

## Overview

### Useful For

Distinguishing primary from secondary membranous nephropathy using an algorithmic approach

Monitoring patients with membranous nephropathy at very low antibody titers

Screening for anti-phospholipase A2 receptor antibodies

### Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
EURO	Phospholipase A2 Receptor, ELISA, S	Yes, (Order PLA2M)	Yes

### Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
PLA2I	PLA2R, Immunofluorescence, S	Yes	No
THSD7	THSD7A Ab, S	Yes	No

### Testing Algorithm

The phospholipase A2 receptor (PLA2R) enzyme-linked immunosorbent assay (ELISA) is initially performed.

If the PLA2R ELISA result is less than 20, then the PLA2R immunofluorescence testing will be performed at an additional charge.

If the PLA2R immunofluorescence result is negative, thrombospondin type-1 domain-containing 7A (THSD7A) antibody testing will be performed at an additional charge.

### Highlights

Anti-phospholipase A2 receptor (PLA2R) antibodies are highly specific for the diagnosis of primary membranous nephropathy.

As many as 70% to 75% of patients with primary membranous nephropathy are positive for anti-PLA2R.

A titer increase, decrease, or disappearance generally precedes a change in clinical status.

### Method Name

EURO: Enzyme-Linked Immunosorbent Assay (ELISA)

PLA2I, THSD7: Indirect Immunofluorescence Assay (IFA)

**NY State Available**

Yes

**Specimen****Specimen Type**

Serum

**Specimen Required****Supplies:** Sarstedt Aliquot Tube, 5 mL (T914)**Collection Container/Tube:****Preferred:** Serum gel**Acceptable:** Red top**Submission Container/Tube:** Plastic vial**Specimen Volume:** 1 mL**Collection Instructions:** Centrifuge and aliquot serum into a plastic vial.**Forms**

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

-[Kidney Transplant Test Request](#)-[Renal Diagnostics Test Request](#) (T830)**Specimen Minimum Volume**

1 mL

**Reject Due To**

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK

**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	14 days	
	Ambient	8 hours	
	Frozen	14 days	

**Clinical & Interpretive**

**Clinical Information**

Membranous nephropathy (MN) is a rare disease in which immune complexes deposit at the glomerular basement membrane, causing damage to the filtration barrier, resulting in proteinuria. Recent studies have shown that in approximately 70% of patients with primary MN (pMN), the immune complexes consist of autoantibodies against the podocyte protein M-type phospholipase A2 receptor (PLA2R).<sup>(1)</sup> There is also evidence that levels of anti-PLA2R autoantibodies correlate well with disease activity and progression.<sup>(2)</sup> The presence of anti-PLA2R antibodies could also potentially be used to differentiate pMN from other causes of nephrotic syndrome if a biopsy is not possible. Among patients with chronic kidney disease awaiting kidney transplantation, higher levels of anti-PLA2R could predict those more likely to recur after transplantation.<sup>(2)</sup>

Mayo Clinic Laboratory data suggest that there is a high-concordance between the enzyme-linked immunosorbent assay (ELISA) and indirect immunofluorescence assay PLA2R results; however, the ELISA assay alone may be preferred for monitoring patients with membranous nephropathy over time for trends in anti-PLA2R antibody levels.

In the remaining 30% of patients with MN who are PLA2R-negative, anti-thrombospondin type-1 domain-containing 7A (THSD7A) was shown to have an approximate 10% prevalence (ie, about 3% of all primary MN patients).<sup>(3)</sup> Mouse podocytes express THSD7A and introduction of anti-THSD7A autoantibodies induces MN in murine models. Mouse podocytes do not express PLA2R so exogenous administration of anti-PLA2R does not recapitulate MN in mice.<sup>(4)</sup> Additionally, THSD7A has been described as a potential tumor antigen and, thus, it has been suggested that THSD7A-positive patients merit a thorough cancer screening.<sup>(5)</sup>

**Reference Values**

ANTI-PHOSPHOLIPASE A2 RECEPTOR (PLA2R) ENZYME-LINKED IMMUNOSORBENT ASSAY:

<14 RU/mL: Negative

14 to 19 RU/mL: Borderline

> or =20 RU/mL: Positive

PLA2R IMMUNOFLUORESCENCE:

Negative

THROMBOSPONDIN TYPE-1 DOMAIN-CONTAINING 7A ANTIBODIES:

Negative

**Interpretation**

Therapy outcome can be monitored by measuring the anti-phospholipase A2 receptor (PLA2R) antibody titer. A titer increase, decrease, or disappearance generally precedes a change in clinical status. Thus, the determination of the antibody titer has a high predictive value with respect to clinical remission, relapse, or risk assessment after kidney transplantation.

According to the manufacturer's package insert, the EUROIMMUN Anti-PLA2R indirect immunofluorescence assay (IFA) was positive in 77.1% of patients with biopsy proven primary membranous nephropathy (pMN).<sup>(6)</sup> This corresponds well with published literature that approximately 70% of patients with pMN will have anti-PLA2R antibodies.

**Cautions**

This test should not be used as a stand-alone test but an adjunct to other clinical information. A diagnosis of primary or secondary membranous nephropathy (MN) should not be made on a single test result. The clinical symptoms, results on physical examination, and laboratory tests (eg, serological tests), when appropriate, should always be taken into account when considering the diagnosis of primary versus secondary MN.

Absence of circulating anti-phospholipase A2 receptor autoantibodies does not rule out a diagnosis of primary MN.

**Clinical Reference**

1. Beck Lh Jr, Bonegio RGB, Lambeau G, et al: M-type phospholipase A2 receptor as target antigen in idiopathic membranous nephropathy. *N Engl J Med.* 2009 Jul 2;361(1):11-21
2. Schlumberger W, Hornig N, Lange S, et al: Differential diagnosis of membranous nephropathy with autoantibodies to phospholipase A2 receptor 1. *Autoimmun Rev.* 2014 Feb;13(2):108-113
3. Tomas NM, Beck LH Jr, Meyer-Schwesinger C, et al: Thrombospondin type-1 domain-containing 7A in idiopathic membranous nephropathy. *N Engl J Med.* 2014 Dec 11;371(24):2277-2287. doi: 10.1056/NEJMoa1409354
4. Tomas NM, Hoxha E, Reinicke AT, et al: Autoantibodies against thrombospondin type 1 domain-containing 7A induce membranous nephropathy. *J Clin Invest.* 2016 Jul 1;126(7):2519-2532. doi: 10.1172/JCI85265
5. Stahl PR, Hoxha E, Wiech T, Schroder C, Simon R, Stahl RAK: THSD7A expression in human cancer. *Genes Chromosomes Cancer.* 2017 Apr;56(4):314-327. doi: 10.1002/gcc.22440
6. Package insert: EUROIMMUN Anti-PLA2R IFA Kit, EUROIMMUN US; V 09/24/2018

**Performance****Method Description**

## Enzyme-Linked Immunosorbent Assay:

The test kit provides microtiter strips, each with 8 break-off reagent wells. In the case of positive samples, specific IgG antibodies (also IgA and IgM) will bind to the antigens. To detect the bound antibodies, a second incubation is carried out using an enzyme-labelled antihuman IgG (enzyme conjugate) catalyzing a color reaction.(Package insert: Anti-PLA2R ELISA [IgG] Kit, EUROIMMUN US; V 07/08/2020)

## Indirect Immunofluorescence Assay:

Diluted patient samples are incubated with combinations of substrates. If the reaction is positive, specific antibodies of classes IgA, IgG, and IgM attach to the antigens. In a second step, the attached antibodies are stained with fluorescein-labelled antihuman antibodies and made visible with a fluorescence microscope.(Package inserts: Anti-PLA2R IFA Kit, EUROIMMUN US; V 09/27/2018; Anti-THSD7A IIFT EUROPattern, EUROIMMUN US;V 06/11/2019)

**PDF Report**

No

**Day(s) Performed**

Monday, Wednesday, Friday

**Report Available**

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3 to 7 days

**Specimen Retention Time**

7 days

**Performing Laboratory Location**

Mayo Clinic Laboratories - Rochester Main Campus

**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**

See Individual Test IDs

**CPT Code Information**

83520

86255 (x1 or x2, if applicable)

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
PMND1	Prim Membranous Nephropathy Diag, S	73737-9

Result ID	Test Result Name	Result LOINC® Value
EURO	Phospholipase A2 Receptor, ELISA, S	73737-9