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GLAXOSMITHKLINE SAFETY ADVISORY

Reminder letter regarding the replacement of Flolan® (epoprostenol) (with Solvent pH 10.5) with Flolan® (with Solvent pH 12)

Date: April 2017

Notification of discontinuation of Flolan (with Solvent pH 10.5) from the end of April 2017 following introduction of new sterile solvent with different pH (pH12)

- Flolan® 0.5 mg Powder and Solvent for Solution for Infusion (PL 10949/0310) pH 10.5 formulation
- Flolan® 1.5 mg Powder and Solvent for Solution for Infusion (PL 10949/0312) pH 10.5 formulation

Dear Healthcare Professional

As you may be aware, a new formulation of Flolan (with Solvent pH 12) has been available in the UK from 14th October 2016 with differences in storage and administration from the previously available formulation (with Solvent pH 10.5). There is currently an overlap in availability of this new formulation with the current one – until April 30th 2017, after which Flolan (with pH 10.5 Solvent) will be no longer available to order.

Reconstituted Flolan with pH 12 Solvent (the new formulation) is more thermostable, which eliminates the need for use of a cold pouch/ice pack during administration.

Key Messages for Healthcare Professionals

- You will not be able to order any new stock of Flolan with Solvent pH 10.5 after 30th April 2017.

- The current Summary of Product Characteristics (SmPC) for Flolan (with Solvent pH 10.5) will remain on the Electronic Medicines Compendium website until the 30th of June 2017 to facilitate the use of any remaining stock in your institution, after which time it will be removed.

- Please use all existing stock of Flolan (with Solvent pH 10.5) by the 30th of June 2017. A cold pouch/ice pack should continue to be used with Flolan (with Solvent pH 10.5) where appropriate (eg in PAH). Failure to do so may result in possible decrease in efficacy due to drug degradation

- When reordering Flolan please only order Flolan (with Solvent pH 12)

- Please transition any remaining patients who are taking Flolan (with Solvent pH 10.5) for Pulmonary Arterial Hypertension (PAH) onto Flolan (with Solvent pH 12) or another prostanoid as soon as possible.

Registered in England & Wales
No. 4310159

Registered office
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- It is recommended that when healthcare professionals are writing a Flolan prescription for a patient with PAH, they should make it clear to the pharmacist/homecare provider, which formulation they are requesting for the patient.

- It is recommended that if a pharmacist receives a prescription, where it is unclear whether it should be dispensed as the pH 10.5 or pH 12 formulation, this should be clarified with the prescribing physician.

- Please ensure patients receiving Flolan for their PAH receive advice and information on the changes in storage/administration and that their dose should be unchanged.

Materials have been provided to healthcare professionals involved in the use of Flolan for PAH to help with smooth transition of patients from the current formulation to the new formulation. These have also been available on the EMC website. Further printed supplies can also be obtained by contacting our UK Customer Contact Centre on 0800 221 441. Please ensure all healthcare professionals who prescribe Flolan in your unit/hospital are aware of this information.

IMPORTANT INFORMATION				
	FLOLAN (with Solvent pH 10.5) **Will be discontinued in UK from 30th April 2017** Flolan solution prepared with Solvent for Solution for Infusion (pH 10.5 solvent)		**FLOLAN (with Solvent pH 12)** **New formulation, available in UK from Oct 2016.** Flolan solution prepared with reformulated Solvent for Solution for Infusion (with pH 12 solvent)	
	0.5 mg	1.5 mg	0.5 mg	1.5 mg
EAN Codes	5010706001923	5010706008663	5000123114498	5000123114504
PIP Codes	338-5978	278-3777	403-4989	403-4997
Availability	**Will be discontinued in UK from 30th April 2017**		**New formulation, available in UK from Oct 2016.**	
Storage (PAH) & Stability during administration	Freshly prepared solutions should be used within 12 hours at 25°C. or May be stored for up to 40 hours between 2°C and 8°C and then used within 8 hours at 25°C. The maximum storage and in-use time when maintained between 2°C and 8°C must not exceed 48 hours. When the infusion pump allows the use of a cold pouch, the solution in the infusion pump must be used within a 24 hour period, provided the cold pouch is changed as necessary throughout the day.		**For solutions ≤ 150,000 ng/mL:** Freshly prepared solutions for infusion (either as a concentrated solution or a further diluted solution) can be administered immediately or stored for up to 8 days at 2°C to 8°C prior to administration. Following this preparation or storage, the solution for infusion should be used within: • 72 hours at up to 25°C or • 48 hours at up to 30°C or • 24 hours at up to 35 °C or • 12 hours at up to 40 °C Discard any unused solution after this time. **For solutions >150,000ng/mL and ≤300,000ng/mL:** Reconstituted solutions that have been stored at 2 to 8°C for up to 7 days can be administered for up to 24 hours at 25°C. Freshly prepared reconstituted solutions, or solutions that have been stored at 2 to 8°C for no longer than 5 days can be administered for up to: • 48 hours at up to 25°C • 24 hours at up to 35°C Discard any unused solution after this time.	

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Storage (Renal)	Reconstituted solutions, prepared in real time, must not be administered over more than 12 hours when they are used at room temperature (between 15°C and 25°C). They should be kept under 25°C and protected from light. It is possible to refrigerate Flolan reconstituted solutions, before they are used at room temperature, ranging between 2°C and 8°C and without exceeding 40 hour storage. In this case, the solutions should not be used over more than 8 hours when administered at room temperature.	Reconstitution and subsequent dilution should be carried out immediately prior to use. Freshly prepared solutions for infusion (either as a concentrated solution or a further diluted solution) can be administered for up to 12 hours at up to 25°C. Discard any unused solution after this time.

PACKAGING		
	Flolan solution prepared with Solvent for Solution for Infusion (pH 10.5)	Flolan solution prepared with reformulated Solvent for Solution for Infusion (pH 12)
0.5 mg pack	 Note: Yellow cap on glass bottle containing Solvent pH 10.5	 Note: Purple cap on plastic bottle containing Solvent pH 12
1.5mg pack	 Note: Yellow cap on glass bottle containing Solvent pH 10.5	 Note: Purple cap on plastic bottle containing Solvent pH 12

TherapeuticIndications of Flolan

	Flolan® (epoprostenol) (with Solvent pH 10.5)	**Flolan® (epoprostenol) (with Solvent pH 12)**
0.5mg vial	• The treatment of pulmonary arterial hypertension (PAH) (idiopathic or heritable PAH and PAH associated with connective tissue diseases) in patients with WHO Functional Class III-IV symptoms to improve exercise capacity and • For use in haemodialysis in emergency situations when use of heparin carries a high risk of causing or exacerbating bleeding or when heparin is otherwise contraindicated	• The treatment of pulmonary arterial hypertension (PAH) (idiopathic or heritable PAH and PAH associated with connective tissue diseases) in patients with WHO Functional Class III-IV symptoms to improve exercise capacity and • For use in haemodialysis in emergency situations when use of heparin carries a high risk of causing or exacerbating bleeding or when heparin is otherwise contraindicated
1.5mg vial	• The treatment of pulmonary arterial hypertension (PAH) (idiopathic or heritable PAH and PAH associated with connective tissue diseases) in patients with WHO Functional Class III-IV symptoms to improve exercise capacity and • For use in haemodialysis in emergency situations when use of heparin carries a high risk of causing or exacerbating bleeding or when heparin is otherwise contraindicated	• The treatment of pulmonary arterial hypertension (PAH) (idiopathic or heritable PAH and PAH associated with connective tissue diseases) in patients with WHO Functional Class III-IV symptoms to improve exercise capacity

Actions Being Taken by GlaxoSmithKline

Packaging:

- The packaging has changed and you will be able to clearly distinguish the reformulated solvent with a statement on the external carton of Flolan highlighting the change to the solvent, “New formulation of solvent (pH 12)- read leaflet inside before use”. This statement will be present on the external carton for approximately 6 months following introduction of the reformulated (pH 12) solvent.

- The predominant colour on the top of the external box packaging has changed from white to blue for 0.5 mg Flolan, and from white to deep red for 1.5 mg Flolan. The flip-top lid colour on the solvent bottle has also been changed from yellow to purple to ensure that the reformulated (pH 12) Solvent for Solution for Infusion looks different from Solvent for Solution for Infusion (pH 10.5). The reformulated Solvent for Solution (pH 12) for Infusion can be further distinguished as it is contained in a plastic vial compared to the glass vial of Solvent for Solution (pH 10.5) for Infusion.

- These changes are intended to minimise any potential for medication errors given the different instructions related to storage and administration of the two formulations.

- The Summary of Product Characteristics (SmPC) and Patient Information Leaflet (PIL) for Flolan have been updated to include information regarding use of the reformulated (pH 12) Solvent for Solution for Infusion.

Summary of Product Characteristics and PIL

- The new full SmPC and copies of the new PIL including information for Flolan solution reconstituted with reformulated (pH 12) Solvent for Solution for Infusion are available from the EMC website http://www.medicines.org.uk/emc/.

- Please note that during the period when both versions of the solvent formulation are available, both sets of SmPC and PIL will be available on http://www.medicines.org.uk/emc/. In addition, the SmPC and PIL for the Flolan (with Solvent pH 10.5) will remain on the EMC website until the 30th of June 2017 to facilitate the use of any remaining stock held by your institution, after which time it will be removed.

Support Materials:

- A range of materials to support the healthcare professional and PAH patient in the transition are available from GSK. If you have not already received these via your local GSK contact, please contact our Customer Contact Centre on 0800 221 441 and we will ensure we send supplies to you directly.

Action required by Health Care Providers

- You are advised to read the revised SmPC (available on (http://www.medicines.org.uk/emc/) relating to preparation and use of the reformulated Flolan (with Solvent pH 12). Please share this information with relevant health care personnel under your supervision/in your unit/hospital.

- Use all remaining Flolan (with Solvent pH 10.5) in your institution by the 30th of June 2017.

- Contact any remaining PAH patients taking Flolan (with Solvent pH 10.5) and arrange for them to transition to Flolan (with Solvent pH 12) or another prostanoid before the end of April 2017.

- You are advised to ensure patients being treated for PAH with Flolan are aware of the reformulated Solvent (pH 12) for Solution for Infusion as well as appropriate instructions for reconstitution, storage and administration of Flolan prepared with the reformulated Solvent (pH 12) for Solution for Infusion.

- Should a patient be transitioned from Flolan prepared with the reformulated Solvent (pH 12) for Solution for Infusion to another intravenous prostanoid therapy in the future, please ensure that the patient understands any differences in reconstitution, storage, and administration occurring as a result of that change.

- Ensure that all new Flolan orders are for Flolan (with Solvent pH 12) with immediate effect.

  If you would like a member of the our Medical team to discuss the content of the letter with you in more detail, please contact the Customer Contact Centre on 0800 221 441.

Adverse event reporting:

Adverse events should be reported. For the UK reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to GlaxoSmithKline on 0800 221 441.

Further Information

- Medical Information for GSK Prescription medicines: Tel: +44 (0)800 221 441. 8:30am to 5:30pm GMT Monday - Friday. An out of hours service is also provided for emergencies which goes to an external provider outside of the times stated.

Yours faithfully

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