



To: Review Committee Chair

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Sponsor/Product: Portola Pharmaceuticals, Inc. / FXa inhibitor antidote, ANDEXXA (andexanet alfa)

Subject: In-support testing to measure the (b) (4) of andexanet alfa against tissue factor pathway inhibitor (TFPI), for licensing action of andexanet alfa, STN 125586

Summary

The potencies of four lots of andexanet alfa drug product (STN 125586) were measured using the (b) (4) Tissue Factor Pathway Inhibitor (TFPI) Inhibition Assay. The andexanet alfa (b) (4) was measured against an in-house reference standard supplied by the sponsor. The assay validity results obtained in CBER met all the assay validity criteria in the sponsor’s SOP. The (b) (4) results from the (b) (4) lots were also within the proposed specifications.

Background

A request was made by the Review Committee Chair to measure the potency of (b) (4) lots of andexanet alfa using the (b) (4) TFPI Inhibition Assay.

Method

The (b) (4) of (b) (4) lots of andexanet alfa was measured at LACBRP/ DBSQC/ CBER using the (b) (4) TFPI Inhibition Assay as described in the document TME-0632 Revision 02 received from the sponsor. This assay measures the ability of andexanet alfa to bind to TFPI, thus reversing the inhibition of FVIIa-Tissue Factor (TF) by TFPI.

(b) (4)

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(b) (4) of the reference standard, assay control and test samples in the range (b) (4) were prepared in (b) (4) and measured in the assay. The mean of the (b) (4) values of the reference standard, provided by the manufacturer (in-house standard), were plotted against concentrations ((b) (4)) to construct the standard curve. Similar plots were also constructed for the control and test samples based on the nominal concentrations provided in the labelling information by the

sponsor. (b) (4) analysis was used to analyze the dose-response curves. The relative potencies of the control and test samples compared to the in-house reference standard were calculated by the (b) (4) software using the measured (b) (4) value, and are expressed as relative (b) (4) as percentage of the standard. The (b) (4) is calculated thus:

(b) (4)

[Redacted]

Reagents Supplied by the Sponsor

- andexanet alfa, In-house Reference Standard, Lot (b) (4) [Redacted], also used as assay control, ((b) (4) [Redacted]).
- Recombinant human TFPI, Lot Number (b) (4) [Redacted].
- Human Factor VIIa, Lot Number (b) (4) [Redacted]
- Human Factor X, Lot Number (b) (4) [Redacted]

Results

The results of the assay validity criteria are shown in Table 1.

Table 1: Assay Validity criteria for the (b) (4) TFPI Inhibition Assay

Assay Validity Criteria	Results
(b) (4)	

Assay Validity Criteria	Results
(b) (4)	

The (b) (4) results of (b) (4) lots of the drug product are presented in Table 2.

Table 2: CBER/ DBSQC potency measurements for andexanet alfa samples using (b) (4) TFPI Inhibition Assay

Sponsor's specifications:

(b) (4)

Lot Number	Sponsor's Result ¹		CBER Results		CBER/Sponsor Results Ratio (%)	
	(b) (4)	(b) (4)	(b) (4)	(b) (4)	(b) (4)	(b) (4)
(b) (4)	(b) (4)		109	1.04	96.5	96.8
(b) (4)			109	1.04	101.9	101.5
(b) (4)			107	1.02	109.2	109.3
(b) (4)			115	1.09	133.7	134.9

¹ Sponsor's results are from Supplemental Information from the Sponsor as 125586/0.82

Conclusions

The results obtained in LACBRP/DBSQC show that the (b) (4) of andexanet alfa measured by the (b) (4) TFPI Inhibition Assay are within the specifications proposed for this assay and comparable with the results obtained by the sponsor.