MEDICATION SAFETY COMMUNICATION

Information for health professionals in NSW public health organisations

Epoprostenol (as sodium) powder for injection – 20 May 2024	
Details of affected product(s)	Epoprostenol sodium (Flolan®) 500 microgram powder for injection vial with diluent vial – ARTG 80342 Epoprostenol sodium (Flolan®) 1.5 mg powder for injection vial with diluent vial – ARTG 80343
Reason for communication	Disruption to supply
Date issue made apparent	April 2024
Estimated resolution date	31 December 2024

Main indications and use

Epoprostenol is indicated for the long-term treatment, via continuous intravenous infusion, in World Health Organisation (WHO) functional class III or class IV patients with:

- idiopathic pulmonary arterial hypertension
- familial pulmonary arterial hypertension
- pulmonary arterial hypertension associated with the scleroderma spectrum of diseases.

Situation

There is an anticipated disruption to the supply of epoprostenol sodium (Flolan) 500 microgram and 1.5 mg powder for injection vial with diluent vial from 1 July 2024 and 10 June 2024 respectively due to manufacturing issues. The estimated return to supply date for both strengths is 31 December 2024.

Alternative agents

At the time of publication, an alternative Australian registered brand, Veletri® remains available:

- Epoprostenol (as sodium) (Veletri) 500 microgram powder for injection vial – ARTG 208316
- Epoprostenol (as sodium) (Veletri) 1.5 mg powder for injection vial – ARTG 207547

Remaining supply of the Flolan brand should be reserved for use where the Veletri brand is not appropriate.

Precautions, safety issues and other considerations associated with alternative products

The Flolan and Veletri brands of epoprostenol are identical in active ingredient, strength and formulation. However, there are differences in excipients, reconstitution instructions, mode of delivery, stability and presentation. **Table 1** has been prepared as a guide to aid a comparison between the two registered products of epoprostenol. Refer to the Product Information for further information.

The differences in formulation are to be considered if the medicine is being administered via any route other than those approved in the Product Information of the Australian registered products (for example, inhalation via nebuliser).
Information for consideration:

- Janssen, the drug sponsor of Veletri, do not endorse the use of their product outside the recommendations listed in the Product Information.
- The presence of arginine as an excipient (which can cause both bronchodilation and bronchoconstriction, inflammation, cytotoxicity and fibrosis) and the pH of the reconstituted solution are cited as concerns with the use of Veletri via the inhaled route.
- Despite this, there are sources of information which support the use of Veletri via the inhaled route including the UpToDate® Lexidrug ™ monograph for epoprostenol.

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Facilities should review their local guidelines/policies containing epoprostenol. This is particularly important in instances where policies/guidelines refer to the Flolan brand specifically. Local Drug and Therapeutic Committees should ensure local processes are in place to minimise risk of incorrect reconstitution and that clinicians are aware of the differences in stability. See **Table 2** for the reconstitution requirements of Flolan and Veletri.

Patients should be informed of the change in brand of epoprostenol prior to its administration and provided with education on the safety considerations. For example, the compatible diluents, type of infusion pump and reconstitution requirements.

Table 1. Comparison of Australian registered products of epoprostenol.

	Flolan (Product Information)	**Veletri** (Product Information)
Active ingredient and strength(s)	Epoprostenol sodium, 500 mcg and 1.5 mg	
Form	Vial and diluent	Vial
Excipients	Glycine, mannitol, sodium chloride, sodium hydroxide.	Sucrose, L-arginine and sodium hydroxide.
Compatible diluent	Use only the diluent supplied, and do not flush the lumen containing epoprostenol, as a bolus dose could be fatal.	Sodium chloride 0.9% or water for injections, and do not flush the lumen containing epoprostenol, as a bolus dose could be fatal.
Reconstitution considerations	Each vial and diluent is for single-use in one patient only. Reconstitution must be carried out under aseptic conditions. Use only the diluent provided for reconstitution. 1. Withdraw approximately 10 mL of the provided diluent into a sterile syringe and inject it into the vial containing the freeze-dried Flolan. 2. Shake the vial gently until the powder has dissolved. 3. Draw up the reconstituted solution in the Flolan vial into the syringe and re-inject it into the remaining volume of the diluent and mix thoroughly.	Each vial is for single-use in one patient only. Reconstitution must be carried out under aseptic conditions. 1. Reconstitute the Veletri vial with 5 mL of a compatible diluent. 2. Withdraw the reconstituted solution in the vial into a syringe. 3. Add the contents in the syringe to a sufficient volume of the identical diluent to make a total of 100 mL.
Administration considerations	The final solution to be administered to the patient must be filtered using a 0.22- or 0.20-micron inline filter. Do not stop the infusion suddenly or make large dose changes except in life-threatening situations. Even brief interruptions to the infusion can lead to rapid deterioration and may be fatal. Extravasation may cause tissue damage.	
Tubing considerations	Flolan is **not** compatible with tubing or containers that contain PET or PETG.	No specific advice provided in Product Information.
Mode of delivery	Use a compatible infusion pump – type not specified in Product Information.	Use a continuous ambulatory delivery device (CADD®) infusion pump.
Storage	Vials and diluent: store below 25°C. Protect from light. Do not store Flolan powder in a bathroom or near a sink, or in the car or on window sills or in the freezer.	Store the Veletri powder in a cool, dry place where it stays below 25°C. Protect from light by keeping it in the carton until use. Do not store Veletri powder in a bathroom or near a sink, in the car or on window sills or in the freezer.

	Flolan (Product Information)	**Veletri (Product Information)**
Stability after reconstitution	Stable for: up to 48 hours if stored at temperatures up to 25°C up to 36 hours if stored at temperatures up to 30°C up to 24 hours if stored at temperatures up to 35°C up to 12 hours if stored at temperatures up to 40°C up to 8 days if kept between 2°C and 8°C. Discard any unused solution after this time.	Stable in the infusion pump for 24 hours at room temperature and up to 30°C. Solutions prepared in a sterile production unit are stable for 8 days at 2 to 8°C. Discard any unused solution after this time.
Presentation	A white to off white powder contained in a glass vial. The diluent is contained in a plastic vial and has a **purple** flip-top cover.	A white to off-white powder in a clear glass vial. The 500 microgram vial has a **white** flip-off cap and the 1.5 mg vial has a **red** flip-off cap.

Table 2. Comparison of reconstitution requirements.

Final concentration required	**Flolan reconstitution requirements**	**Veletri reconstitution requirements**
5,000 nanogram/mL	1 x 500 microgram vial diluted to 100 mL with diluent provided.	1 x 500 microgram vial diluted with 5 mL of compatible diluent. Then withdraw entire vial contents and add to a sufficient volume of the identical diluent to make a total of 100 mL.
10,000 nanogram/mL	1 x 500 microgram vial diluted to 50 mL with diluent provided.	Dilute 2 x 500 microgram vials with 5 mL of compatible diluent each. Then withdraw entire vial contents and add to a sufficient volume of the identical diluent to make a total of 100 mL.
15,000 nanogram/mL	1 x 1.5 mg vial diluted to 100 mL with diluent provided.	1 x 1.5 mg diluted with 5 mL of compatible diluent. Then withdraw entire vial contents and add to a sufficient volume of the identical diluent to make a total of 100 mL.
30,000 nanogram/mL	1 x 1.5 mg vial diluted to 50 mL with diluent provided.	No information provided in Product Information.

Impacts of this communication on clinical practice

- Actions to address the disruption to the supply of epoprostenol (Flolan) should be planned and implemented at a local level by the Drug and Therapeutics Committee in consultation with the relevant clinicians.
- Alternatives are available and can be utilised by facilities after consideration of the above precautions and safety issues in addition to individual patient needs.

Associated regulatory or policy issues

PD2022_032 Medication Handling
PD2019_019 Coordination of responses to urgent system-level medicine or medical device issues

Key contacts

Clinical Excellence Commission (Medication Safety) – CEC-MedicationSafety@health.nsw.gov.au
HealthShare NSW (Category Manager – Strategic Procurement) – Noman.Masood@health.nsw.gov.au