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GLAXOSMITHKLINE SAFETY ADVISORY

Date: 14th December 2017

Dear Healthcare Professional:

Title: FLOLAN (epoprostenol sodium) and leakage of administration sets containing polyethylene terephthalate glycol (PETG) or polyethylene terephthalate (PET)

GSK has recently received reports of leakage of administration materials used with FLOLAN prepared with Sterile Diluent (pH12) due to cracking or damage. The leakage occurred in components containing polyethylene terephthalate glycol (PETG) that were being used in renal dialysis. Polyethylene terephthalate (PET) is not considered to be compatible with highly alkaline solutions, based on reports of administration set damage when used with highly alkaline medications. PETG is thought to be similarly susceptible to alkaline solutions.

GSK would like to advise that such administration materials may develop damage resulting in cracking or leakage of fluids when used for administration of FLOLAN solution prepared with Sterile Diluent (pH12).

Key Messages

- **FLOLAN solution prepared with Sterile Diluent (pH12) must not be used with any preparation or administration materials containing polyethylene terephthalate (PET) or polyethylene terephthalate glycol (PETG).**

Action Being Taken by GlaxoSmithKline

GSK is reviewing the prescribing information for FLOLAN and Sterile Diluent (pH12) to establish whether an update is warranted to highlight the incompatibility of FLOLAN solution

prepared with Sterile Diluent (pH12) and preparation and administration materials containing PET or PETG.

Action required by Health Care Providers

You should confirm if your patients who are receiving FLOLAN solution prepared with Sterile Diluent (pH12) use any preparation or administration materials that contain PET or PETG.

If you are unsure of the materials that are used by your patients for preparation or administration of FLOLAN solution, you should consult the manufacturer of the sets to confirm if they are considered compatible with highly alkaline solutions, such as FLOLAN solution prepared with Sterile Diluent (pH12).

Please share the information in this letter with relevant health care personnel under your supervision.

Supporting Information

During development of Sterile Diluent (pH12) for FLOLAN, GSK performed physical compatibility tests with preparation and administration materials that were reported to be used during preparation or administration of FLOLAN. These tests assessed the potential for an interaction between epoprostenol reconstituted with Sterile Diluent (pH12) and contact materials used during reconstitution and administration of epoprostenol solutions.

In addition, for some materials, compatibility testing with sodium hydroxide solutions is reported in published literature. These test conditions are frequently at higher pH, higher temperature and longer duration than administration components would be exposed during preparation or administration of FLOLAN solution prepared with Sterile Diluent (pH12). It is therefore likely that a material compatible with these extreme conditions will be generally compatible with FLOLAN solution prepared with Sterile Diluent (pH12).

Based on GSK testing with Sterile Diluent (pH12) or published literature with sodium hydroxide solutions, the following materials are likely to be compatible with FLOLAN solution prepared with Sterile Diluent (pH12):

- Modified Acrylic
- Acrylonitrile butadiene styrene (ABS)
- Cyclic olefin polymer
- Polyamide
- Polyethersulfone
- Polyethylene
- Polyisoprene
- Polyolefin
- Polypropylene

- Polytetrafluoroethylene (PTFE)
- Polyurethane
- Polyvinyl chloride (PVC) (plasticised with bis(2-ethylhexyl) phthalate [DEHP])
- Polyvinylidene fluoride (PVDF)
- Silicone

GSK did not test all administration sets that contain the above materials. The use of components of similar composition to those that were tested constitutes a lower risk of incompatibility. Manufacturers of administration sets may sometimes change the components or materials. You should consult the manufacturer of the sets to confirm if they are considered compatible with highly alkaline solutions, such as FLOLAN solution prepared with Sterile Diluent (pH12), if you are unsure of the materials that are used by your patients for preparation or administration of FLOLAN.

Further Information

Further information concerning Flolan is available within the SmPC, which is available on the HPRA website, www.hpra.ie.

Please report all adverse events associated with FLOLAN, including events associated with the preparation or administration materials or central line used to administer FLOLAN. Reporting 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL-Dublin 2; Tel: +3531 6764971; Fax: +3531 6762517; Website: www.hpra.ie; Email: medsafety@hpra.ie.

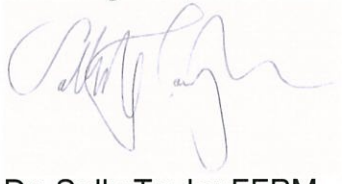
Adverse events should also be reported to GSK on 1800 244 255.

If a problem has occurred with the preparation or administration materials, this should be returned to the manufacturer for further evaluation.

Contact(s) for Further Information or Questions

For all questions, please contact GSK Medical Information at telephone number 1800 244 255.

With regards,



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