Direct Healthcare Professional Communication

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 < *national competent authority*> 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 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. Healthcare professionals are asked to report any suspected adverse reactions directly to:

<Details (name, postal address, fax number, website address) on how to access the national spontaneous reporting system >

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 or telephone. Phone: 0800 069 8041 or +31 20 225 4560.

Sincerely,

Communication Plan for Direct Healthcare Professional Communication

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Ondexxya (andexanet alfa)
Marketing authorisation holder(s)	Portola Netherlands B.V.
Safety concern and purpose of the communication	Andexanet alfa causes unresponsiveness to the anticoagulant effects of heparin. <u>Purpose</u> To increase awareness that use of andexanet prior to heparinization e.g. during surgery should be avoided
DHPC recipients	• Hospital pharmacies • Physicians working on intensive care units • Physicians working on emergency care units • Physicians working in cardiology departments • Surgeons Target groups should be further defined at national level, depending on national health care systems.
Member States where the DHPC will be distributed	The DHPC will be distributed in those countries in which Ondexxya is marketed, currently Austria, Denmark, Finland, Germany, the Netherlands, Sweden and the United Kingdom[1] The DHPC will be distributed in other EU member states at the time of product launch, in agreement with relevant NCAs. [1]As of 1.2.2020, the UK is no longer an EU Member State. However, EU law still applies to the UK during the transition period.

Timetable	Date
DHPC and communication plan (in English) agreed by PRAC	1 October 2020
DHPC and communication plan (in English) agreed by CHMP/CMDh	15 October 2020
Submission of translated DHPCs to the national competent authorities for review	22 October 2020
Agreement of translations by national competent authorities	28 October 2020
Dissemination of DHPC	4 November 2020