National Pulmonary Hypertension Service
Royal Free Hospital

NHS
University Hospitals Sussex
NHS Foundation Trust

IV Epoprostenol infusions (Veletri, Janssen-Cilag)- dosing protocol.

Written from Royal Free London (Specialist centre) protocol.

Pulmonary Arterial Hypertension can be idiopathic where the cause is unknown or associated with other conditions e.g. it can occur as a complication of connective tissue diseases such as Scleroderma. There is evidence that prostacyclin therapy improves both quality of life and survival, especially at higher doses.

Epoprostenol is a prostacyclin used for the treatment of patients with severe Pulmonary Arterial Hypertension with WHO functional Class III-IV symptoms. Epoprostenol is a potent pulmonary and systemic vasodilator, thus improves exercise capacity. The cardiovascular effects during infusion disappear within 30 min of the end of administration.

- Epoprostenol is now available from several different companies in 0.5mg and 1.5mg strengths.
- Epoprostenol should be prescribed by its generic name with the manufacturers name in brackets i.e. epoprostenol (GSK/Flolan12), epoprostenol (Janssen-Cilag/ Veletri) , epoprostenol (Mercury)
- **Each brand has different reconstitution instructions and thermostable data. Therefore, each one should be prepared in accordance to the manufacturer's summary of product characteristics for their respective product.**
- This dosing chart corresponds to the **Veletri®** product only.
- The patient must be maintained on the same brand of epoprostenol to minimise confusion.

Epoprostenol Therapy

- All patients must have NHS England funding (except in cases of patients admitted to the Royal Free London Trust, that are acutely unwell)
- The specific sheet for preparation/administration should be seen for the epoprostenol product prescribed
- Epoprostenol can be administered peripherally (short term only) or via a skin tunnelled line (once inserted)
- Once started the infusion should **NEVER** be stopped (except when changing syringe)
- Aseptic technique should be used when using a skin tunnelled lines to administer drugs, as per trust policy

Starting doses of Epoprostenol (this normally happens at Royal Free in London)

1) Start the infusion running at 2ng/kg/min
2) Increase the rate of infusion by 1ng/kg/min every 24-48hrs as tolerated by the patient. Standard dosing regime available via PH team.
3) Once the patient is stable and competent to administer their own infusion, swap the patient over to their home pump system in collaboration with the PH team and Pharmacist.

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Approved MGC May 2022, Review May 2024

- **NB** Occasionally it may be necessary to increase the rate more quickly if the patient is acutely ill eg by 0.2-0.5ml every 2-6hours until maximum tolerated is reached.

Monitoring

- Monitor (BP, HR, RR, O_2 sats, side effects) every 15 minutes for first hour post increase then 4 hourly thereafter
- If patient becomes hypotensive (BP<80mmHg systolic), feels faint or extremely dizzy, then reduce the rate of infusion by 0.2-0.5ml/hr and contact the senior medical officer

Side effects

Main side effects are headaches, nausea and vomiting, diarrhoea, jaw and shin pain, low blood pressure and flushing.

Due to the high pH of the buffer solutions, peripheral administration should be kept to short term use only (e.g. whilst central or picc line issues resolved) and using low concentrations of Veletri to minimise risk of extravasation.

Dose Changes

Changes in the long-term infusion rate should be based on persistence, recurrence or worsening of the patient's symptoms of pulmonary arterial hypertension or the occurrence of adverse reactions due to excessive doses of Veletri.

In general, the need for increases in dose from the initial long-term dose should be expected over time. Increases in dose should be considered if symptoms of pulmonary arterial hypertension persist, or recur after improving. The infusion rate should be increased by 1 to 2 ng/kg/min increments at intervals sufficient to allow assessment of clinical response; these intervals should be at least 15 min. Following establishment of a new infusion rate, the patient should be observed, and lying and standing blood pressure and heart rate monitored for several hours to ensure that the new dose is tolerated.

During long-term infusion, the occurrence of dose-related pharmacological events similar to those observed during the dose-ranging period may necessitate a decrease in infusion rate, but the adverse reactions may occasionally resolve without dosage adjustment. Dosage decreases should be made gradually in 2 ng/kg/min decrements every 15 min or longer until the dose-limiting effects resolve. Abrupt withdrawal of Veletri or sudden large reductions in infusion rates should be avoided due to the risk of potentially fatal rebound effect. Other side effects include dizziness, asthenia and increased dyspnoea. **Except in life-threatening situations (e.g. unconsciousness, collapse, etc.), infusion rates of Veletri should be adjusted only under the direction of a physician.**

Continuous Infusion Information (most likely to be used at UHS)

Stock solutions are made up dependant on the patient weight and dose (ng/kg/min). Patients admitted to BSUH who are already on these infusions will know their dose. If they are unable to clarify this information please speak to pulmonary hypertension team at the Royal Free London to obtain this information.

- Maximum concentration to be used with the Veletri® brand is 120,000ng/ml
- The reconstituted Veletri® product is stable at 48hrs at room temperature and for 8 days between 2-8°C
- Therefore, the infusion only needs changing every 48 hours

If there are any queries please contact :

UHS Aorthopathy Nurse Specialist (Jo Jessup) on 07557824209 (office hours only)
UHS oncall cardiology registrar bleep 8850
UHS Cardiology ward pharmacists bleep 8226 for 6a or 8112 for level 10
UHS oncall pharmacist (via switchboard out of hours)
Royal Free pulmonary hypertension registrar (at Royal Free our local specialist centre on bleep 1404),
Royal Free pulmonary hypertension nurses ex 38648 or bleep 1529
Royal Free Pulmonary hypertension pharmacist Shalina Dhalla ex 36014 or bleep 2281.

DOSING TABLES (taken directly from Royal Free protocol)

Veletri (Janssen-Cilag) FOR PATIENTS 45-75KG

Stock solution 1

Dilute 1 x1.5mg vial of epoprostenol with 100ml sodium chloride 0.9% as shown. Final concentration 15,000ng/ml

Dose (ng/kg/min)	Rate (ml/hr) according to patient weight						
	45kg	50kg	55kg	60kg	65kg	70kg	75kg
2	0.4	0.4	0.4	0.5	0.5	0.6	0.6
3	0.5	0.6	0.7	0.7	0.8	0.8	0.8
4	0.7	0.8	0.9	1.0	1.0	1.1	1.1
5	0.9	1.0	1.1	1.2	1.3	1.4	1.4
6	1.1	1.2	1.3	1.4	1.6	1.7	1.7
7	1.3	1.4	1.5	1.7	1.8		
8	1.4	1.6	1.8	1.9			
9	1.6	1.8					
10	1.8						

Stock solution 2

Dilute 2 x1.5mg vial of epoprostenol with 100ml sodium chloride 0.9% as shown. Final concentration 30,000ng/ml

Dose (ng/kg/min)	Rate (ml/hr) according to patient weight						
	45kg	50kg	55kg	60kg	65kg	70kg	75kg
2	0.2	0.2	0.2	0.2	0.3	0.3	0.3
3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
4	0.4	0.4	0.4	0.4	0.5	0.6	0.6
5	0.5	0.5	0.6	0.6	0.7	0.7	0.8
6	0.5	0.6	0.7	0.7	0.8	0.8	0.9
7	0.6	0.7	0.8	0.8	0.9	1.0	1.1
8	0.7	0.8	0.9	1.0	1.0	1.1	1.2
9	0.8	0.9	1.0	1.1	1.2	1.3	1.4
10	0.9	1.0	1.1	1.2	1.3	1.4	1.5
11	1.0	1.1	1.2	1.3	1.4	1.5	1.7
12	1.1	1.2	1.3	1.4	1.6	1.7	1.8
13	1.2	1.3	1.4	1.6	1.7	1.8	
14	1.3	1.4	1.5	1.7	1.8		
15	1.4	1.5	1.7	1.8			
16	1.4	1.6	1.8				
17	1.5	1.7					
18	1.6	1.8					
19	1.7						
20	1.8						

Stock solution 3

Dilute 3 x1.5mg vial of epoprostenol with 100ml sodium chloride 0.9% as shown. Final concentration 45,000ng/ml

Dose (ng/kg/min)	Rate (ml/hr) according to patient weight						
	45kg	50kg	55kg	60kg	65kg	70kg	75kg
10	0.6	0.7	0.7	0.8	0.9	0.9	1.0
11	0.7		0.8	0.9	1.0	1.0	1.1
12		0.8	0.9	1.0		1.1	1.2
13	0.8	0.9	1.0		1.1	1.2	1.3
14				1.1	1.2	1.3	1.4
15	0.9	1.0	1.1	1.2	1.3	1.4	1.5
16	1.0	1.1	1.2	1.3	1.4	1.5	1.6
17				1.4	1.5	1.6	1.7
18	1.1	1.2	1.3		1.6	1.7	1.8
19		1.3	1.4	1.5		1.8	
20	1.2		1.5	1.6	1.7		
21	1.3	1.4		1.7	1.8		
22		1.5	1.6	1.8			
23	1.4		1.7	1.8			
24		1.6	1.8				
25	1.5	1.7	1.8				
26	1.6						
27		1.8					
28	1.7						
29							
30	1.8						

Stock solution 4

Dilute 4 x1.5mg vial of epoprostenol with 100ml sodium chloride 0.9% as shown. Final concentration 60,000ng/ml

Dose (ng/kg/min)	Rate (ml/hr) according to patient weight						
	45kg	50kg	55kg	60kg	65kg	70kg	75kg
12	0.5	0.6	0.7	0.7	0.8	0.8	0.9
13	0.6	0.7		0.8		0.9	1.0
14			0.8		0.9	1.0	1.1
15	0.7	0.8		0.9	1.0	1.1	
16			0.9	1.0			1.2
17	0.8	0.9			1.1	1.2	1.3
18			1.0	1.1	1.2	1.3	1.4
19	0.9	1.0					
20			1.1	1.2	1.3	1.4	1.5
21		1.1	1.2	1.3	1.4	1.5	1.6
22	1.0						1.7
23		1.2	1.3	1.4	1.5	1.6	
24	1.1				1.6	1.7	1.8
25		1.3	1.4	1.5		1.8	
26	1.2			1.6	1.7		
27		1.4	1.5		1.8		
28	1.3			1.7			
29		1.5	1.6				
30	1.4		1.7	1.8			
31		1.6					
32			1.8				
33	1.5	1.7					
34							
35	1.6	1.8					
36		1.8					
37	1.7						
38							

39	1.8						

Stock solution 5

Dilute 5 x 1.5mg vial of epoprostenol with 100ml sodium chloride 0.9% as shown. Final concentration 75,000ng/ml

Dose (ng/kg/min)	**Rate (ml/hr) according to patient weight**						
	45kg	**50kg**	**55kg**	**60kg**	**65kg**	**70kg**	**75kg**
20	0.7	0.8	0.9	1.0	1.0	1.1	1.2
21	0.8				1.1	1.2	1.3
22		0.9	1.0	1.1			
23					1.2	1.3	1.4
24	0.9	1.0	1.1	1.2			
25					1.3	1.4	1.5
26					1.4	1.5	1.6
27	1.0	1.1	1.2	1.3			
28					1.5	1.6	1.7
29		1.2	1.3	1.4			
30	1.1				1.6	1.7	1.8
31			1.4	1.5			
32	1.2	1.3			1.7	1.8	
33			1.5	1.6		1.8	
34		1.4			1.8		
35	1.3			1.7	1.8		
36			1.6				
37		1.5		1.8			
38	1.4		1.7	1.8			
39		1.6					
40			1.8				
41	1.5						
42		1.7	1.8				
43							
44	1.6	1.8					
45							
46	1.7	1.8					
47							
48							

49	1.8						

Stock solution 6

Dilute 6 x 1.5mg vial of epoprostenol with 100ml sodium chloride 0.9% as shown. Final concentration 90,000ng/ml

Dose (ng/kg/min)	**Rate (ml/hr) according to patient weight**						
	45kg	**50kg**	**55kg**	**60kg**	**65kg**	**70kg**	**75kg**
26	0.8	0.9	1.0	1.0	1.1	1.2	1.3
27				1.1	1.2	1.3	1.4
28							
29	0.9	1.0	1.1	1.2	1.3	1.4	1.5
30							
31							1.6
32	1.0	1.1	1.2	1.3	1.4	1.5	
33							1.7
34				1.4	1.5	1.6	
35	1.1	1.2	1.3				1.8
36					1.6	1.7	1.8
37			1.4	1.5			
38		1.3				1.8	
39	1.2			1.6	1.7	1.8	
40			1.5				
41		1.4			1.8		
42	1.3			1.7	1.8		
43			1.6				
44		1.5		1.8			
45	1.4		1.7	1.8			
46				1.8			
47		1.6					
48			1.8				
49	1.5		1.8				
50		1.7	1.8				
51							

52	1.6						
53		1.8					
54							
55	1.7	1.8					
56							
57							
58							
59	1.8						
60	1.8						

Veletri (Janssen-Cilag) FOR PATIENTS 85-110KG

Stock solution 1

Dilute 1 x1.5mg vial of epoprostenol with 100ml sodium chloride 0.9% as shown. Final concentration 15,000ng/ml

Dose (ng/kg/min)	Rate (ml/hr) according to patients weight				
	85kg	90 kg	100 kg	105 kg	110 kg
2	0.6	0.6	0.6	0.8	0.9
3	0.8	0.8	0.8	1.3	1.3
4	1.1	1.1	1.1	1.7	1.8
5	1.4	1.4	1.4		
6	1.7	1.7	1.7		

Stock solution 2

Dilute 2 x1.5mg vial of epoprostenol with 100ml sodium chloride 0.9% as shown. Final concentration 30,000ng/ml

Dose (ng/kg/min)	Rate (ml/hr) according to patients weight				
	85 kg	90 kg	100 kg	105 kg	110 kg
2	0.3	0.4	0.4	0.4	0.4
3	0.5	0.5	0.6	0.6	0.7
4	0.7	0.7	0.8	0.8	0.9
5	0.9	0.9	1.0	1.1	1.1
6	1.0	1.1	1.2	1.3	1.3
7	1.2	1.3	1.4	1.5	1.5
8	1.4	1.4	1.6	1.7	1.8
9	1.5	1.6	1.8		

10	1.7	1.8	

Stock solution 3

Dilute 3 x1.5mg vial of epoprostenol with 100ml sodium chloride 0.9% as shown. Final concentration 45,000ng/ml

Dose (ng/kg/min)	**Rate (ml/hr) according to patients weight**				
	85 kg	**90 kg**	**100 kg**	**105 kg**	**110 kg**
10	1.1	1.2	1.3	1.4	1.5
11	1.2	1.3	1.5	1.5	1.6
12	1.4	1.4	1.6	1.7	1.8
13	1.5	1.6	1.7	1.8	
14	1.6	1.7	1.9		
15	1.7	1.8			
16	1.8				

Stock solution 4

Dilute 4 x1.5mg vial of epoprostenol with 100ml sodium chloride 0.9% as shown. Final concentration 60,000ng/ml

Dose (ng/kg/min)	**Rate (ml/hr) according to patients weight**				
	85 kg	**90 kg**	**100 kg**	**105 kg**	**110 kg**
12	1.0	1.1	1.3	1.3	1.3
13	1.1	1.2	1.3	1.4	1.4
14	1.2	1.3	1.4	1.5	1.5
15	1.3	1.4	1.5	1.6	1.7
16	1.4	1.4	1.6	1.7	1.8
17		1.5	1.7	1.8	
18	1.5	1.6	1.8		
19	1.6	1.7			
20	1.7	1.8			
21	1.8				

Stock solution 5

Dilute 5 x 1.5mg vial of epoprostenol with 100ml sodium chloride 0.9% as shown. Final concentration 75,000ng/ml

Dose (ng/kg/min)	**Rate (ml/hr) according to patients weight**				
	85 kg	**90 kg**	**100 kg**	**105 kg**	**110 kg**
16	1.1	1.2	1.3	1.3	1.4
17	1.2		1.4	1.4	1.5
18		1.3		1.5	1.6

19	1.3	1.4	1.5	1.6	1.7
20	1.4		1.6	1.7	1.8
21		1.5	1.7		
22	1.5	1.6		1.8	
23	1.6	1.7	1.8		
24					
25	1.7	1.8			
26	1.8				

Stock solution 6

Dilute 6 x 1.5mg vial of epoprostenol with 100ml sodium chloride 0.9% as shown. Final concentration 90,000ng/ml

Dose (ng/kg/min)	**Rate (ml/hr) according to patients weight**				
	85 kg	**90 kg**	**100 kg**	**105 kg**	**110 kg**
21	1.2	1.3	1.4	1.5	1.5
22		1.3	1.5		1.6
23	1.3	1.4		1.6	1.7
24	1.4		1.6	1.7	1.8
25		1.5	1.7	1.8	
26	1.5	1.6			
27			1.8		
28	1.6	1.7			
29					
30	1.7	1.8			
31	1.8				
32	1.8				

Stock solution 7

Dilute 7 x 1.5mg vial of epoprostenol with 100ml sodium chloride 0.9% as shown. Final concentration 105,000ng/ml

Dose	**Rate (ml/hr) according to patients weight**

(ng/kg/min)	85 kg	90 kg	100 kg	105 kg	110 kg
25	1.2	1.3	1.4	1.5	1.6
26	1.3		1.5	1.6	
27		1.4			1.7
28	1.4		1.6	1.7	1.8
29		1.5	1.7		
30	1.5			1.8	
31		1.6	1.8		
32	1.6				
33		1.7			
34	1.7				
35		1.8			
36					
37	1.8				
38	1.8				

Stock solution 8

Dilute 8 x 1.5mg vial of epoprostenol with 100ml sodium chloride 0.9% as shown. Final concentration 120,000ng/ml

Dose (ng/kg/min)	Rate (ml/hr) according to patients weight				
	85 kg	90 kg	100 kg	105 kg	110 kg
28	1.2	1.3	1.4	1.5	1.5
29			1.5		1.6
30	1.3	1.4		1.6	1.7
31			1.6		
32	1.4			1.7	1.8
33		1.5	1.7		
34				1.8	
35	1.5	1.6	1.8		
36			1.8		
37	1.6	1.7			
38					
39	1.7	1.8			
40		1.8			
41		1.8			
42	1.8				
43	1.8				

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Approved MGC May 2022, Review May 2024