גירסה 2 03.11.2019

תאריך: אוגוסט 2021

רופא /ה, רוקח/ת נכבד/ה

חברת טבע מודיעה על העדכונים הבאים בעלון לצרכן/לרופא של התכשיר

שם התכשיר

Heparin Sodium Teva 25,000 IU/5 ml,

Solution for Injection or Infusion

Contains: ***Heparin sodium 25000 IU/5ml***

עדכון בעלון לרופא ועלון לצרכן חדש

<u>התוויה כפי שאושרה בתעודת הרישום:</u>

- Prevention of thromboembolic disorders.
- As part of the treatment of venous and arterial thromboembolic disorders (including early treatment of heart attacks as well as unstable angina pectoris)
- For the anticoagulation in case of treatment or operation with extracorporeal circulation (e.g. heart-lung machine, hemodialysis)

<u>ברצוננו להודיע שהעלון לרופא עודכן</u>

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להלן השינויים העיקריים (החמרות) בעלון:

4.3 Contraindications

Heparin Sodium Teva 25,000 IU/5 ml must not be used in the following cases:

- Hypersensitivity to the active substance heparin, Benzyl alcohol or to any of the excipients of *Heparin Sodium Teva 25,000 IU/5 ml* listed in section 6.1.
- ~~Current~~ Acute or previous history of heparin-induced allergic thrombocytopenia (type 2).
- Disorders associated with a bleeding diathesis, e.g. thrombocytopenia, coagulopathies, severe hepatic, renal or pancreatic disorders.
- Disorders in which there is a suspected lesion of the vascular system, e.g. gastrointestinal ulcers, hypertension (>105 mmHg diastolic), cerebral haemorrhage, trauma or surgical operations involving the central nervous system (CNS), eye operations, retinopathies, vitreous haemorrhage, aneurysm of the cerebral arteries, infectious endocarditis.
- Threatened miscarriage.
- Spinal anaesthesia, epidural anaesthesia, lumbar puncture.
- Organ lesions associated with a bleeding tendency.

4.4 Special warnings and precautions for use

[…]

~~Benzyl alcohol can trigger toxic and anaphylactoid reactions in infants and children aged up to 3 years.~~

***Heparin Sodium Teva* contains benzyl alcohol**

Benzyl alcohol has been associated with the risk of serious adverse reactions (gasping syndrome) in newborn babies and infants.

In infants (under 3 years of age), the medicinal product should not be used for longer than a week because of accumulation.

Large quantities of benzyl alcohol should be used only with caution and when absolutely necessary because of the risk of accumulation and toxicity (metabolic acidosis), especially in individuals with hepatic or renal impairment and during pregnancy and lactation.

***Heparin Sodium Teva* contains sodium**

This medicinal product contains 28 mg sodium per vial, equivalent to 1.4% of the maximum daily dietary intake of 2 -g recommended by the WHO for an adult.

4.5 Interaction with other medicinal products and other forms of interaction

Antiplatelet drugs (aspirin, ticlopidine, clopidogrel, prasugrel, ticagrelor, dipyridamole in high doses), fibrinolytics, other anticoagulants (coumarin derivatives), oral factor Xa inhibitors (apixaban, rivaroxaban), thrombin inhibitors (bivalirudin, argatroban, dabigatran), hirudin (desirudin), non-steroidal anti-inflammatory drugs (phenylbutazone, indometacin), glycoprotein IIb/IIIa receptor antagonists, high-dose penicillin, dextrans:
Clinically significant increased effect and increased risk of bleeding.

4.6 Fertility, pregnancy and lactation

Pregnancy
Heparin does not cross the placenta. To date, experience in pregnant women has not demonstrated any foetal/neonatal toxicity of heparin. Animal studies have also not shown any evidence of reproductive toxicity (see section 5.3).
There are, however, reports of an increased risk of miscarriages and premature births.
Treatment- or disease-induced complications in pregnant women cannot be ruled out. Daily high-dose heparin administration over a period of more than 3 months can increase the risk of osteoporosis in pregnant women.
Epidural anaesthesia is contraindicated during birth in women treated with anticoagulants. Anticoagulant treatment is also contraindicated if there is a bleeding tendency such as with threatened miscarriage (see section 4.3).
If necessary, use of heparin during pregnancy can be considered.

Lactation
Heparin is not excreted in human milk. Heparin can be used during breast-feeding. Daily high-dose administration of heparin over a period of more than 3 months can increase the risk of osteoporosis in breast-feeding women.

4.8 Undesirable effects

[…]

Very rare:	Type 2 thrombocytopenia can occur after a delay of several weeks after the end of heparin treatment (Spinler S A: New concepts in heparin-induced thrombocytopenia: Diagnosis and management, J Thromb Thrombolysis 21(1), 17-21, 2006: FDA MedWatch Safety Alert. Heparin Sodium Injection. December 8, 2006). If type 2 thrombocytopenia occurs, heparin should be stopped immediately. Other treatment measures depend on the nature and severity of symptoms. Further parenteral heparin administration is absolutely contraindicated.

[…]

~~*Nervous system disorders*~~
~~Spinal and epidural haematomas have been reported in rare cases with the use of heparin sodium in the context of spinal or epidural anaesthesia or postoperative indwelling catheters. These events have resulted in neurological complications of varying severity, such as persistent or permanent paralysis (see also 4.4).~~

[…]

Hepatobiliary disorders
Very common: Elevation of serum transaminases (AST, ALT), gamma-glutamyl transpeptidase (gamma-GT), LDH and lipase~~,~~ / ~~which is not clinically relevant and generally reversible.~~.

Reproductive system disorders
Very rare: Priapism

Skin and subcutaneous tissue disorders
Uncommon: Transient alopecia, skin necrosis.

Musculoskeletal and connective tissue disorders
Not known: Osteoporosis may develop after prolonged use (months), mostly when higher doses are used and especially in patients with a predisposition to it.

[...]

General disorders and administration site conditions
Common: Local tissue reactions at the injection site (induration, redness, discoloration and small haematomas).
Very rare: Calcinosis at the injection site, mainly in patients with severe kidney failure.
Benzyl alcohol can cause allergic reactions.

Reporting of suspected adverse reactions

6.6 Special precautions for disposal and other handling

~~No special requirements.~~

Administration of the subcutaneous injection
The injection should be administered with a fine injection needle held perpendicular to the body axis, into a raised fold of abdominal skin or on the anterior aspect of the thigh; the injection must be strictly subcutaneous.
Any drops adhering to the injection needle should be removed before the injection, as introducing heparin sodium into the injection channel can result in superficial bruising and in rare cases local allergic irritation.