Bundesamt für Sicherheit
im Gesundheitswesen

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Betreff: Alprostadil– hältige Arzneispezialitäten (Indikation: peripheren arteriellen Verschlusskrankheit) – Änderungen der Fach- und Gebrauchsinformationen aufgrund des HBD – PSUR Worksharing Projektes

Sehr geehrte Damen und Herren,

basierend auf der Evaluierung des PSURs im EU-HBD-worksharing Projekt (Verfahrensnummer: AT/H/PSUR/0036/001) kommt es zu der Empfehlung, folgende Ergänzungen in die **Fach- und Gebrauchsinformation** aller Alprostadil– hältige Arzneispezialitäten (Indikation: peripheren arteriellen Verschlusskrankheit) aufzunehmen. Sollten diese bereits aufgenommen worden sein, betrachten Sie dieses Schreiben als gegenstandslos.

Fachinformation

4.3 Contraindications

Hypersensitivity to alprostadil or any excipient of the product.
- Impairment of cardiac function, such as New York Heart Association (NYHA) class III and IV heart failure, hemodynamically relevant arrhythmia, inadequately controlled coronary heart disease, mitral and/or aortic valve stenosis and/or insufficiency. History of myocardial infarction within the last six months.
- Acute pulmonary edema or history of pulmonary edema in patients with heart failure.
- Severe chronic obstructive pulmonary disease (COPD) or pulmonary venoocclusive disease (PVOD).
- Disseminated pulmonary infiltration.
- Bleeding tendency, such as patients with acute erosive or bleeding gastric and/or duodenal ulcer.
- Pregnant women.
- Breastfeeding mothers.
- History of cerebrovascular accident within the last 6 months
- Severe hypotension
- Patients with renal dysfunction (oligoanuria)
- Patients with signs of acute hepatic impairment (elevated transaminases or gamma GT) or with known severe hepatic impairment (including history of the one)
- General contraindication against infusion therapy (like congestive heart failure, pulmonary or cerebral oedema and hyperhydration)

4.4 Special warnings and precautions for use

Patients receiving alprostadil should be closely monitored during each dose. Frequent checks of the cardiovascular function including monitoring of blood pressure, heart rate, and fluid balance should be performed. To avoid symptoms of hyperhydration, the infusion volume of alprostadil should not exceed of 50 – 100 ml/day (infusion pump) and infusion time as outlined in section 4.2 should be strictly followed.
Before discharging the patient a stable cardiovascular condition should be established.
Patients with renal impairment should be closely monitored (e.g. fluid balance and renal function tests).
Alprostadil should only be administered by physicians who are experienced in the treatment of peripheral arterial occlusive disease and who are familiar with monitoring of cardiovascular functions and who have adequate facilities. Alprostadil should not be administrated per bolus injection.
Alprostadil must not be administered to women who may become pregnant.
Alprostadil is not recommended for use in pediatric population.

4.5 Interaction with other medicinal products and other forms of interaction

Since alprostadil has vasodilatator properties and is, in vitro, a weak inhibitor of platelet aggregation, care should be taken in patients receiving other vasodilatators or anticoagulants concomitantly. As alprostadil may enhance the effect of any blood pressure lowering drug (such as antihypertensive drugs, vasodilatator drugs), intensive monitoring of blood pressure should be performed in patients receiving these drugs.

4.6 Fertility, pregnancy and lactation

Alprostadil must not be administered to women who may become pregnant, pregnant women or breastfeeding mothers.
Women of childbearing potential who would receive Alprostadil have to use effective contraception during treatment.
Pre-clinical fertility studies have been conducted and at the recommended clinical dosage of Alprostadil, no effects on fertility are expected.

4.7 Effects on ability to drive and use machines

Alprostadil may cause decrease in systolic blood pressure and thereby can have a moderate influence on the ability to drive and to use machines. Patients should be warned of this possibility and told that caution is needed if driving a car or operating machinery.

4.8 Undesirable effects

Undesirable effects frequencies are defined as: very common (≥1/10), common (≥1/100 <1/10), uncommon (≥1/1,000 <1/100), rare (≥1/10,000 <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).
During administration of Alprostadil the following undesirable effects may be observed:
Blood and lymphatic system disorders
Rare: thrombocytopenia, leukopenia, leukocytosis

Nervous system disorders
Common: headache
Rare: Confusional states, convulsion of cerebral origin
Not known: Cerebrovascular accident

Cardiac disorders
Uncommon: decrease in systolic blood pressure, tachycardia, angina pectoris
Rare: Arrhythmia, Biventricular cardiac failure
Not known: Myocardial infarction
Respiratory, thoracic and mediastinal disorders
Rare: pulmonary edema
Not known: Dyspnoea

Gastrointestinal disorders
Uncommon: gastrointestinal reactions (nausea, vomiting); acceleration properties of alprostadil (diarrhoea, nausea, vomiting)
Hepatobiliary disorders
Rare: liver enzyme abnormalities

Skin and subcutaneous tissue disorders
Common: reddening, edema, flushing
Uncommon: allergic reactions (cutaneous hypersensitivity such as rash, discomfort in joints, febrile reactions, sweating, chills)
General disorders and administration site conditions
Common: Pain, headache, after an intraarterial administration: feeling of warmth, feeling swollen, localized edema, paresthesia
Uncommon: after intravenous administration: feeling of warmth, feeling swollen, localized edema, paresthesia
Very rare: anaphylaxis/ anaphylactoid reactions
Not known: injection site phlebitis, thrombosis at the site of the catheter tip, localized bleeding.

4.9 Overdose

In case of overdosage of alprostadil a fall of blood pressure with tachycardia may occur.
Further symptoms may be observed: vasovagal syncope with paleness, sweating, nausea, and vomiting.
Local symptoms may be pain, edema, and reddening along the infused vein.
If symptoms of overdosage should occur, the infusion should be reduced or stopped immediately. In case of hypotension the legs of the lying patient should be kept in an elevated position. If symptoms persist, cardiac examination/tests should be performed. If necessary, sympathomimetic agents should be administered.

Oben angeführte Textabschnitte stellen eine Mindestanforderung dar, zusätzliche nationale Hinweise in diesen Abschnitten sind zu belassen.