APS IgG

Order Code: APSGD-24

1. INTENDED USE

BlueDot APS IgG is an immunodot kit intended for the detection, in human sera only, of IgG autoantibodies against the antigens Cardiolipin/ß2-GPI complex (CL/ß2-GPI) and ß2-GPI (isolated protein).

This kit is intended to confirm results obtained by Enzyme Immunoassay techniques; the kit is intended as an aid in the diagnosis of several autoimmune diseases (for more details, see 11.5 Autoantibodies diagnostic values*).*

Detection of the different IgG autoantibodies can be either qualitative (see point 10.1) or semi-quantitative (see point 10.2).

The test is intended for a large, routine population. This kit is strictly reserved for professional use in clinical analysis laboratories. Prior training is strongly recommended (please contact your distributor).
It can only be used manually on a platform shaker or in an open automated immunodot processing system, programmed according to the pipetting scheme described in point 9.2.

2. PRINCIPLE OF THE TEST

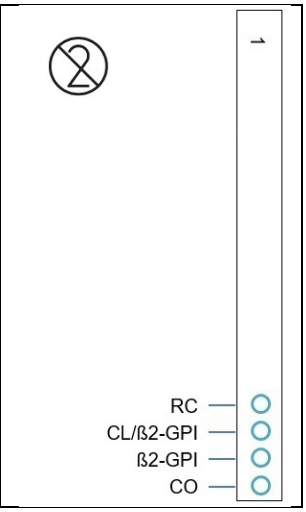
This kit and all its components are intended for exclusive manual use.
The test is based on the principle of an Enzyme Immunoassay. The strips are composed of a membrane fixed onto a plastic support. In the assay procedure, the strips are incubated with diluted patient serum. If present in the sample, the patient's autoantibodies bind to the specific antigen on the membrane. Unbound or excess antibodies are removed by washing in the next step. Then, human anti-IgG immunoglobulins conjugated with alkaline phosphatase are incubated with the strips and bind to the antigen-antibody complexes on the membrane surface. After a second washing step to remove excess conjugate, the chromogen/substrate solution is added, resulting in the appearance of an insoluble coloured product (purple) that precipitates at the site of the enzymatic reaction. The colour intensity is directly proportional to the quantity of antibodies present in the sample. The kit contains 24 single-use tests.

3. KIT CONTENTS

Prior to any use of the kit, please check that all the items listed are present. Please also check if the characteristics of the product are corresponding to those described hereafter. If one of the items is missing or damaged, please do not use the kit and contact your distributor.

3.1 COMPONENTS

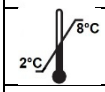
TO BE DILUTED:	**(10 x) Wash Solution**	**1 x 40 ml - 10x concentrated** (colourless) *Contains: H_2O • TBS • NaCl • Tween • Preservatives*
READY TO USE:	**Dot strips**	**24 units (each strip is for single use)** *4 dots each:* *1 negative control* **(CO)** *2 antigens* *1 positive control* **(RC)**
	Sample Diluent	**1 x 40 ml** (green) *Contains: H_2O • TBS • NaCl • Tween • BSA • Preservatives • Dye*
	Conjugate	**1 x 40 ml** (red) *Contains: H_2O • TBS • NaCl • KCl • $MgCL_2$ • AP-conjugated goat anti-human IgG • Preservatives • Dye*
	Substrate	**1 x 40 ml** (brown bottle, pale yellow solution) *Contains: H_2O • Preservatives • $MgCL_2$ • TBS • NBT • BCIP • NBT Stabilizer*
	Incubation trays	**3 units** *with 8 wells for incubation*



Abbreviations in alphabetic order:
AP = Alkaline Phosphatase; BCIP = Bromo-Chloro-Indolyl-Phosphate; BSA = Bovine Serum Albumin; KCl = Potassium Chloride; $MgCl_2$ = Magnesium Chloride; NaCl = Sodium Chloride; NBT = NitroBlue Tetrazolium; TBS = Tris Buffer Saline

For more information on the composition and concentration of the active ingredients used, please refer to the MSDS available on request or on www.d-tek.be.

Symbols used on kit labels

	Consult instructions for use		CE Mark + Notified Body
	In Vitro Diagnostic Medical Device		For 24 uses
	To be stored from 2-8°C		Reference
	Batch Number		To be protected from direct sunlight
	Use-by date		Manufacturer
	Cartridge		Caution
	Strip		

3.2 Antigens used

CL/ß2-GPI Cardiolipin /ß2-GPI Complex (purified from bovine heart, complexed in vitro with natural, human ß2-GPI)

ß2-GPI ß2-GlycoProtein I (isolated protein) (purified from human plasma)

3.3 Reactive ingredients

Substance	Origin	Intend purpose in APS kits	Concentration in APS kits	Purity
Goat anti-human IgG-alkaline phosphatase	Animal (Goat)	Secondary antibody (detection antibody) in conjugate buffer	< 0,1 µg/ml in conjugate buffer	Unknown. No antibody is detectable to non-immunoglobulin serum components.
CL/ß2-GPI antigen	Animal (purified from bovine heart, complexed in vitro with natural, human ß2-GPI)	Biomarker (antigen) coated on strips	0,33 mg/ml One CL/ß2-GPI spot = 0,5µl on each strip	>80%
ß2-GPI antigen	Human (purified from human plasma)	Biomarker (antigen) coated on strips	0,5 mg/ml One ß2-GPI spot = 0,5µl on each strip	>80%
Protein L	Bacterial (from Peptostreptococcus magnus)	Reactive (positive) control	0,01 mg/ml One RC spot = 0,5µl on each strip	>95%
Streptavidin-Alkaline Phosphatase	Bacterial (from Streptomyces avidinii)	Cut-off (negative) control	< 0,1 µg/ml One CO spot = 0,5µl on each strip	Unknown.
NBT-BCIP	Synthetic (chemical substance	Substrate for alkaline phosphatase	0,2 mg/ml	≥ 98%

4. MATERIAL REQUIRED BUT NOT PROVIDED

Platform shaker / Micropipettes / Timer / Graduated cylinder / Distilled or deionised water / Tweezers / Absorbent and/or filter paper.

5. STORAGE

The reconstituted wash solution is stable for at least one month at 2-8°C. Reagents and strips can be stored at 2-8°C until the expiry date indicated on each vial or tube.
Place unused strips back into the provided tube, seal it and store at 2-8°C. Chromogen/Substrate (NBT/BCIP) shall be stored at 2-8°C.
When stored properly, all test kit components are stable until the indicated expiry date.

6. SAFETY PRECAUTIONS

1. All reagents are for in vitro diagnostic and professional use only. The test kit should be processed by trained technical staff only.
2. The reagents in the kit are considered as not dangerous, as the concentrations of potentially dangerous chemicals are below the thresholds specified by European regulations:

Name	CAS	EINECS	Concentration in strip	Classification according to Regulation EC 1272/2008 Significance H Phrases
Cellulose Nitrate	9004-70-0	-	< 5 %	Flam. Sol. 1 H228

Annex VI to Regulation (EC) No 1272/2008: Index N°: 603-037-00-6; Commission Regulation (EU) 2015/830; 3.2.1

Name	CAS	EINECS	Concentration in mixture	Classification (in concentrated form) according to Regulation EC 1272/2008 Significance H Phrases
MIT:	55965-84-9	-	< 0,0015 %	Acute Tox. 2 H330 Acute Tox. 2 H310 Acute Tox. 3 H301 Skin Corr. 1 C H314; C ≥ 0,6% Eye Dam. 1 H318; C ≥ 0,6% Skin Sens. 1 A H317; C ≥ 0,0015% A Aquatic Acute 1 H400 Aquatic Chronic 1 H410

Annex to Commission Regulation (EU) 2018/1480; Index Number: 613-167-00-5 ; Commission Regulation (EU) 2015/830; 3.2.1

Name	CAS	EINECS	Concentration in mixture	Classification (in concentrated form) according to Regulation EC 1272/2008 Significance H Phrases
NaN_3	26628-22-8	247-852-1	< 0.1 %	Acute tox. 2 H300 Acute tox. 1 H310 STOT RE 2 H373 Aquatic acute 1 H400 Aquatic chronic, 1 H410

Annex VI to Regulation (EC) No 1272/2008: Index Number: 011-004-00-7; Commission Regulation (EU) 2015/830; 3.2.1

Name	CAS	EINECS	Concentration in mixture	Classification (in concentrated form) according to Regulation EC 1272/2008 Significance H Phrases
NBT	298-83-9	206-067-4	< 0,01%	Acute tox. 4 H302

Nevertheless, these chemicals are toxic in concentrated form. Therefore, contact with the skin, eyes or mucous membranes should be avoided by using suitable individual protection (gloves, laboratory coat, goggles). As with any chemical containing specific hazards, the product/components of the product should only be handled by qualified personnel and with the necessary precautions.

3. Patient samples should be handled as if they could transmit infectious diseases; they therefore require suitable protection (gloves, laboratory coat, goggles). In any case, GLP should be applied with all the general or individual safety rules in force.
4. Waste disposal: Patient samples, incubated test strips and used reagent vials should be handled as infectious waste. The boxes and other containers do not need to be collected separately, unless stated otherwise in official regulations.
5. The device is containing substances from animal, human, and bacterial origins (cfr 3.3) at very low concentration. All these substances were selected in order to not contain any microbial or transmissible agents and are non-toxic at the concentration used in the device. Nevertheless, laboratory good practice at user site (glasses, gloves) is necessary

7. RECOMMANDATIONS

1. D-tek and its authorized distributors cannot be held responsible for damages caused indirectly or due to: a change or modification in the indicated procedure, an improper use of the kit and / or the use of an incomplete or damaged kit. The use of this kit is reserved for qualified technical personnel only.
2. D-tek's responsibility is limited in all cases to the replacement of the kit.
3. In the event of a serious incident (injury, deterioration in health, or death) with this IVD device, please report it immediately to the manufacturer (see address below) and to the competent authority in your country.

8. SAMPLE COLLECTION, HANDLING AND STORAGE

Sera with particles should be centrifuged at low speed. Blood samples should be collected in dry tubes. Please avoid using a pool of different sera, as this can lead to inconsistent results (see point 10.4). After separation, the serum samples should be used immediately or aliquoted and stored at 2-8 ° C (for maximum 14 days) or frozen at -20°C (for longer storage periods, maximum 13 months). Repeated freezing/ thawing cycles of the samples must be at a maximum of 10 cycles.

9. ASSAY PROCEDURE

BASIC INFORMATION, HANDLING AND TIPS:

The dots are precoloured blue on the strips, ensuring that all antigens have been dotted correctly onto the membrane. This blue coloration disappears during the first step of the incubation. During incubation with the wash solution, a faint pink background coloration appears on the membrane and disappears upon drying at the end of the procedure.
During the procedure, agitation of the incubation tray is necessary to ensure efficient circulation of fluids over the membrane. A Rocking platform is the shaker of choice. Be sure to adjust the movement of the shaker in such a way that no spilling of solutions or cross-contamination between the wells can occur.
After each filling of the wells with solution, agitate manually the incubation tray until the strips are completely immersed in order to remove air bubbles which may be trapped under the strip. Alternatively, floating strips may be forced into the solution by pushing down (with tweezers or pipette tip) on the upper part of the strip (plastic label zone).
Avoid touching the membrane zone of the strip with fingers, tweezers or pipette tips. Always use the plastic label zone for handling or manipulation. The whole procedure must be run **at room temperature (18-25°C)**.

Description of the CONTROLS:

The **Positive Control or RC (Reaction Control)** consists of a protein (protein L) fixing all the immunoglobulins present in the test sample. If the test has been carried out correctly, this control will show a colouring at the end of the test (with an intensity depending on the effective concentration of immunoglobulins in the sample).
The absence of any colouring of this dot at the end of the test may indicate that the sample has not been pipetted on the strip (see 10.4 *Troubleshooting*).

The **Negative Control or CO (Cut-Off Control)** consists of a protein (streptavidin – alkaline phosphatase) reacting with the enzymatic substrate and with certain constituent elements of the tested sample. If the test has been carried out correctly, this control is coloured at the end of the test, with a signal depending on the kinetics of the substrate and the characteristics of the sample. The intensity of this control serves as a threshold value for the final interpretation of the results (see 10 *INTERPRETATION OF RESULTS*).

9.1 Reagents preparation

1. Allow all components to equilibrate at room temperature **(18-25°C)** before use.
2. **Dilute** the concentrated **wash solution 10x** with **distilled water.**
   Prepare 15 ml diluted wash solution per strip tested
   Example: 1,5 ml concentrated wash solution + 13,5 ml distilled water for one strip.
   Do not substitute reagents or mix strips with different batch numbers this may lead to variations in the results.

9.2 Pipetting flow chart

1. **Place** one **strip** per patient into the wells, blue dots **facing up**.
2. Add **2 ml diluted wash solution** per well. **Incubate** (shake) **for 10 min.**
   Upon correct incubation, the blue coloration of the dots completely disappears.
   If not prolong the procedure until the colour of the dots fades completely.
3. **Discard** solution from the wells.
   Remove liquid by slowly inverting the plate. The strips will adhere to the bottom of the wells. Dry the edge of the tray with absorbent paper.
4. Add **1,5 ml sample diluent** per well.
5. Add **10 µl patient sample** per well. **Incubate** (shake) **for 30 min.**
   Avoid touching the membrane with the pipette tip. Preferentially dispense the sample into the solution over the upper part of the strip (plastic label zone).
   Note: Steps 4 and 5 can be combined by pre-diluting the sample in a glass or plastic tube (1,5 ml sample diluent + 10 µl patient sample). Mix (Add to the well)
6. **Discard** solution from the wells.
   Remove liquid by slowly inverting the plate. The strips will adhere to the bottom of the wells. Dry the edge of the tray with absorbent paper.
7. **Wash 3 x 3 minutes** with **1,5 ml diluted wash solution** per well (shake)**.**
   Following each wash step remove liquid from the wells by slowly inverting the plate. The strips will adhere to the bottom of the wells. Dry the edges of the tray with absorbent paper
8. Add **1,5 ml Conjugate** per well. **Incubate** (shake) **for 30 min**.
9. **Discard** solution from the wells.
   Remove liquid by slowly inverting the plate. The strips will adhere to the bottom of the wells. Dry the edge of the tray with absorbent paper
10. **Wash 3 x 3 min.** with **1,5 ml diluted wash solution** (shake)
    Following each wash step remove liquid from the wells by slowly inverting the plate. The strips will adhere to the bottom of the wells. Dry the edges of the tray with absorbent paper.
11. Add **1,5 ml Substrate** per well. **Incubate** (shake) **for 10 min.**
12. **Discard** solution from the wells.
    Remove liquid by slowly inverting the plate. The strips will adhere to the bottom of the wells. Dry the edge of the tray with absorbent paper.
13. **Wash 1 x 3 min.** with **1,5 ml diluted wash solution** per well to stop the reaction.
14. **Collect** the strips from the wells and allow them to dry for 30 minutes on absorbent paper. The interpretation must be done in the 24 hours following the test processing.

10. INTERPRETATION OF RESULTATS

A visual (qualitative) interpretation of the results of the kit is possible, however the use of the BlueScan scanner and the Dr Dot Software is generally recommended for more precision and a semi-quantitative interpretation.

10.1. Qualitative Interpretation

1. Peel off the cover of the adhesive on the back side of each strip and attach strips dots face up onto the marked fields of the interpretation sheet provided with the kit. This will indicate the respective positions of the different controls and antigens on the membrane.
2. The first upper dot (**Positive Control Dot**) must be positive for all patients. Only a clearly coloured Positive Control Dot ensures your results are valid and operation was correct and/or kit components were not degraded. If the first upper dot is not coloured, the test has failed and cannot be interpreted further.
3. Compare the specific **antigen** dots to the **Negative Control Dot** (which always is the last bottom dot). The colour intensity of the antigen dots is directly proportional to the titer of the specific antibody in the patient sample.
   The colour intensity of the Negative Control Dot may vary depending on the sample characteristics. If the sample is free of interfering substances the Negative Control Dot may be even close to uncoloured. In contrast, a highly coloured Negative Control Dot indicates a high rate of unspecific binding in the sample.

> ***POSITIVE RESULT*:**
> A sample is positive for a specific antibody if the colour intensity of the corresponding Antigen dot is higher than the intensity of the Negative Control Dot.
> ***NEGATIVE RESULT*:**
> A sample is negative for a specific antibody if the colour intensity of corresponding Antigen dot is lower than or equal to the intensity of the Negative Control Dot.

NB: A weak coloration of an antigen dot, when close to the colour intensity of the Negative Control Dot may be difficult to differentiate by visual inspection only. In such cases, it is recommended to use Dr Dot Software and scanning system (see 10.2) and refer to the corresponding instructions for more accurate interpretation.

10.2 Results semi-quantification: use of Dr Dot Software and Scanning system (material needed: BlueDiver Clamp, empty stripholders)

The BlueScan scanner is a specially designed system for the reading of D-tek immunodot strips. It allows precise and easy insertion of test strips.

The Dr Dot Software allows a semi-quantification of results. Based on the image obtained, each result will be quantified in grayscale value and compared to the reference scale integrated in the BlueScan Cover.

These grayscale intensities will be transformed and displayed in arbitrary units (AU, from 0 to 100) based on the intensities of the controls (RC and CO, see point 9) present on the strip, according to the following conversion formula:

$$Result\ of\ antigen\ X\ (AU) = \frac{Grayscale\ intensity\ of\ antigen\ X - Grayscale\ intensity\ of\ CO}{Grayscale\ intensity\ of\ RC - Grayscale\ intensity\ of\ CO} * 100$$

1. Prepare a BlueDiver Clamp and load it with as many empty stripholders as there are strips to analyse. Carefully insert a strip into each stripholder, RC showing upwards.
2. Insert the clamp, the reactive side of the strips facing down, into the dedicated emplacement in the cover of the BlueScan scanner.
3. Start scanning the strips using the Dr Dot Software.
4. The software semi-quantifies the results, and the interpretation of the obtained values is as follows

Dr Dot arbitrary unit (AU)	Interpretation
< 5	Negative
5 – 10	Equivocal (*)
>10	Positive

For detailed information about the BlueScan and Dr Dot Software please refer to the Manual of Use of your Dr Dot Software

10.3 Important recommendations for the interpretation of results

1. D-tek's kits constitute a diagnostic aid. In consequence, no diagnosis can be established solely on the basis of our kits. The results should always be interpreted by taking into account the clinical examination, the patient's history and the results obtained by other methods.
   No single technique can rule out the possibility of false positive or false negative results. With this in mind, an indirect immunofluorescence test should, as far as possible, be carried out prior to the use of an immunodot kit (immunofluorescence being recognized as a reference method in autoimmunity).
2. The intensity of a result is not necessarily related to the degree of intensity of the disease, but rather to the level of antibodies detected.
3. Low titers of autoantibodies may occur in healthy patients. For this reason, low positive results (close to the CO, between 5 and 10 Dr Dot AU), although valid, should be considered equivocal. In such cases, the retesting of the patient, preferably by using a new sample, is recommended. If the result remains equivocal on retesting, other diagnostic tests and/or clinical information should be used to help determine the autoimmune status of the patient.
4. For various reasons, and under certain conditions, the kit may show a defect in performance (see 10.4 Troubleshooting). In such cases, the results are not valid and cannot be interpreted. It is recommended to repeat the test. If the error persists, please contact your distributor.
5. The intensity of the results may decrease when the device is used at the end of its life. However, the performance of the kit is not affected (detection of positives and negatives) under normal conditions of use and storage.

6. Sequential sampling (at different dates) of an autoimmune patient can sometimes lead to different results from one sample to another. This difference can have several reasons: the patient's treatment, the evolution of the disease, or a seroconversion. In the specific case of seroconversion, the result can be positive for an autoantibody in an early sampling of the patient and become positive for another autoantibody in a later sampling of the same patient.

10.4 Troubleshooting

Problem	**Possible causes + Action**
Discrepancy of results as compared to a reference method	-Use - incorrect pipetting of serum - incorrect volume dispensed - Use of two different samples of the same patient (see point 10.3.6) or wrong sample handling/storage between tests - erroneous visual interpretation - erroneous Dr Dot reading → repeat the test -Material - Interfering substance in the sample - Sample is a pool of different human sera → repeat the test and confirm by other methods -Method - intrinsic performance of the kit (see 11.2 *Analytical sensitivity and specificity*) - expired kit - stability problem **Please contact your distributor for any further technical support requests.**
Different results in the same batch or between several batches -	-Use - incorrect pipetting of serum - incorrect volume dispensed - erroneous visual interpretation or - bad Dr Dot reading → repeat the test - Method - intrinsic performance of the kit (see 11.1 *Repeatability and Reproducibility*)
Contamination between neighbouring strips	- Use - incorrect pipetting of serum → repeat the test
RC absent or weak	- Use - Serum not pipetted at all → repeat the test - Patient with immunoglobulin deficiency → repeat the test to confirm patient status - Damaged reagents → check the integrity of the reagents → contact your supplier if you suspect a problem - Spot not on the strip → count the number of dots on the strip; if not correct, contact your supplier
CO absent	- damaged reagents → check the integrity of the reagents, contact your distributor if you suspect a problem - Spot absent from the strip → count the number of spots present on the strip, contact your distributor in case of incorrect number
Non-specific bindings / high background / high CO value	Suspected presence of a contaminant or an interfering substance in the patient sample → repeat the test and confirm through another method **Please contact your distributor for any further technical support requests.**
Strips not correctly labelled	Manufacturing problem → please contact your distributor
Kit content incorrect	Manufacturing problem → please contact your distributor

NOTE:

The major residual risks of the kit, as given in the risk analysis of the kit at the end of design (after mitigation), are the following:

1) Risk of false results based on a pipetting error (bad serum)

2) Risk of false results based on an interfering substance contained in the sample

11. PERFORMANCES

11.1 Repeatability and Reproducibility

Reference samples were tested for each antibody in successive statistically representative series, both in the same test as in different tests and between different batches in order to calculate the intra-assay, inter-assay and inter-lot variations respectively. In all the cases, the variations in colour intensity were within the following expected limits:

CV ≤ 10% for intra-assay runs
CV ≤ 15% for inter-assay runs
CV ≤ 20% for inter-lot runs

11.2 Analytical sensitivity

Measurement range (semi-quantified results): From 0 AU (negative) to 100 AU (high positive).
Limit of detection: the lowest measured value of the test is 5 AU (considered as equivocal following the interpretation algorithm, see point 10.2)
As not any international standard is available for the autoantibodies, trueness of measurement and linearity are not applicable on this product.

11.3 Analytical specificity

1. The main known interfering substances were tested on each biomarker of the present kit.
   For each concentration of interfering substance tested, the difference between the result of the sample without the interfering substance and the result obtained in the presence of the interfering substance did not exceed 15%.

Interfering substance	Maximum Concentration	Intermediate Concentration	Minimum Concentration	Difference <15%
Bilirubin	100 mg/dL	50 mg/dL	25 mg/dL	Yes
Haemoglobin	200 mg/dL	100 mg/dL	50 mg/dL	Yes
Cholesterol	224.3 mg/dL	112 mg/dL	56 mg/dL	Yes
Rheumatoid factor IgM	~500IU/ml	~300IU/ml	~100IU/ml	Yes

2. Note: It is impossible to test all the possible interfering substances described in the literature. Other interferences, amongst others drug-induced interferences, are possible. The high analytical specificity of the test is guaranteed by the quality of the antigen used. This kit detects IgG antibodies against Cardiolipin/ß2-GPI complex (CL/ß2-GPI) and ß2-GPI (isolated protein). No cross reactions with other autoantibodies have been found.

11.4 Clinical sensitivity and specificity

Sensitivity and Specificity were calculated from combined results obtained on clinically defined positive and negative EQAS controls and from historical data (external clinical evaluation on clinically defined positive and negative patients). These characterized samples (confirmed positive or negative for specific antibodies by reference laboratories and/or methodologies) were assayed following the test instructions. A detailed clinical report is available upon request.

Sensitivity:
The percentage is established with the following calculation:

$$Sensitivity = \frac{True\ Positive\ Results}{True\ Positive\ Results + False\ Negative\ Results}$$

Antigen	True Positive Results	False Negative Results	Sensitivity (%)
CL/ß2-GPI	67	0	>99
ß2-GPI	53	9	85

Specificity:
The percentage is established with the following calculation:

$$Specificity = \frac{True\ Negative\ Results}{True\ Negative\ Results + False\ Positive\ Results}$$

Antigen	True negative results	False positive results	Specificity (%)
CL/ß2-GPI	99	1	99
ß2-GPI	98	0	>99

Note: Sensitivity and specificity values of 100 % are strictly related to sample cohorts used in clinical evaluations. In theory, a diagnostic kit shouldn't be 100% sensitive or specific (at least > 99%).

It is imperative to repeat positive antiphospholipid (aPL) antibody tests in 12 weeks to exclude the possibility of infection-related antibody induction.

11.5 Autoantibodies diagnostic values

Anti-CL/ß2-GPI	Anti-CL/ß2-GPI of the IgG isotype are marker antibodies and classification criteria of the anti-phospholipid syndrome (APS). They are also present in up to 60% in patients with Systemic Lupus Erythematosus, and are found in variable frequency (4-50%) in various other diseases. It is imperative to repeat positive antiphospholipid (aPL) antibody tests in 12 weeks to exclude the possibility of infection-related antibody induction, and to ensure a correct diagnosis of the antiphospholipid syndrome.
Anti-ß2-GPI	Anti-B2GPI of the IgG isotype are marker antibodies and classification criteria of the anti-phospholipid syndrome (APS), and are characterized by arterial or venous thrombosis and fetal miscarriage. They are more specific but less sensitive for the anti-phospholipid syndrome than anti-CLs. The prevalence of anti-B2GPIs is higher in patients with Systemic Lupus Erythematosus. They are rarely detected in infectious diseases.

Publication references:

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2: Chayoua W, Kelchtermans H, Moore GW, Musiał J, Wahl D, de Laat B, Devreese KMJ. Identification of high thrombotic risk triple-positive antiphospholipid syndrome patients is dependent on anti-cardiolipin and anti-β2glycoprotein I antibody detection assays. J Thromb Haemost. 2018 Oct;16(10):2016-2023. doi: 10.1111/jth.14261. Epub 2018 Aug 24. PMID: 30079628.

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6: Raimondo MG, Pericleous C, Radziszewska A, Borghi MO, Pierangeli S, Meroni PL, Giles I, Rahman A, Ioannou Y. Oxidation of β2-glycoprotein I associates with IgG antibodies to domain I in patients with antiphospholipid syndrome. PLoS One. 2017 Oct 19;12(10):e0186513. doi: 10.1371/journal.pone.0186513. PMID: 29049363; PMCID: PMC5648189.

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12. TEST LIMITATIONS

1. The results obtained with this confirmatory test are dependent on the intrinsic performance of the kit and must be considered as an aid to the final diagnosis, taking into account the results obtained by a reference technique and the clinical data of the patient.
2. In case of hyper-lipemic samples, it is recommended to centrifuge it before the pipetting of the 10µl of sample, which must be done into the supernatant.
3. Other confirmatory tests targeting IgM anti-cardiolipin and anti-β2GPI antibodies, as well as other anti-phospholipid antibodies (anti-phosphatidylethanolamine antibodies, anti-phosphatidylinositol antibodies, anti-phosphatidylserine antibodies, anti-phosphatidylserine prothrombin antibodies) should be performed in negative patients showing clinical signs and symptoms suggestive of antiphospholipid syndrome. It is imperative to repeat positive anti-phospholipid antibody tests in 12 weeks to exclude the possibility of infection-related antibody induction.
4. The concentration of autoantibodies in a serum sample is not relative to the results provided by the device.
5. There is no link between the concentration of the different autoantibodies detected by the device, and the severity of its associated auto-immune diseases.

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