DABIGATRAN PLASMA CALIBRATOR

Ref 222801

CE IVD

HYPHEN BioMed
www.hyphen-biomed.com
155, rue d'Eragny
95000 NEUVILLE SUR OISE
FRANCE
Tel. : +33 (0)1 34 40 65 10
Fax : +33 (0)1 34 48 72 36
info@hyphen-biomed.com

Calibration plasma for the assay of Dabigatran with anti-IIa method

Not for Sale in the US

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ENGLISH:

INTENDED USE:

Dabigatran Plasma Calibrator is a set of calibration plasmas for Dabigatran measurements, titrated and optimized using the anti-IIa clotting assay **HEMOCLOT THROMBIN INHIBITORS (CK002K/CK002L).**
When required, Dabigatran Plasma Calibrator allows calibrating the assays of Dabigatran using clotting anti-IIa method, especially when HEMOCLOT Thrombin Inhibitors kit is used, with the **standard range protocol**.

SUMMARY AND EXPLANATION:

Dabigatran is the active moiety of the oral anticoagulant pro-drug, Dabigatran etexilate (Pradaxa®). When required, Dabigatran can be measured in plasma in case of suspicion of excess of anticoagulant activity.

REAGENTS:

12 vials (4 sets of 3 vials) of 1 ml human plasma supplemented with different concentrations of Dabigatran (4 vials for each concentration).

CAL 1: Calibrator 1: Human plasma, lyophilized, supplemented with Dabigatran (level 1 at **about 50 ng/mL**) – 4 vials of 1mL
CAL 2: Calibrator 2: Human plasma, lyophilized, supplemented with Dabigatran (level 2 at **about 250 ng/mL)** – 4 vials of 1mL
CAL 3: Calibrator 3: Human plasma, lyophilized, supplemented with Dabigatran (level 3 at **about 500 ng/mL**) – 4 vials of 1mL.

The exact concentration of Dabigatran in each vial is indicated on the flyer provided in each kit. The calibration curve covers the range from <50 to 500 ng/mL.

CAUTIONS AND WARNINGS:

- Any product of biological origin must then be handled with all the required cautions, as being potentially infectious.
- Calibrator plasmas contain preservative.
- Each donor unit used for the preparation of calibration plasmas is a human plasma, which has been tested with registered methods for the presence of Hepatitis B Surface Antigen, Hepatitis C Antibodies (HVC) and antibodies to HIV 1 and 2 and was found negative. However, no test can completely exclude the presence of infectious agents. Any product of human origin, and more especially plasma, must be considered as being potentially infectious and must be handled with all the required cautions for this kind of material.
- The disposal of waste materials must be carried out according to current local regulations
- In order to improve stability, reagents must be closed with their original screw caps following each use.
- Reagents must be handled with care, in order to avoid any contamination during use. Take care to limit as much as possible any evaporation of the reagents during use, by limiting the liquid-air surface exchange. Evaporation reduces reagent stability on instrument board.
- It is recommended to homogenize each vial before use, in order to have a good reproducibility, all the time.
- Stability studies for 3 weeks at 30°C show that the reagents can be shipped at room temperature for a short period without damage.
- For in vitro diagnostic use.

PREPARATION AND STABILITY OF REAGENTS:

Calibrator:
Reconstitute each vial with exactly **1mL** of distilled water, shake thoroughly for complete homogenization.
Let the reagent stabilize for 30 min at room temperature (18-25°C); while shaking the vial from time to time.
Homogenize before each use.
Stability of reagent, provided that any contamination or evaporation is avoided, kept in its original vial or in a closed plastic microcentrifuge tube:

- **7 days** at 2-8°C.
- **48 hours** at room temperature (18-25 °C).
- **Up to 6 months** frozen at -20°C or below*

*At around ≤ -20°C: plasma in a tightly closed container can be frozen and thawed once. Freeze as rapidly as possible. Thaw at +37°C; adapt duration to the volume of plasma. Use within 2 hours. The stability of the thawed reagent should be verified in the working conditions of the user laboratory.

STORAGE CONDITIONS:

Reagents must be stored at 2-8°C, in their original packaging box. They are then usable until the expiration date printed on the box.

TRACEABILITY:

These concentrations are accurately determined against an Internal Reference Standard, initially validated against fresh reference preparations of Dabigatran, spiked into a normal human citrated plasma pool, and confirmed with a physico-chemical method (LC-MS).

QUALITY CONTROL:

If used with anti-IIa assays from other manufacturers, measured values can vary according to the assay reactivity and its standardization: each laboratory must then determine and validate the appropriateness of using this calibrator in its specific assays conditions.

CHARACTERISTICS:

Dabigatran Plasma Calibrators allow establishing the calibration curve for the measurement of Dabigatran in plasma, especially with Anti-IIa method. Using the **HEMOCLOT Thrombin Inhibitors (ref. CK002K/L)** kit, Dabigatran is measured with the **standard range protocol**, and the assay is linear up to about 500 ng/mL using the manual method or the STA-R instrument.
The calibration curve obtained covers the usual concentrations currently observed during Dabigatran therapy.
Dabigatran Control Plasma (ref 224701) can be used in order to obtain an homogeneous quality control system.
The HEMOCLOT Thrombin Inhibitors anti-IIa method, used according to the **standard range protocol**, for the measurement of Dabigatran concentrations in plasma, offers a sensitivity threshold of about ≤20 ng/mL.
If used with other kits, results can vary according to the assay reactivity and its standardization: each laboratory must then determine and validate the suitability for use in its specific test conditions.

LIMITATION:

- Like all lyophilised plasmas, the calibration plasmas are more or less cloudy after reconstitution. This is due essentially to the lipids that, after lyophilisation, become less soluble and can form a light deposit.
- If necessary, let each vial 10 minutes at room temperature and shake gently before use in order to homogenise the content.
- Any plasma containing a coagulum or contamination must be rejected.
- Performances should be verified in the exact laboratory working conditions.

REFERENCES:

1 Product Monograph Pradaxa® (Dabigatran etexilate) based on EU approval (Boehringer Ingelheim)
2 Oral Dabigatran etexilate vs subcutaneous enoxaparin for the prevention of venous thromboembolism after total knee replacement: the Re-MODEL randomized trial" Eriksson et al., J Thromb Haemost, 2007, 5:2178-85.
3 Dabigatran etexilate vs enoxaparin for the prevention of venous thromboembolism after total hip replacement: a randomised, double-blind, non inferiority trial" Eriksson et al., Lancet, 2007, 370:949-956.
4 Clinical Pharmacokinetics and Pharmacodynamics of the Oral Direct Thrombin Inhibitor Dabigatran Etexilate, J Stangier, Clin Pharmacokinet 2008; 47(5): 285-295.
5 The pharmacokinetics, pharmacodynamics and tolerability of Dabigatran etexilate, a new oral direct thrombin inhibitor, in healthy male subjects, J Stangier et al, Br J Clin Pharmacol 2007, vol 63.
6 A new oral direct thrombin inhibitor, Dabigatran etexilate, compared with enoxaparin for prevention of thromboembolic events following total hip or knee replacement: the BISTRO II randomized trial; Eriksson et al, J Thromb Haemost 2005, 3: 103-111.
7 Woodhams B, Girardot O, Blanco M-J, Colesse G, Gourmelin Y.Stability of coagulation proteins in frozen plasma. Blood coagulation and Fibrinolysis. 2001. Vol 12, No 4. 229-236.

SYMBOLS:

Used symbols and signs listed in the ISO standard 15223-1.