2025/06/20
A02A00002GEN

REF 1300036373

REAGENT 12 x 4 mL

IVD CE

HORIBA ABX SAS
Parc Euromédecine
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FRANCE

Yumizen G PT Liq 4

- **Yumizen G200**
- **Yumizen G400/G400 DDi/G405**
- **Yumizen G800/G800h/G850h**
- **Yumizen G1500/G1550/G1500h/G1550h**

In vitro diagnostic reagent for determination of prothrombin time test by coagulometry.

Application Release

	Test name
Yumizen G1500/G1550	PT Liq
Yumizen G1500h/G1550h	PT Liq
Yumizen G800	PT Liq
Yumizen G800h/G850h	PT Liq
Yumizen G405	PT Liq
Yumizen G400/G400 DDi	PT
Yumizen G200	PT

Intended Use

For *in vitro* diagnostic use only.
Yumizen G PT Liq 4 is a liquid, ready to use, rabbit brain thromboplastin reagent used for determination of Prothrombin Time (PT).

Clinical Interest (1)

The PT test according to Quick is a sensitive screening test for the common and extrinsic coagulation pathway.
Yumizen G PT Liq 4 as a reagent for PT is highly sensitive to VKA, decreased level of factors in common and extrinsic pathway (factor FII, FV, FVII, and FX), hereditary or acquired coagulation disorders and liver failure.

Method

Yumizen G PT Liq 4 reagent as a calcium thromboplastin, induces the formation of fibrin clot when added to patient's plasma.

The time of this clotting process is measurable manually or with optical and mechanical coagulation analyzers.

Reagents

Yumizen G PT Liq 4 is ready-to-use.
This reagent is a tissue thromboplastin extract from rabbit brain, which contains tissue factor, lipid, calcium ion and preservative.

Suspended rabbit brain powder	< 25 g/L
$CaCl_2$*$2H_2O$	< 2 g/L
Sodium azide	< 1.2 g/L

Yumizen G PT Liq 4 should be used according to this notice.
The manufacturer cannot guarantee its performance if used otherwise.

Handling

1. Wait until the reagent reaches the working temperature.
2. Mix thoroughly the vial horizontally (5 - 10 times).
3. **For automated analyzers only:** place the vial in the reagent holder without cap.

For optimal performance remove the reagent from the instrument after use, close the vial and store at 2 - 8°C.
An analysis of the control must be carried out on a daily basis at the same time as the patient samples, including each time a calibration is carried out.
The frequency of the controls depends on the laboratory requirements.
Each laboratory must establish the quality assurance procedures to be followed. These must conform to the

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current accreditation requirements and pertinent regulations.

Care should be taken not to interchange the caps with others products.

Calibrator

For the calibration, use the master curve provided or the calibrator:
Yumizen G CAL (1300036416) (not included, optional)
12 x 1 mL
To calculate the ratio of the test (PT), you could use the mean value (MNPT) provided in the enclosed annex.
According to the CLSI H47-A2 document every laboratory should determine its own MNPT value. (2)

Control

For internal quality control, use:

- **Yumizen G CTRL I & II** (1300036412) (not included)
  5 x 1 mL + 5 x 1 mL

The frequency of controls and the confidence intervals should correspond to laboratory guidelines and country-specific directives. You should follow federal, state and local guidelines for testing quality control materials. The results must be within the range of the defined confidence limits. Each laboratory should establish a procedure to follow if the results exceed these confidence limits.
Each control should be assayed daily and/or after a calibration.

Semi-Automated Analyzers Procedure

Yumizen G PT Liq 4 can be used on semi-automated analyzers (Yumizen G Line), according to the following procedure.
Duplicated measurement is recommended.

1	Incubate the **Yumizen G PT Liq 4** at 37°C.	~30 min
2	Add the sample into the cuvette.	50 µL
3	Incubate at 37°C.	2 min
4	Add the **Yumizen G PT Liq 4**.	100 µL
5	Start immediately the measurement at 640 nm.	~1 min

For manual testing use the same protocol with double volumes. (3)

In case of determination by any other hemostasis analyzers, please follow the instructions of the manual.

Materials Required but not Provided

- HORIBA analyzers (Yumizen G Line) are recommended.
- Calibrator (optional): **Yumizen G CAL** (1300036416)
- Control: **Yumizen G CTRL I & II** (1300036412)
- Standard laboratory equipment

Specimen

Plasma

- 3.2% (109 mmol/L) sodium-citrate anticoagulated plasma in primary tube.
- 3.2% (109 mmol/L) sodium-citrate, theophylline, adenosine and dipyramidole (CTAD) anticoagulated plasma in primary tube.

Mix the blood carefully.

Specimen centrifugation

Speed	Time	Temperature
1500 g	15 min	room temperature

Specimen Stability (4)

- At 20 - 25°C°C: 24 hours
- Between -22°C to -26°C: 12 months (only the plasma)

Do not store on ice or at 2 - 8°C as cold activation of factor VII may alter results.
If the patient is on both heparin and coumarin-based anticoagulant therapy, the results may vary with time of storage.
To thaw plasma:

1. Place the sample in a water bath: not more than 5 min at 37°C.
2. Centrifuge the sample.

For additional information, please refer to CLSI document H21-A5.

Reference Range (5)

Each laboratory should establish its own reference ranges.
The values given here are used as guidelines only.

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Normal range	Mean	From	To
INR	1.00	0.80	1.20

The therapeutic reference range for INR may vary depending on the clinical indication of OAT by VKA.

Storage and Stability

Stability before opening

Stable up to the expiry date on the label if stored at 2 - 8°C.

Stability after opening

	20 - 25°C	2 - 8°C
Yumizen G PT Liq 4	4 days	12 days

Stability on board

Automated Analyzers

	15 - 19°C
Yumizen G PT Liq 4	5 days

Semi-automated Analyzers

	37°C
Yumizen G PT Liq 4	2 days

Expected Results [a]

Yumizen G PT Liq 4 test results can be reported in the following units:

- **Second:** observed clotting time of the sample.
- **Ratio (PT / MNPT):** clotting time of the sample divided by the mean normal prothrombin time (MNPT).
- **Percentage:** proportional part of the normal PT activity, which is calculable from the calibration curve. Method dependent master curve in the enclosed annex can be used for the calculation.
- **International Normalized Ratio (INR):** ratio raised to the power of International Sensitivity Index (ISI).
  $INR = (PT / MNPT)^{ISI}$
  The ISI value in the enclosed annex can be used for the calculation.
  The ISI value assignment follows the guidelines of World Health Organisation (WHO).

Precautions of Calculation

- The MNPT value depends on the population (race, gender) and measuring circumstances (sampling tube, etc.).
  Our value, which is identical with the 100% point of the calibration curve, is for information only.
  According to the CLSI H47-A2 document every laboratory should determine its own MNPT value. (2)
- By calculating with inappropriate data or using the supplied data improperly, erroneous results can be obtained.
- The system is validated only for OAT patients by VKA. (2)
- Accurate and general conversion of percentage into INR (or back) is not possible.

Waste Management

- Please refer to local legal requirements.
- This product contains less than 0.2% of sodium azide as a preservative. Sodium azide may react with lead and copper to form explosive metal azides.

General Precautions

- This product is for professional *in vitro* diagnostic use only.
  For laboratory use.
- For prescription use only.
- This reagent is classified as non-hazardous in compliance with regulation (EC) N°.1272/2008.
- **Warning:** This product is obtained from substances of animal origin. Consequently, it should be treated as potentially infectious and handled with the appropriate cautions in accordance with good laboratory practices (6).
- Do not pipette by mouth.
- Do not replenish the products.
- Do not swallow. Avoid contact with skin and mucous membranes.
- Observe the standard laboratory precautions for use.
- The product vials should be discarded after use. Disposal of all waste material should be in accordance with local guidelines.
- Please refer to the SDS associated with the product.
- Do not use the product if there is visible evidence of biological, chemical or physical deterioration.
- Do not use the product if the recommended storage conditions, including temperature, are not followed.

[a]Modification: § "Expected Results" changed.

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- User must be trained by a HORIBA representative before attempting to operate the device.
- It is the user's responsibility to verify that this document is applicable to the product used.
- For technical assistance, you can call +33 (0)4 67 14 15 16.
- Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the country in which the user and/or the patient is established.
- Using of third-party hemostasis analyzers may cause a risk of system un-harmonization.
- It is the user's responsibility to evaluate the risk of using a third-party hemostasis analyzers.

Performance

The performance data listed below are representative of performance on HORIBA systems.

Lot to Lot Variability

The comparison of plasma samples tested consecutive lots of reagent shows that the lot to lot variability is within specification.

Sample Volume

Instrument	Volume
Yumizen G1500/G1550	50 µL
Yumizen G1500h/G1550h	50 µL
Yumizen G800	50 µL
Yumizen G800h/G850h	50 µL
Yumizen G405	50 µL
Yumizen G400/G400 DDi	50 µL
Yumizen G200	50 µL

Precision

Repeatability (on automated analyzers)

Repeatability according to the recommendations found in the CLSI (NCCLS), EP15-A3 (7), EP05-A3 (8), H47-A2 (9) (data obtained on internal study).

- 2 controls (10 runs)
- 2 specimens (20 runs)

	Mean value Second	CV %
Control specimen 1	11.3	0.590
Control specimen 2	18.3	0.387

	Mean value Second	CV %
Specimen 1	14.4	0.643
Specimen 2	32.9	0.990

Maximum acceptance criteria (CV %): < 2%

Reproducibility (on automated analyzers)

Reproducibility according to the recommendations found in the CLSI (NCCLS), EP05-A3 (8), H47-A2 (9) (data obtained on internal study).

- 2 controls (10 runs)

	Mean value Second	CV %
Control specimen 1	11.3	1.521
Control specimen 2	19.0	1.094

Maximum acceptance criteria (CV %): < 5%

Measuring Range

The measuring range is 10 - 120s on the Yumizen G Line instruments.

Correlation

Specimens are correlated with a commercial reagent taken as reference on HORIBA analyzers (Yumizen G Line).

- Passing-Bablok regression: 1.020 (slope)
- Bland et Altman plot procedure: 0.047 (INR difference)

Interferences (10)

Haemoglobin: No significant influence is observed up to 6.80 g/L.
Triglycerides: No significant influence is observed up to an Intralipid® concentration (representative of lipemia) of 8.0 mmol/L.
Bilirubin: No significant influence is observed up to 270 µmol/L.
Heparin: No significant influence is observed up to 0.75 IU/mL.

Clinical Performance

Clinical sensitivity and specificity, positive predictive value and negative predictive value are not commonly reported for this test.
This is largely attributed to the fact that this test is a screening test.
To arrive at a diagnosis and a course of treatment, results from others routine coagulation tests should be used in conjunction with other diagnostic information and the

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attending health-care professional's evaluation of the patient's condition.

Precautions of Characteristics

The measurement data was generated during a performance evaluation and is not recommended as an acceptance criterion.

Reference

1. De Caterina R, Husted S Wallentin L, Andreotti F, Arnesen H, Bachmann F, Baigent C, Huber K, Jespersen J, Kristensen SD, Lip GYH, Morais J, Rasmussen LH, Siegbahn A, Verheugt FWA, Weitz JI. Vitamin K antagonists in heart disease: Current status and perspectives (Section III). Thromb Haemost (2013) **110**: 1087-1107.
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3. Van Den Besselaar et al. Paving the way for establishing a reference measurement system for standardization of plasma prothrombin time: Harmonizing the manual tilt tube method. J Thromb Haemost. (2020 Aug); **18** (8): 1986-1994.
4. Collection, Transport, and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Hemostasis Assays. Approved Guideline, 5th ed., CLSI (NCCLS) document H21-A5 (2008).
5. Hirsh J, Dalen J, Anderson DR, Poller L, Bussey H, Ansell J, Deykin D. Oral anticoagulants: Mechanism of action, clinical effectiveness, and optimal therapeutic range. Chest (2001) **119**: 8S-21S.
6. Council Directive (2000/54/EC). Official Journal of the European Communities. No. L262 from October 17, 2000: 21-45.
7. User Verification of Precision and Estimation of Bias. Approved Guideline, 3rd ed., CLSI (NCCLS) document EP15-A3 (2014).
8. Evaluation of Precision of Quantitative Measurement Procedures. Approved Guideline, 3rd ed., CLSI (NCCLS) document EP05-A3 (2014).
9. One-Stage Prothrombin Time (PT) Test and Activated Partial Thromboplastin Time (APTT) Test. Approved Guideline, 2nd ed., CLSI (NCCLS) document H47-A2 (2008).
10. Interference Testing in Clinical Chemistry. Approved Guideline, 2nd ed., CLSI (NCCLS) document EP07-A2 (2005).