MAYO CLINIC LABORATORIES

Test Definition: RIVAR

Rivaroxaban, Anti-Xa, Plasma

Overview

Useful For

Measuring rivaroxaban concentration in selected clinical situations (eg, kidney insufficiency, assessment of compliance, periprocedural measurement of drug concentration, suspected overdose, advanced age, and extremes of body weight)

Special Instructions

- Coagulation Guidelines for Specimen Handling and Processing

Method Name

Chromogenic Assay

NY State Available

Yes

Specimen

Specimen Type

Plasma Na Cit

Ordering Guidance

This assay is not indicated for monitoring low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH) concentrations. The presence of UFH and LMWH will cause the rivaroxaban anti-Xa level to be falsely elevated.

This assay is optimized to measure rivaroxaban concentration in presence of coagulation factor Xa recombinant, inactivated-zhzo (andexanet alfa, Andexxa).

Specimen Required

Specimen Type: Platelet-poor plasma
Collection Container/Tube: Light-blue top (3.2% sodium citrate)
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL
Collection Instructions:
1. Specimen should be collected 2 to 4 hours (peak) after a dose or just prior (trough) to the next dose for rivaroxaban concentrations.
2. For complete instructions, see Coagulation Guidelines for Specimen Handling and Processing
3. Centrifuge, transfer all plasma into a plastic vial, and centrifuge plasma again.
4. Aliquot plasma into a plastic vial leaving 0.25 mL in the bottom of centrifuged vial.
5. Freeze plasma immediately (no longer than 4 hours after collection) at -20 degrees C or, ideally, below -40 C degrees.
Additional Information:
1. A double-centrifuged specimen is critical for accurate results as platelet contamination may cause spurious results.

2. Each coagulation assay requested should have its own vial.

Forms

If not ordering electronically, complete, print, and send a Coagulation Test Request (T753) with the specimen.

Specimen Minimum Volume

0.5 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma Na Cit	Frozen	42 days	

Clinical & Interpretive

Clinical Information

Rivaroxaban, an oral anticoagulant that directly inhibits factor Xa, has been approved by the US Food and Drug Administration for prophylaxis of thrombosis in atrial fibrillation and surgical patients and treatment of venous thromboembolism (VTE). Unlike warfarin, it does not require routine therapeutic monitoring. However, in selected clinical situations, measurement of drug level would be useful (eg, kidney insufficiency, assessment of compliance, periprocedural measurement of drug concentration, suspected overdose, advanced age, and extremes of body weight).

Table**. Plasma Concentrations of Rivaroxaban in Patient Populations Studied(1)**

Patient population/clinical setting	**Rivaroxaban dose**	**C-min (ng/mL)*** trough plasma concentration (predose)	**C-max (ng/mL)** peak plasma concentration** (postdose)
VTE prevention after total hip replacement surgery	10 mg once daily	9 (1-38)	125 (91-196)
DVT treatment (continued treatment)	20 mg once daily	26 (6-87)	270 (189-419)
Stroke prevention in patients with non-valvular AF (CR-CL > or =50 mL/min)	20 mg once daily	44 (12-137)	249 (184-343)
Stroke prevention in patients with non-valvular AF (CR-CL 30-49 mL/min)	15 mg once daily	57 (18-136)	229 (178-313)
Secondary prevention in patients with acute coronary syndrome	2.5 mg twice daily	17 (6-37)	46 (28-70)

Median (5th-95th percentile)
*Defined as samples collected 20-28 hours after dosing
**Defined as samples collected 2-4 hours after dosing
Abbreviations not previously defined:
Atrial fibrillation (AF)
Creatinine clearance (CR-CL)
Deep vein thrombosis (DVT)

Reference Values
An interpretive report will be provided.

Interpretation
The lower limit of detection of this assay is 4 ng/mL.

Therapeutic reference ranges have not been established. See Clinical Information section for peak and trough drug concentrations observed from clinical trials.

Cautions
Routine monitoring of rivaroxaban is not indicated. Therapeutic reference ranges have not been established, however, peak and trough levels observed in clinical trials at different dosing are available. Rivaroxaban concentration may be affected by drug interactions and liver or kidney disease.

Clinical Reference
1. Mueck W, Stampfuss J, Kubitza D, Becka M. Clinical pharmacokinetic and pharmacodynamic profile of rivaroxaban. Clinical Pharmacokinetics. 2014;53(1):1-16 doi:10.1007/s40262-013-0100-7
2. Xarelto (rivaroxaban) Summary of Product Characteristics. Package insert. Bayer Pharma AG; 2013. Available at www.ema.europa.eu/en/documents/product-information/xarelto-epar-product-information_en.pdf
3. EINSTEIN Investigators, Bauersachs R, Berkowitz SD, et al. Oral rivaroxaban for symptomatic venous thromboembolism. N Engl J Med. 2010;363(26):2499-2510
4. EINSTEIN-PE Investigators, Buller HR, Prins MH, et al. Oral rivaroxaban for the treatment of symptomatic pulmonary embolism. N Engl J Med. 2012;366(14):1287-1297
5. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011;365(10):883-891
6. Siegal DM, Curnutte JT, Connolly SJ, et al. Andexanet alfa for reversal of factor Xa inhibitor activity. N Engl J Med. 2015;373:2413-2424
7. Martin K, Beyer-Westendorf J, Davidson BL, Huisman MV, Sandset PM, Moll S. Use of the direct oral anticoagulants in obese patients: guidance from the SSC of the ISTH. J Thromb Haemost. 2016;14(6):1308-1313

Performance

Method Description
The rivaroxaban, anti-Xa assay is performed on the Instrumentation Laboratory ACL TOP Family using the HemosIL Liquid Anti-Xa kit. The liquid Anti-Xa kit is a 1-stage chromogenic assay based on a synthetic chromogenic substrate and on factor Xa inactivation. Factor Xa is neutralized directly by rivaroxaban. Residual factor Xa is quantified with a synthetic

chromogenic substrate. The para-nitroaniline released is monitored kinetically at 405 nm and is inversely proportional to the rivaroxaban in the sample.(Package insert: HemosIL Liquid Anti-Xa kit. Instrumentation Laboratory Company; REV 06/2017)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
1 to 3 days

Specimen Retention Time
7 days

Performing Laboratory Location
Rochester

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test has been modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
80299

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
RIVAR	Rivaroxaban, Anti-Xa, P	74871-5

Result ID	Test Result Name	Result LOINC® Value
RIVA1	Rivaroxaban, Anti-Xa, P	74871-5
RIVA2	Interpretation	69049-5
RIVA3	Cautions	62364-5