prostavasin® 20 µg should be used only by physicians who have angiologic experience and are familiar and equipped with modern facilities for the continuous monitoring of the cardiac and circulatory functions.

INTRA-ARTERIAL INFUSION OF PROSTAVASIN® 20 µg

Based on present information, the following dosage regimen can be used for the intra-arterial therapy with prostavasin® 20 µg:

The contents of one ampoule of prostavasin® 20 µg dry substance (equivalent to alprostadil 20 µg) are dissolved in 50 ml of physiological saline.

Unless otherwise prescribed, 1/2 ampoule of prostavasin® 20 µg (equivalent to alprostadil 10 µg) is infused into an artery with an infusion pump over a period of 60 to 120 minutes. Dependent on the tolerance, the dose can be elevated to 1 ampoule (alprostadil 20 µg), in particular if necroses are present. The drug is usually given once daily.

If an indwelling catheter is used for the intra-arterial infusion, it is recommended to give, dependent on the tolerance and the seriousness of the disease, a dosage of 0.1 to 0.6 ng/kg BW/min. with an infusion pump over a period of 12 hours (equivalent to 1/4 to 1 1/2 ampoules of prostavasin® 20 µg).

INTRAVENOUS INFUSION OF PROSTAVASIN® 20 µg

Based on present information, the following dosage regimen can be used for the intravenous therapy with prostavasin® 20 µg, unless otherwise prescribed:

The contents of two ampoules of prostavasin® 20 µg dry substance (equivalent to alprostadil 40 µg), dissolved in 50 to 250 ml of physiological saline, are given as a 2-hour intravenous infusion. This dose is administered twice daily. An alternative is the once-daily administration of 3 ampoules of prostavasin® 20 µg (alprostadil 60 µg), dissolved in 50 to 250 ml of physiological saline, as a 3-hour intravenous infusion.

The intravenous therapy of patients with impaired renal function (renal insufficiency with creatinine values >1.5 mg/dl) should start with two-hour infusions of one ampoule of prostavasin® 20 µg twice daily (alprostadil 20 µg b.i.d.). In accordance with the overall clinical picture, the dose can be raised to the above-mentioned normal dose within 2 to 3 days.

In patients with renal insufficiency as well as in those at a cardiac risk, the infusion volume should be limited to 50 to 100 ml/day, and the infusion be given by means of an infusion pump.

The ready-made solution has to be prepared fresh immediately prior to use.

How long should prostavasin® 20 µg be used?

After 3 weeks of therapy with prostavasin® 20 µg, a decision has to be taken, whether continuing the infusion therapy with prostavasin® 20 µg will be of clinical benefit. If no therapeutic success has been reached, the therapy has to be discontinued.

A total therapy period of 4 weeks should not be exceeded.

OVERDOSAGE AND OTHER CASES OF FAULTY USE

What has to be done, if too much prostavasin® 20 µg has been used?

Symptoms of overdosage

Overdosage of prostavasin® 20 µg can result in fall of blood pressure and subsequent elevated heart rates. Other symptoms include: vasovagal reactions with pallor, sweats, nausea and vomiting, myocardial ischaemia and heart failure. Local symptoms are pain, swelling and reddening near the site of infusion.

THERAPY OF OVERDOSAGE

When symptoms of overdosage (heavy pain, fall of blood pressure) occur, the dose of prostavasin® 20 µg has to be reduced; if necessary the infusion of prostavasin® 20 µg has to be discontinued. If blood pressure has decreased, the first measure is to elevate the supine patient's legs. If the symptoms persist, cardiac diagnostics must immediately be performed and may be followed by the administration of sympathomimetics.

SIDE-EFFECTS

The following frequencies are used in the side-effects listings:

What side-effects may appear during the therapy with prostavasin® 20 µg?

Very common: More than 1 in 10 patients treated	**Common:** More than 1 in 100 patients treated
Uncommon: More than 1 in 1000 patients treated	**Rare:** More than 1 in 10,000 patients treated
Very rare: 1 or less in 10,000 patients treated including isolated cases	

Alterations at the site of application

Very common: Pain, erythemas and oedemas at the limb used for intra-arterial infusion

Common: Similar symptoms are also seen on intravenous administration; reddening of the infused vein is seen in addition

These substance- or infusion-related side-effects subside after reduction of the dose or discontinuation of the infusion.

THE FOLLOWING SYMPTOMS ARE OBSERVED ALMOST IRRESPECTIVE OF THE ROUTE OF ADMINISTRATION

Central and peripheral nervous system

Common: Headache, sensory disturbances in the diseased limb

Uncommon: States of confusion

Rare: Cerebral convulsive seizures

Gastrointestinal tract

Uncommon: Gastrointestinal complaints, e.g. diarrhoea, nausea, vomiting

Cardiovascular system, cardiac rhythm and vascular alterations

Common: Flushing

Uncommon: Fall of blood pressure, tachycardia, angina pectoris

Rare: Cardiac arrhythmia, development of acute pulmonary oedema or global heart failure

Hepatic alterations

Uncommon: Increase in liver enzyme values (transaminases)

Haematologic alterations

Rare: Decrease and increase in WBC, and decrease in the number of platelets

Generalized disorders

Uncommon: Increase in temperature, sweats, chill, fever, allergic reactions; CRP (C-reactive protein) alterations, rapid normalization after termination of the therapy.

Very rare: Cases of serious hypersensitivity reactions

Muscular and skeletal system

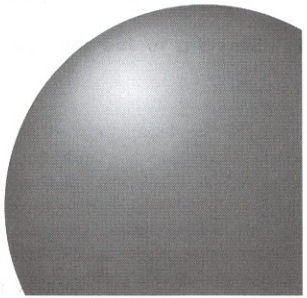
Uncommon: Joint complaints

Very rare: Reversible hyperostosis of the long bones after more than 4 weeks of therapy

Inform your doctor or physician of any side-effects not mentioned in this package insert.

prostavasin® 20 µg

ALPROSTADIL



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Patient information

Dear patient,

Please read the following patient information carefully, because it contains important information on what you should consider when using this drug. Please ask your doctor or pharmacist in case of any questions.

prostavasin® 20 µg

Active ingredient: alprostadil

COMPOSITION

One ampoule with 48.2 mg of dry substance contains:

pharmacologically active ingredient: alprostadil 20 µg (as alfadex clathrate complex)

OTHER INGREDIENTS

alfadex, lactose

PRESENTATION AND CONTENTS

Dry substance in ampoules. Packs of 10, 15 (N3), 30 and 60 ampoules, and hospital-size packs of 20 (2 x 10) ampoules

SUBSTANCE OR INDICATION GROUP OR MODE OF ACTION

Prostaglandin E1, substance promoting blood flow

NAME AND ADDRESS OF THE PHARMACEUTICAL COMPANY AND OF THE MANUFACTURER

Manufacturer: SCHWARZ PHARMA AG
Alfred-Nobel-Straße 10
40789 Monheim, Germany
Phone: + 49 2173 48 0
Fax: + 49 2173 48 1608
Internet: http://www.schwarzpharma.com

INDICATIONS

Therapy of chronic arterial occlusive disease of stages III and IV.

CONTRAINDICATIONS

When must you not use prostavasin® 20 µg?

prostavasin® 20 µg must not be used in cases of hypersensitivity to alprostadil or to any other ingredient of the drug.

prostavasin® 20 µg must not be used in patients with prior cardiac damage such as heart failure without adequate therapy, cardiac arrhythmia without adequate therapy, higher-degree valvular defects, coronary heart disease without adequate therapy, state following myocardial infarction within the past 6 months, nor in patients who are suspected, on the basis of clinical or radiologic evidence, of presenting with pulmonary oedema or pulmonary infiltration, or in patients with serious chronic obstructive lung disease or diseases with constriction of the pulmonary veins.

Patients with signs of liver damage (elevated transaminase or gamma-GT values) or patients known to suffer from liver disease have to be excluded from a therapy with prostavasin® 20 µg, as have to be patients who are feared to show haemorrhagic complications due to the effects of prostavasin® 20 µg (e.g. patients with fresh gastric/intestinal ulcers, polytrauma).

Particular precautions have to be observed in risk patients (see section "Special warnings and precautions of use").

What do you have to observe during pregnancy and lactation?

prostavasin® 20 µg must not be used during pregnancy and lactation.

SPECIAL WARNINGS AND PRECAUTIONS OF USE

Which precautions have to be observed?

Patients with an age-dependent tendency towards heart disease or with coronary heart disease have to be monitored in hospital throughout the therapy with prostavasin® 20 µg and for one day after its termination. For symptoms of hyperhydration to be avoided in such cases, the volumes of carrier solution should not exceed 50 to 100 ml/day (infusion pump) whenever possible, and the cardiac and circulatory functions (e.g. blood pressure and heart rate) should be checked frequently, if necessary including measurements of body weight, fluid balance and central venous blood pressure, and echocardiographic examinations.

The same monitoring is necessary in patients with

– peripheral oedemas and
– renal dysfunction (serum creatinine >1.5 g/dl).

What do you have to observe when driving a motor-vehicle or operating machinery or working in unsafe places?

Even when used in accordance with the instructions, this drug can alter the reactivity such as to impair the ability required to drive a motor-vehicle or to operate machinery or to work in unsafe places.

INTERACTION WITH OTHER DRUGS

How are the effects of other drugs affected by prostavasin® 20 µg?

The effects of antihypertensive agents and vasodilator substances can be enhanced during a therapy with prostavasin® 20 µg. This is also true for agents used to treat coronary heart disease. In patients receiving prostavasin® 20 µg and such substances concomitantly, the cardiac and circulatory parameters must be closely monitored.

The simultaneous use of prostavasin® 20 µg and drugs delaying blood clotting (anticoagulants, platelet aggregation inhibitors) may result in an elevation of the haemorrhagic tendency.

Please note that this information may also apply to drugs you took a short time ago.

DOSAGE, MODE AND DURATION OF ADMINISTRATION

At which dosage and how often should you take prostavasin® 20 µg?