Anticoagulant management

Simple and efficient anticoagulant management with 24/7 availability: one reagent for all anti-Xa drug activities

Together for a better
healthcare journey

Key benefits at a glance

- Liquid, ready-to-use
- Fully automated on Sysmex analysers, with 24/7 availability
- Factor Xa (FXa) -based chromogenic assay design
- No antithrombin (AT) dependency within the normal range (50% - 170%)
- No PF4 interference up to 1 µg/mL
- Extended stability
- One universal solution; a single reagent to measure a broad range of anti-Xa drug activities:
  - Heparins (unique, calibration curve for UFH & LMWH)
  - Direct oral anti-Xa inhibitors (drug specific calibrators and controls for Rivaroxaban, Apixaban, Edoxaban)

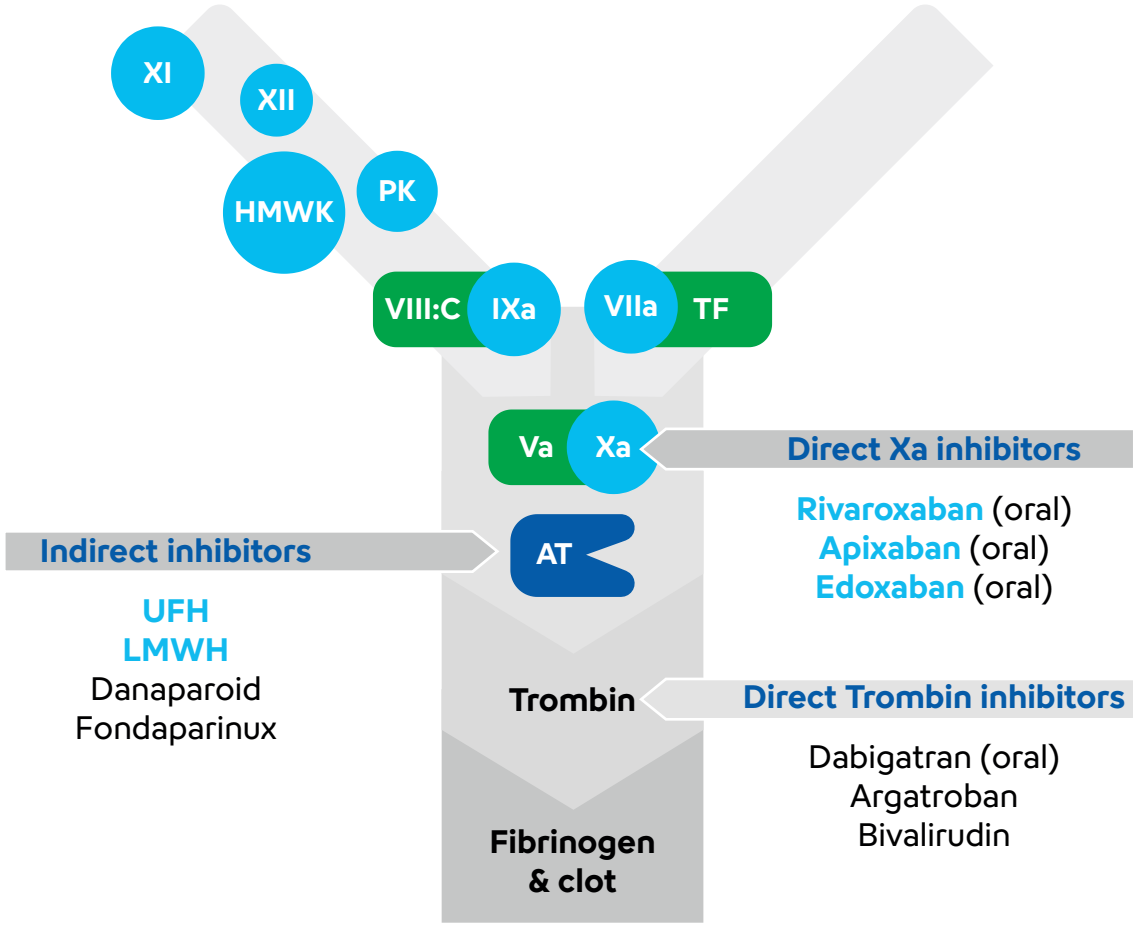
Introduction

Anticoagulation therapy is recommended and widely used to prevent the recurrence of venous thromboembolism (VTE) and stroke in patients with atrial fibrillation (AF).

Heparin anticoagulants (UFH and LMWH) are currently used for many preventive or curative indications. Measuring concentrations of this drug in patient plasma enables therapy monitoring and dosage adjustments. Besides heparin, the direct oral factor Xa inhibitors, Rivaroxaban, Apixaban and Edoxaban, are used as first-line agents for eligible patients to prevent recurrent VTE and stroke in those with nonvalvular AF. Although monitoring is not needed in treated patients, measurement in human plasma may be of use in certain clinical situations, such as emergency surgery, suspected overdosing (bleeding risk) or non-compliance (thrombosis risk).

The Revohem Anti-Xa LRT is an anti-Xa chromogenic method designed as a universal solution for measuring:

- Unfractionated heparin (UFH) and low molecular weight heparin (LMWH) using a single calibration curve derived from superimposition.
- The three major direct anti-Xa inhibitors, Rivaroxaban, Apixaban and Edoxaban, through the additional use of specific calibrations.



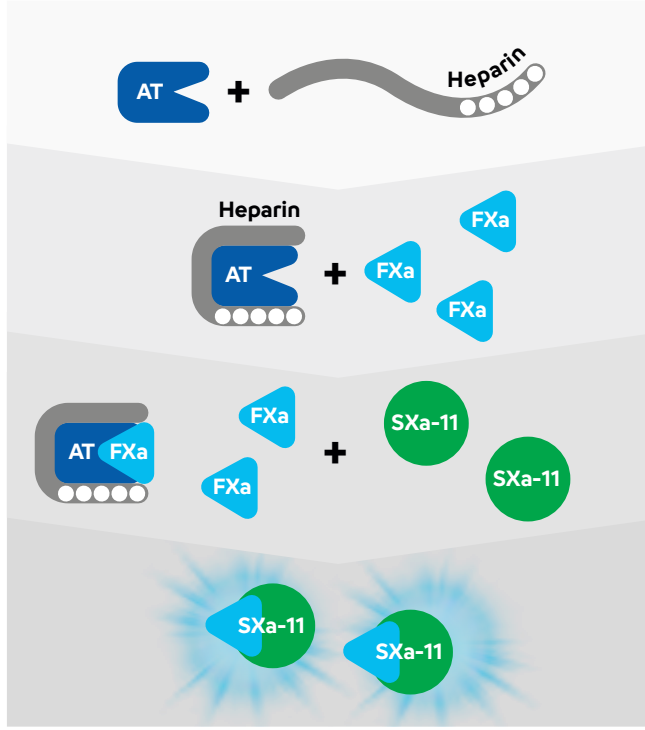
Assay principle

The Revohem Anti-Xa LRT method is a liquid, ready-to-use, one-stage chromogenic assay based on the inhibition of a constant, excessive amount of FXa in the presence of endogenous AT.

It is suitable for the quantification of indirect and direct anti-Xa inhibitors.

The residual FXa hydrolyses a specific chromogenic substrate (CS-11(32)) releasing paranitroaniline (pNA).

The amount of pNA released, which is measured by absorbance at 405 nm, is inversely proportional to the concentration of indirect or direct anti-Xa inhibitors present.



Heparin and Heparin analogues

Heparin anticoagulants (UFH and LMWH) are currently used for many preventive or curative indications. Heparin analogues (Fondaparinux & Danaparoid) are also used in specific clinical situations as alternative anticoagulant therapy, such as in the occurrence of heparin-induced thrombocytopenia (HIT). Measuring these drug concentrations in patient plasma allows for therapy monitoring and dose adjustments.

Why use a specific anti-Xa assay for Heparin monitoring?

To monitor Heparins, an anti-Xa assay is the method of choice over the APTT due to its greater precision and rapidity. Additionally, it boasts more specificity and linearity over a wider measuring range, which reduces the amount of adjustments required during dosage.

"True" unique calibration

Revohem Anti-Xa LRT was developed to be capable of determining UFH & LMWH through using a single hybrid calibration curve, which has been verified to have the ability to superimpose two individual curves onto each other. As a result, the single calibration can be used to measure both UFH and/or LMWH reflecting true dose-response curve through all levels.

The laboratory can obtain accurate results in Anti-Xa activity in IU/mL regardless of any type of heparin used or whether the type is even known.

Standardised, accurate, easy-to-adapt

Revohem Anti-Xa LRT offers a wide measurement range and excellent linearity, ensuring accuracy over the entire therapeutic range of commercially available heparins and corresponding heparin analogues. Our calibrators are aligned to the WHO International Standards. Furthermore, no interference of released heparin-neutralising proteins has been observed with the Revohem Anti-Xa LRT kit, due to the use of dextran sulfate. Validated assay applications are available for the Sysmex CS-Series and CN-Series.

DOACs

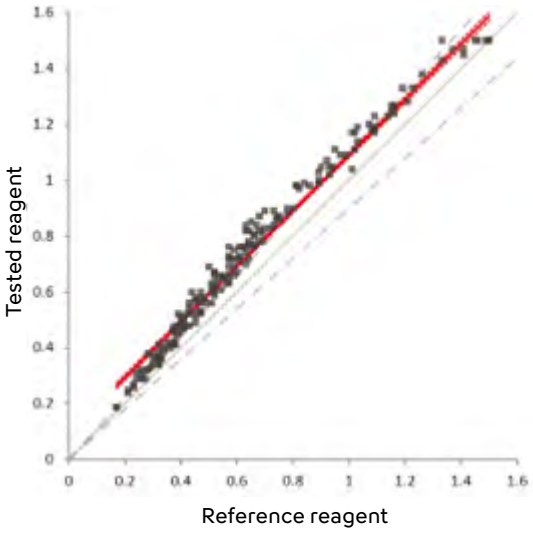
Rivaroxaban, Apixaban and Edoxaban are direct oral anticoagulants (DOACs) that inhibit activated Factor X (FXa). They have been increasingly used as first-line agents for eligible patients to prevent recurrent VTE and stroke in those with nonvalvular atrial fibrillation. Since their introduction into the market, the number of indications and direct oral Factor Xa inhibitors have continued to grow. Due to their superior pharmacological and clinical profile, therapy monitoring is not required since frequent individual patient dosage adjustments have been rendered obsolete.

Though monitoring is not a necessity in treated patients, measurements of human plasma may still be required in certain cases, particularly in the event of emergency surgery, suspected overdosage due to renal impairment (bleeding risk) or suspected non-compliance (thrombosis risk). Due to the continuous evolution of the anticoagulant market, our portfolio expanded accordingly and will continue to grow alongside the market to ensure that we can always offer complete, universal solutions for laboratory measurement.

The benefits of using specific anti-Xa assays for DOACs: Direct FXa inhibitors (DiXals)

The liquid chromatography-tandem mass spectrometry (LC-MS/MS) method is the gold standard for DOAC measurement; however, it is challenging to adapt the method into lab routines at reasonable TAT and cost. The routine coagulation assays, such as PT or APTT, are not suitable for quantitative assessment of DOAC level, since they lack sufficient levels of sensitivity and thus could potentially lead to erroneous interpretation. Therefore, the anti-Xa assay is recommended for assessing the aforementioned drugs.

Method comparison



Reference method	INNOVANCE Anti-Xa (Sysmex CN-6000)
Tested method	Revohem Anti-Xa LRT (Sysmex CN-6000)
Number of samples (n)	200
Linear regression	y = 0.993x+0.096
Coefficient of correlation (r)	0.991
Standard error of the estimate (Sy.x)	0.05

Performance

	Heparin (UFH/LMWH)	Rivaroxaban	Apixaban	Edoxaban
Measuring range	0.05-1.80 IU/mL	15-516 ng/mL	20-601 ng/mL	20-499 ng/mL
LoQ/LoD	0.05/0.00	15/14.7	20/19.8	20/15
Precision	CV% ≤10 %	CV% ≤10 %	CV% ≤10 %	CV% ≤10 %
Onboard stability on Sysmex analysers	7 days	7 days	7 days	7 days

Interferences	Heparin	Rivaroxaban	Apixaban	Edoxaban
Haemoglobin	300 mg/dL	1000 mg/dL	1000 mg/dL	1000 mg/dL
Bilirubin (free/conjugated)	25 mg/dL	60 mg/dL	60 mg/dL	60 mg/dL
Triglycerides	875 mg/dL	875 mg/dL	875 mg/dL	875 mg/dL

Contact your Sysmex representative today to simplify anticoagulant testing with the Anti-Xa assay.

Reagent:

Product	Description	Kit presentation	Order number
Revohem Anti-Xa LRT	**R1:** Liquid form Chromogenic substrate specific for Factor Xa (CS-11(32)) **R2:** Liquid form Bovine Factor Xa, contains BSA and Dextran Sulphate.	R1: 3mL x 3, R2: 3mL x 3	CG217097
		R1: 5mL x 4, R2: 5mL x 4	AL064127
		R1: 7.5mL x 4, R2: 7.5mL x 4	BU634799

Calibrators and controls:

Product	Description	Kit presentation	Order number
Revohem Heparin Hybrid Calibrator	CAL 1: Lyophilised human plasma without LMWH. CAL 2: Lyophilised human plasma containing approx 0.4 IU/mL of LMWH. CAL 3: Lyophilised human plasma containing approx 0.8 IU/mL of LMWH. CAL 4: Lyophilised human plasma containing approx 1.2 IU/mL of LMWH. CAL 5: Lyophilised human plasma containing approx 1.6 IU/mL of LMWH.	1 mL x 4, 5 levels (approx 0, 0.4, 0.8, 1.2, 1.6 IU/mL)	BQ221064
Revohem UFH Control Plasma	C1: Lyophilised human plasma containing approx 0.20 IU/mL of UFH C2: Lyophilised human plasma containing approx 0.50 IU/mL of UFH	1 mL x 6, 2 levels	AZ296682
Revohem LMWH Control Plasma	C1: Lyophilised human plasma containing approx 0.50 IU/mL of LMWH C2: Lyophilised human plasma containing approx 1.20 IU/mL of LMWH	1 mL x 6, 2 levels	CE227688
Revohem Rivaroxaban Calibrator	CAL 1: Lyophilised human plasma without Rivaroxaban CAL 2: Lyophilised human plasma containing approx 250 ng/mL of Rivaroxaban CAL 3: Lyophilised human plasma containing approx 500 ng/mL of Rivaroxaban	1 mL x 3, 3 levels	AC222492
Revohem Rivaroxaban Control	C1: Lyophilised human plasma containing approx 80 ng/mL of Rivaroxaban. C2: Lyophilised human plasma containing approx 300 ng/mL of Rivaroxaban.	1 mL x 6, 2 levels	BB808578
Revohem Apixaban Calibrator	CAL 1: Lyophilised human plasma without Apixaban CAL 2: Lyophilised human plasma containing approx 300 ng/mL of Apixaban CAL 3: Lyophilised human plasma containing approx 500 ng/mL of Apixaban.	1 mL x 3, 3 levels	AY519357
Revohem Apixaban Control	C1: Lyophilised human plasma containing approx 80 ng/mL of Apixaban. C2: Lyophilised human plasma containing approx 200 ng/mL of Apixaban.	1 mL x 6, 2 levels	AY519357
Revohem Edoxaban Calibrator	CAL 1: Lyophilised human plasma without Edoxaban. CAL 2: Lyophilised human plasma containing approx 250 ng/mL of Edoxaban. CAL 3: Lyophilised human plasma containing approx 500 ng/mL of Edoxaban.	1 mL x 3, 3 levels	CE077977
Revohem Edoxaban Control	C1: Lyophilized human plasma containing approx 80 ng/mL of Edoxaban C2: Lyophilized human plasma containing approx 300 ng/mL of Edoxaban	1 mL x 6, 2 levels	AD713277

Auxiliary Reagent:

Product	Description	Kit presentation	Order number
Revohem Anti-Xa Diluent	Sample diluent for anti-Xa chromogenic assay. Solution containing Sodium chloride.	20 mL x 4	AF018369
		20 mL x 10	CW518576

Other related products:

Product	Description	Applicable	Order number
BIOPHEN DiXaI	Chromogenic assay for quantitative determination of anti-Xa activity. Insensitive to Heparin.	Rivaroxaba Apixaban Edoxaban	221030
HEMOCLOT Thrombin Inhibitors	Clotting assay for quantitative determination of Direct Thrombin Inhibitor activity.	Dabigatran Bivalirudin Argatroban	CK002K/ CK002L
BIOPHEN DTI	Chromogenic assay for quantitative determination of Direct Thrombin Inhibitor activity.	Dabigatran Bivalirudin	220202

Availability may be dependent on country – please contact your local Sysmex representatives.

References

[1] Amiral J, *et al.* Optimization of Heparin Monitoring with Anti-FXa Assays and the Impact of Dextran Sulfate for Measuring All Drug Activity. Biomedicines 2021, 9, 700.

[2] Levy JH, *et al.* Defining heparin resistance: communication from the ISTH SSC Subcommittee of Perioperative and Critical Care Thrombosis and Hemostasis. J Thromb Haemost. 2023 Aug 22:S1538-7836(23)00641-4.

[3] Whitman-Purves E *et al.* Performance of anti-factor Xa versus activated partial thromboplastin time for heparin monitoring using multiple nomograms. Clin Appl Thromb Hemost. 2018;24:310–6.

[4] Gosselin RC *et al.* International Council for Standardization in Haematology (ICSH) Recommendations for Laboratory Measurement of Direct Oral Anticoagulants. Thromb Haemost. 2018 Mar;118(3):437-450.

[5] Hvas AM *et al.* Heparin-induced thrombocytopenia: pathophysiology, diagnosis and treatment. Expert Rev Hematol. 2021 Apr;14(4):335-346.

[6] Shinohara S *et al.* Performance evaluation of a new anti-Xa assay which utilises hybrid calibration curve for the monitoring of unfractionated and low molecular weight heparin. ISTH Virtual. Shinohara S. 06/23/2024; 423551; PB0097

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