May 18, 2020

To all physicians, haematologists, and other healthcare professionals

It has become apparent in the recent weeks that COVID-19 patients with severe disease may develop associated coagulopathy, similar to disseminated intravascular coagulopathy (DIC).

It has been reported that the most common pattern of coagulopathy observed in patients that require hospitalisation due to severe COVID-19 is characterised by elevations in fibrinogen and D-dimer levels, correlating with a rise in inflammation markers.

In many hospitals, low-molecular-weight heparin is routinely used in these patients for thromboprophylaxis.

It is recommended to monitor platelet count, D-dimer, fibrinogen, and PT/aPTT.

How this may affect haemophilia patients that become infected with the novel coronavirus SARS-CoV-2 is so far unknown.

However, we would like to raise awareness for healthcare practitioners that one-stage clotting assay results can be significantly affected by the type of activated partial thromboplastin time (aPTT) reagent used, which can result in over or under-estimation of Factor IX activity. Avoid the use of silica-based reagents, as some may overestimate the activity of REBINYN®. If a validated one-stage clotting or chromogenic assay is not available locally, then use of a reference laboratory is recommended. Specifically, Rebinyn®, a modified Factor IX product used for the treatment of haemophilia B, is known to interact with the reagents used for the aPTT analysis causing either erroneous shortening or prolongation of clotting time (1).

The following table lists common coagulation assays that may be used to diagnose and monitor patients with COVID-19-associated coagulopathy and indicates whether these assays may be affected by Rebinyn®, providing potential alternatives, where possible. This information is in line with the Rebinyn® FDA-approved Prescribing Information

If a haemophilia B patient on Rebinyn® requires treatment for COVID-19, we recommend to proactively inform the treating healthcare provider about their factor IX treatment and provide them with the below table for increased awareness of its impact on coagulation assays.

Assay/Analyte	Interference with Re-fixia®	Recommended alternatives
aPTT	**Yes** (over/under-estimation of clotting potential when using silica-based aPTT reagents), **avoid if possible**	- Chromogenic anti-Xa assay
PT	No	
D-dimer	No	
Fibrinogen (Clauss method or PT-derived)	No	
FIX activity (one-stage-clotting aPTT based)	**Yes**	- Chromogenic FIX assay - aPTT assays: SynthAFax® or Cephascreen®
FIX activity (chromogenic)	No	
Antithrombin activity	No	
Protein C assay (aPTT based)	**Yes**	Chromogenic Protein C assay
Protein C assay (chromogenic)	No	

Reference:

Rosén P, Rosén S, Ezban M, et al. J Thromb Haemost 2016;14:1420–1427
https://onlinelibrary.wiley.com/doi/full/10.1111/jth.13359

REBINYN®, Coagulation Factor IX (Recombinant), GlycoPEGylated, is a recombinant DNA-derived coagulation Factor IX concentrate indicated for use in adults and children with hemophilia B for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding

For more information please consult full Rebinyn® Prescribing information

To report SUSPECTED ADVERSE REACTIONS, contact Novo Nordisk Inc. at 1-877-668-6777 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*