

Portola Netherlands B.V.  
Prins Bernhardplein 200  
1097 JB Amsterdam  
Netherlands

04 November 2020

**Ondexxya (andexanet alfa): Avoid use of andexanet prior to heparinization.**

Dear Healthcare professional,

Portola Netherlands, B.V., in agreement with the European Medicines Agency and the Medicines and Healthcare products Regulatory Agency would like to inform you of the following information regarding Ondexxya (andexanet alfa):

***Summary***

- **avoid the use of andexanet alfa before heparinization (e.g. during surgery)**
- **andexanet alfa causes unresponsiveness to the anticoagulant effects of heparin;**
- **results of coagulation tests might be misleading when andexanet alfa and heparin are given within a short time of one another. Monitoring of andexanet alfa's effect has not been validated while heparin is active;**
- **use of andexanet alfa for anti-FXa reversal before urgent surgery has not been evaluated.**

***Background on the safety concern***

Andexanet alfa is indicated for adult patients treated with a direct FXa inhibitor (apixaban or rivaroxaban) when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding.

Off-label use of andexanet alfa to reverse FXa anticoagulation prior to surgery with intended heparin anticoagulation has been reported to cause unresponsiveness to heparin. In-vitro data suggest binding of andexanet alfa to the heparin-anti- thrombin III (ATIII) complex and neutralisation of the anticoagulant effect of heparin.

Extent and duration of the interaction have not been evaluated.

### **Call for reporting**

Ondexxya ▼ is subject to additional monitoring and healthcare professionals are asked to report any suspected adverse reactions to the Yellow Card Scheme using the Yellow Card website <https://www.gov.uk/yellowcard>, the free Yellow Card app available from the Apple App Store or Google Play Store, and some clinical IT systems (EMIS, SystemOne, Vision, MiDatabank). Suspected side effects can also be reported by calling 0800 731 6789 for free.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.

### **Company contact point**

If you have any questions about this letter or for more information about Ondexxya, please contact Portola Medical Information. Email: [info@portolaEU.com](mailto:info@portolaEU.com) or telephone. Phone: 0800 069 8041 or +31 20 225 4560.

Sincerely,

DocuSigned by:  
*Ulrich Goldmann*

 Signer Name: Ulrich Goldmann  
Signing Reason: I approve this document  
Signing Time: 02-Nov-2020 | 12:38:52 EST  
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Ulrich Goldmann  
SVP Global Medical Affairs and CMO