Iloprost - Intravenous Infusion - Full Clinical Guideline - Derby Only

Reference no.:CG-CLIN/3788/24

Purpose of guideline

To ensure good clinical practice when prescribing Iloprost for use in critical limb ischaemia (CLI) and severe Raynauds syndrome

Background

Iloprost is a prostacyclin analogue which acts as both a vasodilator and a platelet aggregation inhibitor.

Iloprost is indicated for the treatment of patients with severe peripheral arterial occlusion at risk of amputation and in whom surgery or angioplasty is not possible.

It is also indicated for the treatment of severe Raynaud's phenomena.

Aim and Purpose

- To provide guidance for the prescribing doctor when iloprost treatment is recommended by a consultant vascular surgeon (or hand surgeon in the case of ischaemic digits or rheumatologist for severe Raynaud's phenomena).
- To provide a guide for nursing staff on the methods of administration, titration and monitoring.

This guideline is split into two sections:

1. Guidance for prescribing doctor

2. Guidance for nurse administering the infusion

1. *Guidance for Prescribing Doctor*

Assessment prior to therapy

Full blood count

Pulse & blood pressure

History & examination to elicit presence of infection or previous adverse reaction to treatment.

Review of current medicines; including anticoagulants, antiplatelets, NSAIDs and antidepressants

Contraindications[1]

1. Hypotension
2. Previous severe adverse reaction
3. Pregnancy and lactation
4. Conditions where the effects of iloprost on platelets might increase the risk of haemorrhage (e.g. active PUD, trauma, intracranial haemorrhage)
5. Severe coronary artery disease and unstable angina or CCF
6. Myocardial infarction within the last 6 months or cerebrovascular event (e.g., TIA, stroke) within the last 3 months
7. Pulmonary oedema

Cautions

- Counselling of patient regarding side effects of iloprost treatment should take place before the first treatment. The patient should be discussed with the consultant if systemically unwell.
- The rate of infusion should be halved in patients with liver cirrhosis.[1]
- As iloprost inhibits platelet function, use with heparin and warfarin (and inhibitors of platelet aggregation) may increase the risk of bleeding. If bleeding occurs then iloprost should be stopped.
- Review all current medicines that increase risk of bleeding upon initiation of iloprost

Access: A 21 gauge (green) cannula sited in a large vessel (e.g. forearm or anticubital fossa) is advised due to recognised problems with local irritation at the IV site. A 5mg GTN patch may be used proximal to infusion site if IV access is poor and should be applied at least 2 hours prior to the infusion and removed as soon as the 6 hour infusion is complete.

Prescription:

- Prescribe the iloprost infusion on the electronic prescribing system as iloprost 50micrograms intravenous infusion over 6 hours in the morning.
- Routine medication can be administered concurrently though caution with anticoagulant (see cautions above) and consider withholding antihypertensives if baseline BP is low. Prophylactic doses of LMWH may be continued if the consultant deems this appropriate.
- Anticipatory analgesia and antiemetics (usually Paracetamol and Metoclopramide) may help to minimise side effects and therefore optimise the rate of infusion.

Length of Course

The length of course previously used within the trust has generally been 5-7 days. Longer courses have been reported in the literature for critical limb ischaemia[1,2,3,5,6] and extended treatment may be considered at the discretion of the consultant.

Dose reductions or cessation of treatment:

For mild effects tolerated by patient (e.g. flushing, headache, nausea): Continue & Monitor

For moderate effects (hypotension, vomiting, pain in affected limb): Reduce rate by one increment in table 2 according to the patient's body weight & Monitor

For severe effects (e.g. significant drop in BP/confusion/agitation/ arrhythmias)
Stop infusion – discuss with consultant.

2. Guidance for Nurse administering the infusion

- The full course of iloprost will be supplied by pharmacy as vials (1 x 50 micrograms/0.5 mL iloprost injection).
- Refer to the drug monograph on Net-I on guidance on how to prepare the iloprost infusion.
- Treatment is continued for **6 hours each day** and is then discontinued irrespective of the volume remaining in the syringe. The syringe may then be discarded.
- The patient should remain lying or sitting down in bed, during and immediately after receiving the infusion and should be escorted to and from the bathroom where possible.

Table 1 - Dose Titration. All changes to the infusion rate should be signed for on the infusion checklist in the patients nursing file.

	Time	**Monitoring**	**Infusion**
Step 1	Before treatment	Take baseline pulse & BP. Counsel patient on side-effects and to remain sitting/lying	Start infusion based on body weight - see table 2 for infusion rate
2	After 30 mins	Check for side effects, Pulse & BP*	If OK Increase rate to the next infusion rate in table 2
3	60 mins	Check for side effects, Pulse & BP*	If OK Increase rate to the next infusion rate in table 2
4	90 mins	Check for side effects, Pulse & BP*	If OK Increase rate to the next infusion rate in table 2
5	2 hours	Check for side effects, Pulse & BP*	If OK Maintain rate as above as patient will be receiving the maximum rate for their body weight
6	4 hours	Check for side effects, Pulse & BP*	If OK Maintain rate as above
7	6 hours END OF INFUSION	Only continue to monitor after 6 hours if side effects persist	Stop infusion & discard any remaining contents in the syringe
***If side-effects or BP/pulse changes occur then reduce rate by one increment on table 2.** The rate reduction may not be necessary if mild side-effects such as facial-flushing/headache occur and are tolerated by the patient. In the event of serious side-effects (e.g. dramatic drop in BP, agitation, arrhythmias) the infusion should be stopped and a doctor in the team bleeped to review patient.			

Table 2 - Infusion rate table according to body weight. Based on the iloprost being made up to a solution of 50micrograms in 25mL as per the drug monograph on Net-I. All changes to the infusion rate should be signed for on the infusion checklist in the patients nursing file.

	Infusion rate (ml/hr)			
Body Weight (kg)*	**Step 1 (initial infusion rate)**	**Step 2**	**Step 3**	**Step 4 (maximum infusion rate)**
40	0.60	1.20	1.80	2.4
45	0.68	1.35	2.03	2.7
50	0.75	1.50	2.25	3.0
55	0.83	1.65	2.48	3.3
60	0.90	1.80	2.70	3.6
65	0.98	1.95	2.93	3.9
70	1.05	2.10	3.15	4.2
75	1.13	2.25	3.38	4.5
80	1.20	2.40	3.60	4.8
85	1.28	2.55	3.83	5.0
90	1.35	2.70	4.05	5.0
95	1.43	2.85	4.28	5.0
100	1.50	3.00	4.50	5.0
105	1.58	3.15	4.73	5.0
≥110	1.65	3.30	4.95	5.0

*Round patient's body weight to the nearest 5kg.

Summary of Side Effects[1]

Headaches, cough facial flushing, hypotension, nausea, vomiting, diarrhoea, dizziness, hyperhidrosis, paraesthesia, pain in affected limb(s), local irritation at site of IV infusion. Confusion, agitation and arrhythmias have been reported. Allergic reactions may occur. Angina may be provoked.

Once the infusion has finished[7]

Do not flush the central venous access device. After the infusion is stopped, disconnect the administration set, aspirate the cannula contents, and then flush with sodium chloride 0.9%.

References

1. Colonis Pharma Ltd. Summary of Product Characteristics: Iloprost 100 micrograms/ml concentrate for solution for infusion. 2023.
2. Dormandy JA. Prostanoid drug therapy for peripheral arterial occlusive disease: The European experience. Vascular medicine 1996, 1;2:155-158
3. Melillo E & Nuti M et al. Medical therapy in critical lower limb ischaemia when revascularisation is not feasible. Giornale iltaliano di cardiologia 2006 7;5:317- 335
4. Loosemore TM et al. A meta-analysis of randomised placebo controlled trials in Fontaine stages III & IV peripheral occlusive arterial disease. Int Angiol 1994; 13: 133-42
5. Banyai S, Jenelten R et al. Outpatient treatment of severe peripheral ischaemia with intravenous intermittent low-dose iloprost. An open pilot study. Int Angiol 2002 21;1:36-43
6. Sabovic M. Treatment of chronic ischaemia of a replanted thumb. Journal of Hand Surgery 2002 27;5:481-483
7. Medusa monograph: Iloprost. https://medusa.wales.nhs.uk/IVGuideDisplayNewFormat.asp (Accessed May 2023)

Documentation Controls

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