



Monitoring heparin therapy and measuring direct Xa inhibitors: **Simple, fast, 24/7**

- Liquid formulation, ready-to-use
- One-stage, chromogenic anti-Xa assay
- Universal calibration for UFH and LMWH
- Drug specific calibrators and controls for measurement of Rivaroxaban and Apixaban

Monitoring heparin and measuring direct Xa inhibitors



Unfractionated and low molecular weight heparin

Heparin is a highly sulfated polysaccharide characterized by a wide molecular weight range and a potent anticoagulant activity. It exists either as unfractionated heparin (UFH) or as depolymerized low molecular weight heparin (LMWH). UFH and LMWH have a rapid anticoagulant effect and are used in the prevention and treatment of venous thrombosis and acute coronary syndrome.

UFH and LMWH anticoagulant activity occurs when a complex with antithrombin (AT) is formed, potentiating its anticoagulant activity up to 1,000 fold, which inactivates both thrombin (IIa) and Factor Xa (FXa). UFH acts through both FIIa and FXa inhibition, while LMWH is a more efficient catalyst for FXa inhibition.

Laboratory monitoring is extremely important to assess the appropriate level of anticoagulation in patients. Anti-Xa is recommended for monitoring both UFH and LMWH.

Anti-Xa testing for monitoring UFH helps improve quality of care and patient experience while reducing costs, when compared to APTT testing.¹ The advantages include:

- Higher precision
- Lower levels of discordant results^{1,2,4}
- Faster time to achieve therapeutic levels^{1,3,4}
- Fewer tests and dosage changes^{1,3,4,5}

Direct Xa Inhibitors

Direct oral anticoagulants (DOAC), such as rivaroxaban and apixaban, do not require routine monitoring. However, there are specific instances when an understanding of the DOAC concentration in a patient sample may be useful.

Clinical scenarios where DOAC measurement may be warranted¹

- Bleeding
- Before surgery or an invasive procedure when the patient has taken the drug in the previous 24 hours, or longer if creatinine clearance (CrCl) is < 50 mL/min
- Identification of subtherapeutic or supratherapeutic levels in patients taking other drugs that are known to significantly affect pharmacokinetics

- Identification of subtherapeutic or supratherapeutic levels in patients at the extremes of body weight
- Patients with deteriorating renal function
- Perioperative management
- Reversal of anticoagulation
- Suspicion of overdose
- Assessment of compliance in patients suffering thrombotic events while on treatment

Chromogenic anti-Xa assays are recommended for the measurement of rivaroxaban and apixaban levels.⁶

Promoting effective prophylaxis and treatment for patients on heparin

One calibration curve for UFH and LMWH

HemosIL Liquid Anti-Xa is optimized for testing UFH and LMWH with a single calibration curve, saving time and resources by eliminating the need to set up and prepare multiple calibration curves for each heparin type.

The data below demonstrate excellent recovery for all heparin preparations tested on Instrumentation Laboratory (IL) Hemostasis testing systems.

| Heparin recoveries on IL systems | | | | |
|---|-----------------------|-----------------------|----------------------|--------------------------------------|
| Heparin type | Target values (IU/mL) | Calibration with LMWH | Calibration with UFH | Calibration with heparin calibrators |
| Fragmin® (dalteparin sodium) | 0.40 | 0.40 | 0.42 | 0.44 |
| | 0.80 | 0.77 | 0.80 | 0.78 |
| | 2.00 | 1.80 | 1.83 | 1.83 |
| Innohep® (tinzaparin sodium) | 0.40 | 0.40 | 0.46 | 0.44 |
| | 0.80 | 0.77 | 0.83 | 0.81 |
| | 2.00 | 1.83 | 1.87 | 1.87 |
| Lovenox® (enoxaparin sodium) | 0.40 | 0.39 | 0.42 | 0.39 |
| | 0.80 | 0.83 | 0.86 | 0.84 |
| | 2.00 | 1.87 | 1.92 | 1.97 |
| LMWH standard | 0.40 | 0.40 | 0.43 | 0.40 |
| | 0.80 | 0.84 | 0.84 | 0.87 |
| | 2.00 | 1.93 | 1.97 | 1.97 |
| UFH standard | 0.40 | 0.42 | 0.44 | 0.42 |
| | 0.80 | 0.77 | 0.80 | 0.77 |
| | 2.00 | 1.93 | 1.97 | 1.97 |

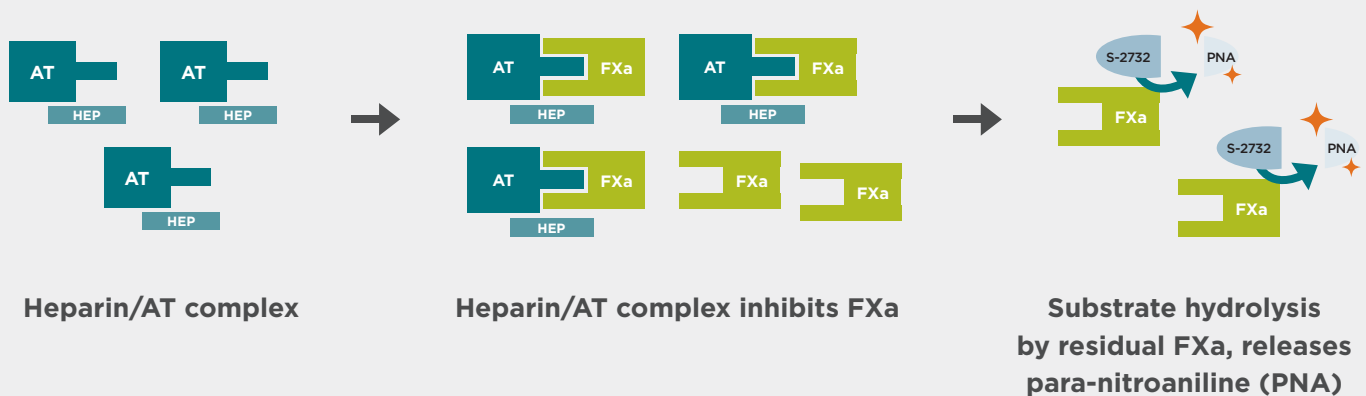
*IL, data on file.

In addition to the three brands of LMWH above, heparin calibrators can be used with Fraxiparine (nadroparin calcium) and with UFH, including Calciparin and Leo synthetic heparins. Arixtra (fondaparinux) and Orgaran (danaparoid) have not been standardized against LMWH; Heparin Calibrators can be used upon establishment of a local conversion factor.*

HemosIL Liquid Anti-Xa

one-stage, universal heparin assay

With the one-stage Liquid Anti-Xa assay, heparin is measured as a complex using only the AT present in the sample (no excess AT is added). FXa is then added to the sample in excess, along with a chromogenic substrate (S-2732). Two competing reactions occur simultaneously:



The resulting absorbance is inversely proportional to the heparin concentration in the plasma.

Greater efficiency and simplicity

With its ready-to-use format and wide linear range, Liquid Anti-Xa provides accurate results with greater efficiency, in less time. Innovative and simple, the Liquid Anti-Xa kit, along with Heparin Calibrators and UF and LMW Heparin Controls, requires only one calibration curve for the determination of both UFH and LMWH activity, over a wide linear range.

- Liquid, ready-to-use
- Available 24 hours/day, 7 days/week, in the routine lab
- Fully automated on ACL Hemostasis systems
- Single calibration curve for UFH and LMWH
- Linear up to 2.0 IU/mL for UFH and LMWH
- Measures effective heparin activity

| Calibrators | Controls |
|---|---|
| <ul style="list-style-type: none"> • Tri-level calibrator traceable to World Health Organization standards for UFH and LMWH • Predetermined heparin concentration: 0.0, 0.8 and 2.0 IU/mL | <ul style="list-style-type: none"> • Bi-level assayed Low and High • Values near the therapeutic ranges |

Promoting effective prophylaxis and treatment for patients taking DOAC therapy

High-performance, automated solution for rivaroxaban and apixaban testing

HemosIL Rivaroxaban and Apixaban Calibrators and Controls, used in conjunction with the HemosIL Liquid Anti-Xa assay, deliver an automated solution for reliable results.

Superior linearity

- Rivaroxaban (20-1000 ng/mL)
- Apixaban (15-1000 ng/mL)

Excellent sensitivity

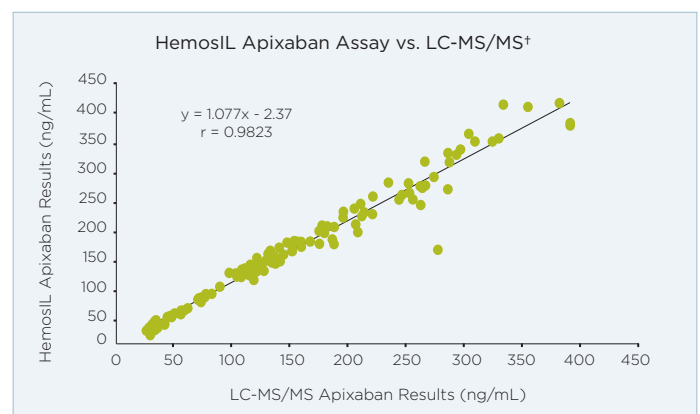
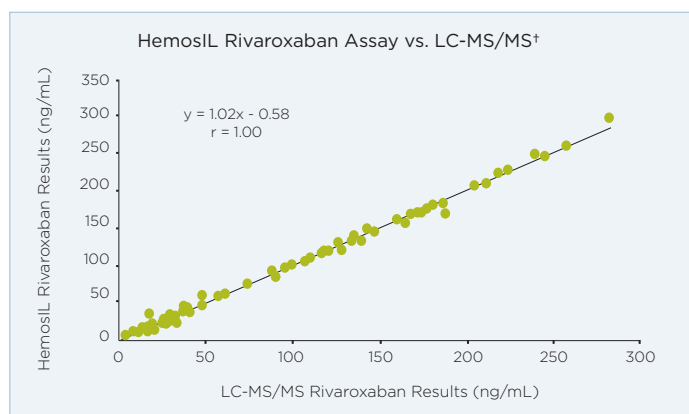
- Rivaroxaban (LoQ:20 ng/mL, LoD:10 ng/mL)
- Apixaban (LoQ:10 ng/mL, LoD:6 ng/mL)

Analytical performance on ACL TOP® Testing Systems

Fully validated and automated on ACL TOP Family and ACL TOP Family 50 Series Hemostasis Testing Systems, the HemosIL Liquid Anti-Xa assay offers reduced interference and extended onboard stability for superior efficiency.

| | Liquid Anti-Xa | | | |
|---|---|---------------------------------|---|---------------------------------|
| | Apixaban | | Rivaroxaban | |
| Linearity | 15-1000 ng/mL | | 20-1000 ng/mL | |
| Imprecision | Low control High control | % CV Total 4.0 1.9 | Low control High control | % CV Total 4.4 2.2 |
| Interference Hemoglobin Bilirubin Triglycerides | ≤ 300 mg/dL ≤ 25 mg/dL ≤ 1156 mg/dL | | ≤ 550 mg/dL ≤ 40 mg/dL ≤ 1151 mg/dL | |
| Onboard Stability on ACL TOP Family Testing Systems | Liquid Anti-Xa: 7 days at 15-25° C Calibrator/Control: 8 hours at 15-25° C | | Liquid Anti-Xa: 7 days at 15-25° C Calibrator/Control: 8 hours at 15-25° C | |

Demonstrates excellent agreement with the “gold standard” liquid chromatography-tandem mass spectrometry (LC-MS/MS) method



†Data on file, IL.

HemosIL Liquid Anti-Xa, and Heparin/DOAC Calibrators/Controls

| Reagent | Part Number | Kit Configuration |
|---|-------------|--|
| Liquid Anti-Xa* | 0020302600 | 5 x 2.5 mL Factor Xa Reagent (liq) 5 x 3 mL Chromogenic Substrate (liq) |
| Liquid Anti-Xa** (for Heparin and Direct Xa inhibitors) | 0020302601 | 5 x 2.5 mL Factor Xa Reagent (liq) 5 x 3 mL Chromogenic Substrate (liq) |
| Heparin Calibrators | 0020300600 | 3 x 1 mL Calibrator 1-3 (lyo) |
| UF Heparin Controls | 0020300300 | 5 x 1 mL Low UF Heparin Control (lyo) 5 x 1 mL High UF Heparin Control (lyo) |
| LMW Heparin Controls | 0020300200 | 5 x 1 mL Low LMW Heparin Control (lyo) 5 x 1 mL High LMW Heparin Control (lyo) |
| Rivaroxaban Calibrators** | 0020013600 | 5 x 1 mL Rivaroxaban Calibrator 1 (lyo) 5 x 1 mL Rivaroxaban Calibrator 2 (lyo) |
| Rivaroxaban Controls** | 0020013700 | 5 x 1 mL Rivaroxaban Low Control (lyo) 5 x 1 mL Rivaroxaban High Control (lyo) |
| Apixaban Calibrators** | 0020014200 | 5 x 1 mL Apixaban Calibrator 1 (lyo) 5 x 1 mL Apixaban Calibrator 2 (lyo) |
| Apixaban Controls** | 0020014300 | 5 x 1 mL Apixaban Low Control (lyo) 5 x 1 mL Apixaban High Control (lyo) |

*Not saleable in all countries.

**Not FDA 510(k)-cleared. Not saleable in the US. Not available in all countries.

References

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