SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Iloprost 100 micrograms/ml concentrate for solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of concentrate for solution for infusion contains 100 micrograms iloprost equivalent to 134 micrograms of iloprost trometamol

Excipient(s) with known effect
Each ml of concentrate for solution for infusion contains 8.1 mg ethanol 96%.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for infusion.
Clear, colourless solution.

Osmolality: 420-480

mOsmol/kg pH: 7.5-8.5

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Iloprost concentrate for solution for infusion is indicated in adults for:

- Treatment of severe chronic ischaemia of lower limbs in patients at risk of amputation, in whom surgical revascularisation or angioplasty has failed or is not indicated, following an interdisciplinary meeting of physicians, surgeons and radiologists.
- Treatment of severe Raynaud’s phenomenon in patients with progressive trophic disorders

4.2 Posology and method of administration

Iloprost concentrate for solution for infusion is **NOT** ready to use and requires dilution before administration.
Iloprost concentrate for solution for infusion should be administered under strict monitoring in a hospital or out-patient clinic setting with adequate facilities.
Pregnancy should be excluded before the start of treatment in women.
Iloprost concentrate for solution for infusion is administered after dilution as described in section 6.6 as an intravenous infusion over 6 hours via a peripheral vein or a central venous catheter. The dose is adjusted according to individual tolerability within the range of 0.5 to 2.0 nanograms iloprost /kg body weight/min.
The infusion solution should be made up just before the infusion to ensure sterility.
Iloprost concentrate for solution for infusion should only be used diluted. To avoid incompatibility, no other products should be added to the infusion prepared for injection.
The content of the ampoule and the diluent must be mixed thoroughly.

Posology

Blood pressure and heart rate should be monitored at the start of the infusion and subsequently at every dose increase.
During the first 2-3 days, the individually tolerated dose is established. For this reason, treatment should be started at an infusion rate of 0.5 nanograms /kg/min for 30 minutes. The dose should then be increased at intervals of 30 minutes by 0.5 nanograms /kg/min to a maximum of 2.0 nanograms /kg/min. The exact infusion rate should be calculated on the basis of body weight to reach an infusion within the range of 0.5 to 2.0 nanograms /kg/min (see tables below for use with infusion pump or syringe driver).

Method of administration

Iloprost concentrate for solution for infusion is NOT ready to use and requires dilution before administration. Depending on the occurrence of adverse effects such as headache and nausea or an undesired blood pressure drop, the infusion rate should be reduced until the optimal tolerated dose is found.
If the adverse effects are severe, the infusion should be temporarily interrupted. The treatment course can then be continued with the dose based on the optimal tolerated dose reached in the first 2 to 3 days of treatment.
Depending on the infusion technique used, there are two different methods to dilute the content of the ampoule. One of those two dilutions are 10-fold less concentrated than the other (0.2 micrograms/ml vs 2 micrograms/ml) and may only be administered with an infusion pump (e.g. Infusomat®). A more concentrated solution may be administered via a syringe driver. For instructions on the use/handling see section 6.6.
Infusion rates (ml/hour) for different doses using an automatic infusion pump.

In general, the ready-to-use infusion solution is administered intravenously using an automatic infusion pump (For instructions on the dilution for use with an infusion pump see section 6.6).
In case of an Iloprost concentrate for solution for infusion concentration of 0.2 micrograms/ml, the required infusion rate must be determined according to the below described scheme, to reach a dose within the range of 0.5 to 2.0 nanograms /kg/min.
The following table (Table 1) can be used to calculate the infusion rate corresponding to the individual weight of the patient and the dose to be administered. Match the

patient's actual body weight on the table, then set the infusion rate on the pump, based on the desired dose in nanograms/kg/min.

Table 1:

Body weight [kg]	Dose [ng/kg/min]			
	0.5	1.0	1.5	2.0
	Infusion rate [ml/h]			
40	6.0	12	18.0	24
50	7.5	15	22.5	30
60	9.0	18	27.0	36
70	10.5	21	31.5	42
80	12.0	24	36.0	48
90	13.5	27	40.5	54
100	15.0	30	45.0	60
110	16.5	33	49.5	66

Infusion rates (ml/hour) for different doses using a syringe driver

A syringe driver with a 50 ml injection syringe (e.g. Perfusor®) may also be used to infuse iloprost. For instructions on the dilution for use with a syringe driver see section 6.6.

In case of an Iloprost concentration of 2 micrograms/ml, the required infusion rate must be determined according to the below described scheme (Table 2), to reach a dose within the range of 0.5 to 2.0 nanograms/kg/min.

The following table (Table 2) can be used to calculate the infusion rate corresponding to the individual weight of the patient and the dose to be infused. Match the patient's actual body weight on the table, then set the infusion rate on the syringe driver based on the desired dose to be delivered in nanograms/kg/min.

Table 2:

Body weight [kg]	Dose [ng/kg/min]			
	0.5	1.0	1.5	2.0
	Infusion rate [ml/h]			
40	0.60	1.2	1.80	2.4
50	0.75	1.5	2.25	3.0
60	0.90	1.8	2.70	3.6

70	1.05	2.1	3.15	4.2
80	1.20	2.4	3.60	4.8
90	1.35	2.7	4.05	5.4
100	1.50	3.0	4.50	6.0
110	1.65	3.3	4.95	6.6

The duration of treatment is up to 4 weeks.
The safety and efficacy of Iloprost concentrate for solution for infusion have not been studied after treatment longer than 4 weeks or after repetitive treatment cycles.*Treatment of severe chronic ischemia of the lower limbs*
The recommended dosage varies between 0.5 to 2.0 nanograms/kg/min for an infusion of 6h /per day depending on the patient's tolerance.
Continue the treatment in general for four weeks, using the tolerated dose determined during the first two or three days of treatment.
The duration of treatment is usually four weeks. It may be less in case of early efficacy. The efficacy and safety of Iloprost concentrate for solution for infusion has not been established for treatment times of more than four weeks or repeated courses of treatment in this indication. Continuous infusion over several days is not recommended. Although there were no clinical consequences, a tachyphylaxis of the effects on the platelets as well as a hyperaggregability at the stop of the treatment can occur.
Treatment of Severe Raynaud's Phenomenon

The recommended dosage varies between 1.5 to 2.0 nanograms/kg/min depending on the patient's tolerance. Treatment should be started at 0.5 nanograms/kg/min (i.e. 10 ml / h) and increased gradually every 30 minutes, according to the scheme proposed above, to reach the maximum tolerated dose by the patient. The duration of the infusion will be 6h/per day for 5 consecutive days, using the maximum tolerated dose determined during the first days of treatment.
Repeat cycles should preferably take place at intervals of 6 to 12 weeks (and never less than 4 weeks).

Special populations

Renal and Hepatic impairment

In patients with renal insufficiency requiring dialysis or severe hepatic impairment, cautious initial titration with a reduced dose is required (e.g. half the normal dose see Section 4.4 and 5.2).
Paediatric population

Safety and efficacy of Iloprost concentrate for solution for infusion in children aged up to 18 years have not been established

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Pregnancy and Lactation (see section 4.6)
- Conditions where the effects of iloprost platelets might increase the risk of haemorrhage (e.g. active peptic ulcer, trauma, intracranial haemorrhage).
- Severe coronary heart disease or unstable angina
- Myocardial infarction within the last six months
- Decompensated cardiac failure if not under close medical supervision
- Acute or chronic congestive heart failure (NYHA II-IV)
- Severe arrhythmias
- Cerebrovascular events (e.g. transient ischemic attack, stroke) within the last 3 months
- Pulmonary oedema
- Congenital or acquired valvular defects with clinically relevant myocardial function disorders not related to pulmonary hypertension.

4.4 Special warnings and precautions for use

Warnings

Surgery should not be delayed in patients requiring urgent amputation (e.g. in cases of infected gangrene).
Patients who are smokers should be strongly advised to stop smoking.
In patients with renal insufficiency requiring dialysis or severe hepatic impairment, it should be taken into account that iloprost plasma levels may be increased due to less elimination of the product (see section 5.2). In these patients, cautious initial titration with dose reduction (see section 4.2) and close clinical monitoring are required.
In patients with low blood pressure care should be taken to avoid further hypotension. Also, patients with significant heart disease should be closely monitored.
The possibility of orthostatic hypotension should be considered in patients getting up from the lying to an upright position after the end of administration.
For patients with a cerebrovascular event, a careful benefit-risk assessment should be undertaken (see also section 4.3 risk of haemorrhage, intracranial haemorrhage).
Special precautions

Accidental infusion of undiluted iloprost may result in local changes at the injection site. Therefore, a dedicated intravenous cannula should be placed for the infusion of iloprost and the patency of the line should be checked during infusion.
Oral ingestion and contact with the mucous membranes should be avoided. On contact with the skin, iloprost may cause long-lasting but painless erythema. Suitable precautions should therefore be taken to avoid iloprost contact with the skin. In the event of such contact, the affected area should be washed immediately with copious amounts of water or saline. Excipients
This medicinal product contains 8.10 mg of alcohol (ethanol) in each 1 ml vial of concentrate and 4.05 mg in each 0.5 ml vial of concentrate respectively. The amount in 1 ml of this medicinal product is equivalent to less than 1 ml beer or wine. The small amount of alcohol in this medicinal product will not have any noticeable effects.
This medicinal product contains 7.08 mg sodium in 1 ml of the concentrate, that is to say essentially “sodium-free”.

4.5 Interaction with other medicinal products and other forms of interaction

Iloprost may increase the anti-hypertensive activity of β- blockers, calcium antagonists, vasodilators and ACE inhibitors. In case of significant hypotension, this can be corrected by dose reduction of iloprost.
Because iloprost inhibits platelet aggregation, concomitant use with oral anticoagulants, and/ or heparin and related molecules (coumarin-type anticoagulants), and/ or thrombolytics and/or other inhibitors of platelet aggregation (such as acetylsalicylic acid, ticlopidine, clopidogrel, and /or anti IIB/ IIIA) may increase the risk of bleeding. The possible increase in haemorrhagic risk should be taken into account by maintaining close clinical monitoring. If this occurs, iloprost administration should be stopped.
Iloprost infusions do not affect the pharmacokinetics of multiple oral doses of digoxin.

4.6 Fertility, pregnancy and lactation

Pregnancy

Iloprost concentrate for solution for infusion is contraindicated during pregnancy (see section 4.3).
Women of childbearing potential have to use effective contraception during treatment.
There are no or limited amount of data from the use of iloprost in pregnant women.
Studies in animals have shown embryotoxicity in rats but not in rabbits and monkey (see section 5.3).
Breastfeeding

Iloprost concentrate for solution for infusion is contraindicated during breast-feeding (see section 4.3). It is unknown whether iloprost is excreted in human milk.
A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Iloprost concentrate for solution for infusion therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.
Fertility

There is no fertility data available.

4.7 Effects on ability to drive and use machines

Iloprost has major influence on the ability to drive and use machines for patients experiencing hypotensive symptoms such as dizziness.
Care should be exercised during initiation of therapy until any effects on the individual have been determined.

4.8 Undesirable effects

Summary of safety profile

The overall safety profile of iloprost is based on data from post-marketing surveillance as well as on pooled clinical trial data. The raw incidence was based on the cumulative database of 3,325 patients having received iloprost either in controlled or uncontrolled clinical trials or in a compassionate use program from generally elderly and multimorbid patients with peripheral arterial occlusive disease (PAOD) in advanced stages III and IV, and patients with thromboangitis obliterans (TAO); for details see Table 1.

The most common observed adverse events (≥ 10%) in patients receiving iloprost in clinical trials are headache, flushing, nausea, vomiting and hyperhidrosis. These undesirable effects are likely to occur during the dose titration at the start of treatment to identify the best tolerable dose for the individual patient. Usually, these undesirable effects resolve with dose reduction.

Overall, the most severe undesirable effects (life-threatening or fatal) in patients receiving iloprost are cerebrovascular stroke, myocardial infarction, pulmonary embolism, cardiac failure, convulsion, hypotension, tachycardia, asthma, angina pectoris, dyspnoea, and pulmonary oedema.

Another group of side effects is related to the local infusion site reactions. For example, infusion site redness and infusion site pain may occur or a cutaneous vasodilation may give rise to a linear erythema above the infusion vein.

Tabulated list of adverse reactions

The table below shows the frequencies of adverse reactions which have been reported in clinical studies and post-marketing experience.

The frequencies are defined as follows: 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) Very rare (<1/10,000) and Not known (frequency cannot be estimated from available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System organ class	**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)
Blood and lymphatic disorders			Thrombocytopenia	
Immune system disorders			Hypersensitivity	
Metabolism and nutrition disorders		Decreased appetite		
Psychiatric disorders		Bradypsychia Confusional state	Anxiety Depression Hallucination	

Nervous system disorders	Headache	Dizziness/Vertigo Paraesthesia/ Palpitations/ Hyperaesthesia/ Burning sensation, Nervousness/Restlessness/ drowsiness	Convulsion* Syncope Tremor Migraine	
Eye disorders			Vision blurred Eye irritation Eye pain	
Cardiac disorders		Tachycardia* Bradycardia Angina pectoris*	Myocardial infarction* Cardiac failure* Arrhythmia/ Extrasystoles*	
Vascular disorders	Flushing	Hypotension* Blood pressure increased	Cerebrovascular event*/ Cerebral ischaemia Pulmonary embolism* Deep vein thrombosis	
Respiratory, thoracic and mediastinal disorders		Dyspnoea*	Asthma* Pulmonary oedema*	Cough
Gastrointestinal disorders	Nausea Vomiting	Diarrhoea Abdominal discomfort/ Abdominal pain	Diarrhoea Haemorrhagic Rectal haemorrhage Dyspepsia Rectal tenesmus Constipation Dysphagia Dry mouth/Dysgeusia	Proctitis
Hepatobiliary disorders			Hepatic impairment	
Skin and subcutaneous disorders	Hyperhidrosis		Pruritus	
Musculoskeletal		Pain in	Tetany/Muscle	
System organ class	**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)
and connective		jaw/Trismus	spasms	

tissue disorders		Myalgia/Arthralgia		
Renal and urinary disorders			Kidney pain Dysuria	
General disorders and administration site conditions		Pain, Pyrexia/Body temperature increased, Feeling hot, Asthenia, Chills, generalised warmth, Thirst Infusion site reactions (infusion site erythema, infusion site pain, infusion site phlebitis)		
Injury, poisoning and procedural complications				

*life-threatening and/or fatal cases have been reported

Iloprost may cause angina pectoris, especially in patients with coronary artery disease. The risk of bleeding is increased in patients when inhibitors of platelet aggregation, heparin or coumarintype anticoagulants are given concomitantly. Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms

The following symptoms might be possible: pronounced facial flush, severe headache, sometimes limb and back pain, vagal reaction with sudden pallor, sweating, nausea, vomiting, abdominal pain, cramps, diarrhoea, decreased or increase of blood pressure, bradycardia or tachycardia.

Management

No specific antidote is known.

Interruption of iloprost administration, monitoring and symptomatic measures are recommended.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Platelet aggregation inhibitors excl. heparin, ATC Code: B01AC
Iloprost is a synthetic prostacyclin analogue. The following pharmacological effects have been observed:

- Inhibition of platelet aggregation, platelet adhesion and release reaction
- Dilation of arterioles and venules
- Increase of capillary density and reduction of vascular hyperpermeability caused by mediators such as serotonin or histamine in the microcirculation.
- Stimulation of endogenous fibrinolytic potential

Anti-inflammatory effects such as inhibition of leukocyte adhesion after an endothelial lesion and of leukocyte accumulation in injured tissue, and reduced release of tumour necrosis factor (TNF).

5.2 Pharmacokinetic properties

Distribution

Steady-state plasma levels are achieved as early as 10-20 minutes after the start of an intravenous infusion. The steady-state plasma levels are linearly related to the infusion rate. Plasma levels of about 135 ± 24 picograms/ml are obtained at an infusion rate of 3 nanograms/kg/min. The plasma concentration of iloprost drops very rapidly after the end of the infusion, because of the high rate of metabolism. The metabolic clearance of the substance from plasma is about 20 ± 5 ml/kg/min. The half-life of the terminal elimination phase from plasma is 0.5 hours, as a result of which the plasma level falls to less than 10% of the steady-state concentration, just two hours after the end of infusion.
Interactions with other medicines at the level of plasma protein binding are minimal, because the greater portion of iloprost is bound to the plasma albumin (protein binding: 60%) and only very low iloprost concentration is reached.
An effect of iloprost therapy on the biotransformation of other medicines is also extremely unlikely because of the metabolic pathways and the low absolute dose.
Metabolism

Iloprost is extensively metabolised principally via β-oxidation of the carboxyl side chain. No unchanged substance is eliminated. The main metabolite is tetranor-iloprost, which is found in the urine in free and conjugated form in 4 diastereoisomers. Tetranor-iloprost is pharmacologically inactive as shown in animal experiments. *In vitro* studies suggest that metabolism of iloprost in the lungs is similar following intravenous administration or inhalation.
Elimination

In subjects with normal renal and hepatic function, the disposition of iloprost following intravenous infusion is characterised in most cases by a two-phase profile with mean half lives of 3 to 5 minutes and 15 to 30 minutes. The total clearance of

iloprost is about 20 ml/kg/min, which indicates extrahepatic contribution to the metabolism of iloprost. A mass-balance study was conducted using 3H-iloprost in healthy subjects. Following intravenous infusion, the recovery of total radioactivity is 81%, and the respective recoveries in urine and faeces are 68% and 12%. The metabolites are eliminated with plasma and with urine in 2 phases for which halflives of about 2 and 5 hours (plasma) and 2 and 18 hours (urine) have been calculated.

Pharmacokinetics in special patient groups

Renal impairment

In a study with intravenous infusion of iloprost, patients with end stage renal failure undergoing intermittent dialysis treatment are shown to have a significantly lower clearance (mean CL = 5 ± 2 ml/min/kg) than that observed in patients with renal failure not undergoing intermittent dialysis treatment (mean CL = 18 ± 2 ml/min/kg).

Hepatic impairment

Because iloprost is extensively metabolised by the liver, the plasma levels of the medicine are affected by changes in hepatic function. In an intravenous administration study, results were obtained involving 8 patients suffering from liver cirrhosis. The mean clearance of iloprost was estimated to be 10 ml/min/kg.

Age and Gender

Age and gender are not of clinical relevance to the pharmacokinetics of iloprost.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, and carcinogenicity. Preclinical study effects were observed only at exposures considered considerably higher than the maximum human exposure indicating little relevance to clinical use.

Systemic Toxicity

In acute toxicity studies, single intravenous and oral doses of iloprost caused severe symptoms of intoxication or death (IV - intravenous delivery) at dosages about two orders of magnitude above the intravenous therapeutic dose. Considering the high pharmacological potency of iloprost and the absolute doses required for therapeutic purposes, the results obtained in acute toxicity studies do not indicate a risk of acute adverse effects in humans. As expected for a prostacyclin, iloprost produced haemodynamic effects (vasodilatation, reddening of skin, hypotension, inhibition of platelet function, respiratory distress) and general signs of intoxication such as apathy, gait disorders, and postural changes.

In systemic toxicity studies with repeated (continuous) intravenous infusion, a slight reduction of the blood pressure occurred at doses above 14 nanograms/kg/min and severe adverse effects (hypotension, respiratory function disorder) occurred only after extremely high doses.

Continuous intravenous/subcutaneous infusion of iloprost up to 26 weeks in rodents and nonrodents at dose levels which exceeded the human therapeutic systemic exposure by 14-47 times (based on plasma levels) did not cause any organ toxicity. Only expected pharmacological effects such as hypotension, reddening of skin, dyspnoea and increased intestinal motility were observed.

Genotoxic potential tumourigenicity

In vitro and in vivo studies for genotoxic effects have not produced any evidence of mutagenic potential.
No tumorigenic potential of iloprost could be demonstrated in tumorigenicity studies in rats and mice.
Reproductive Toxicity

In early and late embryo- and fetotoxicity studies in rats, continuous intravenous administration of iloprost led to anomalies of single phalanges of the forepaws in a few pups without dosedependence.
These alterations are not considered as true teratogenic effects, but are most likely related to iloprost-induced growth retardation in late organogenesis due to haemodynamic alterations in the fetoplacental unit. It can be assumed that this growth retardation is widely reversible during the postnatal development. In comparable embryotoxicity studies in rabbits and monkeys, no such digit anomalies or other macroscopic abnormalities in the gross body structure were observed even after considerably higher doses, which exceeded the human dose by multiple times.
In rats, extremely low levels of iloprost excretion into the milk were observed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trometamol
Ethanol 96%
Sodium chloride
Hydrochloric acid (for pH adjustment)
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

24 months.
Chemical and physical in-use 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 the dilution has taken place in controlled and validated aseptic conditions

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions. For storage conditions after dilution of the medicinal product, see section 6.3

6.5 Nature and contents of container

Type I clear glass vial ampoule containing 0.5 ml or 1.0 ml of concentrate for solution for infusion.
Pack sizes

- Box of 1 or 5 ampoules containing 0.5 ml concentrate for solution for infusion
- Box of 1 or 5 ampoules containing 1 ml concentrate for solution for infusion

Not all pack sizes may be marketed

6.6 Special precautions for disposal other handling

Iloprost 100 micrograms/ml concentrate for solution for infusion should be used only after dilution. Due to possible interactions, no other medicinal product should be added to the readyto-use solution for infusion.
In order to ensure sterility, the ready-to-use solution for infusion should be prepared every day.

Instructions for dilution

The ampoule contents and diluent must be thoroughly mixed.
Dilution of Iloprost 100 micrograms/ml concentrate for solution for infusion with an infusion pump.

For this, the content of 1 ml Iloprost ampoule (i.e. 100 micrograms) is diluted with **500 ml** sterile 0.9% sodium chloride solution or a 5% glucose solution.
The content of 0.5 ml Iloprost ampoule (i.e. 50 micrograms) is diluted with **250 ml** sterile 0.9% sodium chloride solution or a 5% glucose solution, respectively.
Dilution of Iloprost 100 micrograms/ml concentrate for solution for infusion with an infusion syringe pump.

For this, the contents of 1 ml Iloprost ampoule (i.e. 100 micrograms) must be diluted with **50 ml** sterile 0.9% sodium chloride solution or 5% glucose solution.
The contents of 0.5 ml Iloprost ampoule (i.e. 50 micrograms) must be diluted with **25 ml** sterile 0.9% sodium chloride solution or 5% glucose solution, respectively.

Handling

Keep this medicine out of the sight and reach of children.
Do NOT let Iloprost solution come into contact with your skin or eyes. If it does, rinse the skin or your eyes immediately with plenty of water.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Galvany Pharma Limited
Business & Technology Centre, Bessemer Drive,
Stevenage, SG1 2DX,

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 56809/0021

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