

BIOPHEN™ Edoxaban**Control Low**

REF 225401

CI CII 6 x 1 mL



Human plasmas at 2 levels of Edoxaban for the quality control of Edoxaban measurements by chromogenic method.

Not for Sale in the US

English, Last revision: 05-2017

INTENDED USE:

The BIOPHEN™ Edoxaban Control Low kit is a set of control plasmas intended for the quality control of Edoxaban measurements, and lyophilized. They are titrated and optimized for anti-Xa chromogenic assays (low range) such as BIOPHEN™ Heparin LRT (221011, 221013 and 221015) and BIOPHEN™ DiXal (221030).

SUMMARY AND EXPLANATION:

Edoxaban is an oral anticoagulant drug, used for curative or preventive indications. Although monitoring of this treatment is not necessary, when required, measuring the Edoxaban concentration in patients' plasma is helpful in some clinical cases: emergency surgery, adherence to treatment... These control plasmas are then proposed for the quality control of Edoxaban measurements in plasma using anti-Xa chromogenic assays.

REAGENTS:

CI Control I: Lyophilized human plasma containing a titrated quantity of Edoxaban of approximately 25 ng/mL.
6 vials of 1 mL.

CII Control II: Lyophilized human plasma containing a titrated quantity of Edoxaban of approximately 75 ng/mL.
6 vials of 1 mL.

The control concentrations may vary slightly from one batch to the next. For the assay, see the exact values provided on the flyer provided with the kit used.

WARNINGS AND PRECAUTIONS:

- Control plasmas contain stabilizing agents.
- Each pouch of human plasma used for kit preparation was obtained from healthy donors. Each plasma used was screened for the presence of the HBs antigen, of anti-HIV1, anti-HIV2 and anti-HCV antibodies, using approved methods, and found to be negative. Nevertheless, no tests can totally exclude the presence of infectious agents. For this reason, every precaution required for the use of potentially infectious products should be taken when handling and disposing of plasma.
- Waste should be disposed of in accordance with applicable local regulations.
- Handle the reagents with care to avoid contamination during use. If possible, avoid reagent evaporation during use by limiting the liquid-air exchange surface. Evaporation reduces the reagent's stability in the analyzer.
- To ensure reagent stability, seal the vials after use with their respective caps, or close the plastic micro-containers into which the plasmas may have been transferred, depending on the protocol used.
- Aging studies, conducted over a 3-weeks period at 30°C, show that the reagents can be shipped at room temperature over a short period of time, without degradation.
- For *in vitro* diagnostic use.

REAGENT PREPARATION AND STABILITY:

The reagents are lyophilized under a vacuum in their vials. To avoid any product loss when opening the vial of lyophilized reagents, gently remove the freeze-drying stopper.

CI CII

Reconstitute the contents of each vial with exactly **1 mL distilled water**, shake vigorously until fully dissolved.

Allow to stabilize for 30 min. at room temperature (18-25°C), shaking occasionally.

Homogenize prior to use.

Reagent stability after reconstitution, free from any contamination or evaporation, and stored in the original vial, is of:

- **7 days** at 2-8°C.
- **24 hours** at room temperature (18-25°C).
- **2 months** frozen at -20°C or less*

*Thaw only once, as rapidly as possible at 37°C, adapting the incubation period to the volume of reagent. The stability of the thawed reagent should be checked under laboratory work conditions.

STORAGE CONDITIONS:

Unopened reagents should be stored at 2-8°C in their original packaging. Under these conditions, they can be used until the expiry date printed on the kit.

REAGENTS AND MATERIALS REQUIRED BUT NOT PROVIDED:**Reagents:**

- Distilled water.

Materials:

- Calibrated pipettes.

TRACEABILITY:

The Edoxaban control plasmas are qualified against an Internal Standard Reference, whose qualification is linked to the reference method by HPLC-MS/MS.

PROPERTIES:

The BIOPHEN™ Edoxaban Control Low is used for the quality control of Edoxaban assays by chromogenic methods (low range), such as those provided by BIOPHEN™ Heparin LRT (221011, 221013 and 221015) and BIOPHEN™ DiXal (221030).

The controls target values are determined from multi-reagent (BIOPHEN™ Heparin LRT and BIOPHEN™ DiXal) and multi-instrument (Sysmex CS-series or equivalent) tests.

The use of quality controls serves to validate method compliance, along with between-series assay homogeneity for a given batch of reagents.

Include the quality controls with each series, as per good laboratory practice, in order to validate the test.

If the controls fall outside of the acceptable range, the series of assays must be invalidated and the analyses repeated. Check all system parameters before repeating the series.

LIMITATIONS:

- Like all lyophilized plasmas, control plasmas are more or less turbid once resuspended. This turbidity is mainly due to plasma lipids that, after freeze-drying, become "less" soluble and may form a slight deposit.
- Any plasma displaying a coagulum or showing signs of bacterial or fungal contamination must be rejected.
- If the controls are used under measurement conditions other than those validated by HYPHEN BioMed, the test results may vary. The laboratory is responsible for validating the use of these controls in its own analytical system.

REFERENCES:

1. Bathala MS et al. Pharmacokinetics, biotransformation, and mass balance of edoxaban, a selective, direct factor Xa inhibitor, in humans. *Drug Metab Dispos.* 2012 Dec;40(12):2250-5.
2. Bounameaux H and Camm AJ. Edoxaban: an update on the new oral direct factor Xa inhibitor. *Drugs.* 74(11):1209-31. 2014.
3. Furugohri T et al. DU-176b, a potent and orally active factor Xa inhibitor: in vitro and in vivo pharmacological profiles. *J Thromb Haemost.* 6(9):1542-9. 2008.
4. Patel MR, Washam JB. Edoxaban and the need for outcomes-based NOAC dosing. *Lancet.* 385(9984):2232-3. 2015.
5. Honda Y and Morishima Y. Thrombin generation induced by tissue factor plus ADP in human platelet rich plasma: A potential new measurement to assess the effect of the concomitant use of an oral factor Xa inhibitor edoxaban and P2Y12 receptor antagonists. *Thromb Res.* 135(5):958-62. 2015.
6. Ogata K et al. Clinical safety, tolerability, pharmacokinetics, and pharmacodynamics of the novel factor Xa inhibitor edoxaban in healthy volunteers. *J Clin Pharmacol.* 50(7):743-53. 2010.
7. Ruff CT et al. Association between edoxaban dose, concentration, anti-Factor Xa activity, and outcomes: an analysis of data from the randomised, double-blind ENGAGE AF-TIMI 48 trial. *Lancet.* ;385(9984):2288-95. 2015.
8. Zalpour A and Oo TH. Update on Edoxaban for the Prevention and Treatment of Thromboembolism: Clinical Applications Based on Current Evidence. *Adv Hematol.* 920361. 2015

SYMBOLS:

Symbols used and signs listed in the ISO 15223-1 standard, see Symbol definitions document.