimbulkan efek samping, meski tidak semua orang mendapatkannya.
Efek samping yang terlihat pada ibu umumnya ringan derajatnya. Tidak ada efek samping yang diketahui pada bayi yang ada di kandungan atau yang baru dilahirkan.

Efek samping berikut mungkin terjadi dengan obat ini:

**Sangat umum** (mengenai lebih dari 1 dari 10 orang)
- Mual

**Umum** (mengenai kurang dari 1 dari 10 orang)
- Sakit kepala
- Pusing
- Kulit merah
- Mual dan ingin muntah
- Detak jantung cepat
- Tekanan darah rendah. Tanda-tanda bisa termasuk rasa pusing atau pening.
- Reaksi di lokasi injeksi
- Gula darah tinggi

**Tidak Umum** (mengenai kurang dari 1 dari 100 orang)
- Suhu badan tinggi (demam)
- Kesulitan tidur (insomnia)
- Gatal
- Ruam

**Jarang** (mengenai kurang dari 1 dari 1.000 orang)
- Rahim Anda mungkin kurang dapat berkontraksi setelah bayi Anda lahir. Ini bisa menyebabkan pendarahan.
- Reaksi alergi

Anda mungkin mengalami sesak napas atau edema paru (akumulasi cairan di paru-paru), terutama jika Anda hamil lebih dari satu bayi dan/atau diberikan obat yang dapat menunda kelahiran bayi Anda, seperti obat yang digunakan untuk tekanan darah tinggi.

**Pelaporan efek samping**

Jika Anda mendapatkan efek samping diatas, hubungi dokter, bidan atau perawat Anda. Hal yang sama berlaku untuk efek samping yang tidak tercantum dalam leaflet ini. Anda juga dapat melaporkan efek samping tersebut ke sistem pelaporan nasional dibawah ini. Dengan melaporkan efek samping, Anda dapat membantu memberikan informasi lebih lanjut tentang keamanan obat ini.

**Pusat MESO/Farmakovigilans Nasional**

Direktorat Pengawasan Distribusi Produk Terapetik dan PKRT Badan POM RI
Jl. Percetakan Negara 23 Jakarta Pusat, 10560
No Telp : 021 - 4244 755 ext.111
Fax : 021 - 4288 3485
Email : pv-center@pom.go.id dan Indonesia-MESO-BadanPOM@hotmail.com
5. Bagaimana cara menyimpan TRACTOCILE


6. Isi kemasan dan informasi lainnya

Apa isi TRACTOCILE

- Zat aktif adalah atosiban.
- Setiap vial larutan TRACTOCILE 6,75 mg/0,9 ml untuk injeksi mengandung atosiban asetat yang setara dengan 6,75 mg atosiban dalam 0,9 ml.
- Setiap vial konsentrat TRACTOCILE 37,5 mg/5 ml untuk larutan infus mengandung atosiban asetat yang setara dengan 37,5 mg atosiban dalam 5 ml.
- Bahan lainnya adalah manitol, asam klorida dan air untuk injeksi.

Tampilan TRACTOCILE dan bagaimana isi kemasannya

- Larutan TRACTOCILE 6,75 mg/0,9 ml untuk injeksi adalah larutan yang jernih, tanpa warna dan tanpa partikel. Satu pak berisi satu vial yang berisi larutan 0,9 ml. No.Reg: xxxxxxxxxxx
- Konsentrat TRACTOCILE 37,5 mg/5 ml untuk larutan infus adalah suatu larutan yang jernih, tanpa warna dan tanpa partikel. Satu pak berisi satu vial yang berisi larutan 5 ml. No.Reg: xxxxxxxxxxx

Pemegang Hak Pemasaran dan Produsen

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HARUS DENGAN RESEP DOKTER

Leaflet ini terakhir direvisi pada bulan May 2018.