Please read. MWA 03DEC15

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INFORMATION ONLY

Re-introduction of IGIVnex®

Customer Letter # 2015-30

2015-12-02

Dear Customer:

Please see attached letter from Grifols pertaining to the resumed distribution of IGIVnex® (Immune Globulin Intravenous (Human), 10%).

This Customer Letter can also be viewed at www.blood.ca in the "Hospitals" section. If you have questions about this Customer Letter, or if you require it in an accessible format, please contact your local Hospital Liaison Specialist.

Sincerely,

Dana Devine, Ph.D.
Chief Medical & Scientific Officer

Rick Prinzen
Chief Supply Chain Officer

GRIFOLS

Grifols Canada Ltd.
5060 Spectrum Way, Suite 405
Mississauga, ON L4W 5N5
1-866-482-5226

October 30, 2015

Dear Canadian Blood Services Customer:

The purpose of this communication is to notify customers that we have resumed distribution of IGIVnex® (Immune Globulin Intravenous (Human), 10%). This decision is based on the results from a joint Canadian Blood Services - Grifols investigation into the apparent higher rates of allergic/hypersensitivity-type adverse reactions for four IGIVnex® lots. We would like to take this opportunity to provide a summary update regarding IGIVnex® and the findings from this investigation.

Background:

IGIVnex® is manufactured from Canadian donor plasma supplied by Canadian Blood Services, and this product is distributed in Canada by Grifols.

As previously communicated, Grifols recalled IGIVnex® Lot No. 26NP0R1 in February 2014, and quarantined three subsequent lots of IGIVnex® (Lot No. 26NP691, ECGE400021 and ECGE400051), all due to an apparent higher rate of hypersensitivity-type adverse reactions.

Hypersensitivity and anaphylactic/anaphylactoid reactions are a known risk with IVIG products in post-marketing experience and in the clinical trial setting. The nature and severity of the adverse reactions reported were consistent with the safety information in the Product Monograph however the increased reporting was considered a safety signal.

All IGIVnex® lots distributed met required manufacturing and quality standards, and were released through Health Canada's lot release program. Grifols completed a review of all manufacturing records, confirmed that results met specifications and did not identify any manufacturing issues potentially impacting the quality or safety of this product. Grifols also completed extended product characterization and investigational testing, which indicated no unusual differences in the processing, or in the final drug product composition, that may have caused the higher rate of allergic/hypersensitivity-type reactions.

Distribution and use of other IGIVnex® lots during this time period were not associated with any cluster of adverse reaction reports, and there was no similar cluster of reports of these type of adverse events for Grifols' Gamunex® (Immune Globulin Intravenous (Human), 10%) product, which is manufactured using pools of source plasma from donors in the United States, but which uses the same manufacturing process after plasma pooling.

After finding no assignable cause with manufacturing, Canadian Blood Services and Grifols combined scientific, medical and technical expertise and launched a joint investigative team in January 2015 with oversight from an executive steering committee. This team was created to elucidate a potential root-cause through a comprehensive plan investigating the plasma source material and complete supply chain from Canadian Blood Services through to Grifols finished product. At that time, Grifols had also made the decision to hold the release of any new IGIVnex® lots to the market, pending further information from the joint investigative team. Grifols worked with Canadian Blood Services and Health Canada to ensure continued availability of sufficient supply of Gamunex® for Canadian patients.

Investigation Findings and Actions:

A multivariate analysis of data from Canadian Blood Services identified seven whole blood donors whose plasma was common to all recalled/quarantined lots (Lot No. 26NP0R1, 26NP691, ECGE400021 and ECGE400051), but who had not previously donated plasma used in the manufacture of IGIVnex®. Although Canadian Blood Services had not received any reported blood component adverse events through the normal reporting mechanisms, a transfusion safety review of medical records of patients who had received blood components (i.e., red blood cell and platelets) from these seven donors, identified one donor whose blood components were associated with an unusually high frequency of severe anaphylactoid transfusion reactions in recipients. This implicated donor had met all required donor screening and testing criteria, including viral testing of donations and plasma pools. It has been determined that this donor is a potential cause of the high rate of hypersensitivity-type reactions for these IGIVnex® lots.

In response to the findings of the investigative team, Canadian Blood Services has deferred the single implicated donor identified, and Grifols has resumed release and distribution of IGIVnex® product that excludes the plasma from this single donor.

At this time, IGIVnex® Lot No. 26NP691, ECGE400021 and ECGE400051 will remain in quarantine. Actions for these lots will be initiated after the reintroduction of IGIVnex®.

Grifols Pharmacovigilance continues to routinely monitor adverse reactions reports for all Grifols products.

We apologize for the inconvenience this issue has caused and we greatly appreciated your patience, as we maintain our focus on patient safety.

Should you have questions regarding this communication, please contact Grifols Medical Information at 1-866-482-5226.

Sincerely,

Martha Gillies
Director, Contract Operations, Quality & Logistics
Grifols Canada Ltd.

John Parrish
Vice President, Quality Operations
Grifols Therapeutics Inc.