MAYO CLINIC LABORATORIES

Test Definition: RIVAR

Rivaroxaban, Anti-Xa, P

Overview

Useful For

Measuring rivaroxaban concentration in selected clinical situations (eg, renal 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).

Necessary Information

If priority specimen, mark request form, give reason, and request a call-back.

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 in Special Instructions.

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, < or =-40 degrees C.

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.

Reject Due To

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

Specimen Minimum Volume

0.5 mL

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Rivaroxaban, an oral anticoagulant that directly inhibits factor Xa, has been approved by the FDA 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, renal insufficiency, assessment of compliance, periprocedural measurement of drug concentration, suspected overdose, advanced age, and extremes of body weight).

Plasma Concentrations of Rivaroxaban in Patient Populations Studied(1)

Patient population/clinical setting	**Rivaroxaban dose**	**C-min (ng/mL)*** trough plasma conc (predose)	**C-max (ng/mL)** peak plasma conc** (2-4 hours 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

AF-atrial fibrillation, CR-CL-creatinine clearance, DVT-deep vein thrombosis, VTE-venous thromboembolism

Reference Values

<4 ng/mL

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 renal disease.

Clinical Reference

1. Mueck W, Stampfuss J, Kubitza D, Becka M: Clinical pharmacokinetic and pharmacodynamic profile of rivaroxaban. Clinical Pharmacokinetics. 2014 Jan;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/docs/en_GB/document_library/EPAR_-_Product_Information/human/000944/WC500057108.pdf

3. EINSTEIN Investigators, Bauersachs R, Berkowitz SD, et al: Oral rivaroxaban for symptomatic venous thromboembolism. N Engl J Med. 2010 Dec 23;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 Apr 5;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 Sep 8;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 Dec 17;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 Jun;14(6):1308-1313

Performance

Method Description

The rivaroxaban, anti-Xa assay is performed on the Instrumentation Laboratory ACL TOP 700 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 paranitoaniline 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

Specimen Retention Time

7 days

Performing Laboratory Location

Rochester

Fees & Codes

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	Reporting Name	LOINC®
RIVA1	Rivaroxaban, Anti-Xa, P	74871-5
RIVA2	Interpretation	69049-5
RIVA3	Cautions	62364-5