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Re: FLOLAN - IMPORTANT SAFETY INFORMATION

12 March 2007

Dear Healthcare Professional,

GSK has been notified of reports of catheter occlusion originating from the US and Canada in patients using the CADD-Legacy 1 pump to infuse Flolan (epoprostenol) for treatment of pulmonary arterial hypertension. In some instances, replacement of the central venous catheter was required and several patients have reported recurrent incidents. Although catheter occlusion is a recognized problem with chronic intravenous drug administration, the number of incidents reported in the last several months is atypical (approximately 1.5% of Flolan users in the US).

GSK has reviewed the manufacturing records of Flolan drug product and Sterile Diluent. No issues related to the quality of Flolan or the Sterile Diluent have been identified. The only reports that GSK has received regarding catheter occlusions have involved the CADD-Legacy 1 pump, manufactured by Smiths Medical MD, Inc. of St. Paul, Minnesota, USA. This pump is one of the most widely used pumps for the administration of reconstituted Flolan. GSK is not aware of any problems associated with the delivery of reconstituted Flolan using any other type of infusion pump.

It is GSK's understanding, from Smiths Medical, that a change was made in reservoir cassette product contact material beginning in May 2006. The cassettes with lot number ending X16 contain the new material. According to the manufacturer, the modified product contact material was shown to be equivalent to the previous material. As a precaution, in the United States and Canada, GSK understands that Smiths Medical has agreed with local specialty pharmacies that distribute Flolan and infusion supplies to provide replacement cassettes for lot number ending X16 for all Flolan patients.

While investigations are ongoing to identify the cause of catheter occlusion, physicians with Flolan patients can contact Smiths Medical (Local Distributors in Ireland, please contact Fannin Healthcare on 01 2944500 or Medivent Ltd on 01 628 0338) regarding replacement cassettes for lot number ending X16, if necessary.

Please discuss this important information with your Flolan patients for whom GSK have also enclosed an information letter that you may use in conjunction with your discussion as appropriate.

Patient safety is of utmost importance to GSK. We remind you that any suspected adverse reactions, including catheter occlusion, should be reported to the

GlaxoSmithKline (Ireland) Ltd.

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D.S. Redfern (GB)

Pharmacovigilance Section of the Irish Medicines Board and/or the local GSK office on according to the national spontaneous reporting system.

Should you have any questions or require additional information, please contact your the GSK medical information department on 1800 244 255.

Yours sincerely,

Martina Dempsey

Dr, Martina Dempsey
Director of Medical & Regulatory Affairs

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Dear Patient,

GlaxoSmithKline, who makes Flolan, has recently learned of a number of occurrences of blockage in the catheters of a number of patients using Flolan, which could disrupt the flow of Flolan.

The cause of the catheter blockages is currently under investigation by GSK. However, to date, we can confirm that these reports have come from patients in the United States and Canada who are using a specific type of infusion pump, the CADD-Legacy 1 pump manufactured by Smiths Medical MD, Inc. of St. Paul, Minnesota, USA. If you use this type of infusion pump, your physician may ask you to check to see if you have any cassettes with an identification lot number ending in X16. This number can be found on the lower right corner of the cassette package. If you have any of these X16 cassettes, please speak with your physician or pharmacy about obtaining alternative cassettes. This recommendation is a precautionary measure; the cause of the catheter blockages is still under investigation.

If you have concerns or questions about your health or the use of Flolan, please contact your physician or other health care provider. If you have any problems with your catheter or infusion pump, then please discuss this with your physician immediately.

If you have any other concerns or questions, please call 1800 244 255.

Yours sincerely,

Martina Dempsey

Dr. Martina Dempsey PhD
Director of Medical & Regulatory Affairs

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