This package insert follows the Pharmaceuticals, Medical devices and Other Therapeutic Products Act of Japan.

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In Vitro Diagnostics
Certification No. 227ADEZX00129000

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This package insert must be read carefully prior to use.

Glycated Albumin Kit
(Classification code No. 44153000)

NORUDIA GA

General Precautions**

1. This product is for in vitro diagnostic use only, and must not be used for any other purposes.
2. Clinicians should make a comprehensive clinical decision based on assay results in conjunction with clinical symptoms and other examination results.
3. This product should be used only as directed in this package insert. Reliability of results cannot be guaranteed if there are any deviations from the instructions in this package insert.
4. If the reagent accidentally comes in contact with eyes and/or mouth, rinse immediately with ample water as first aid, and consult the doctor if required.
5. Carefully read the operating instructions for each type of automated analyzers prior to using this product. Parameters for each type of analyzers are available, and can be requested from SEKISUI MEDICAL CO., LTD. if required.

Description (Kit Components)**

Component:	Ingredients
GA Enzyme Solution 1:	Protease 4-Aminoantipyrine
GA Enzyme Solution 2:	Fructosyl amino acid oxidase N,N-bis (4-sulfobutyl)-m-toluidine disodium
ALB Buffer Solution 1:	Succinic acid
ALB Coloring Solution 2:	Bromocresol purple
Calibrator 1:	Human serum
Calibrator 2:	Human serum

Intended Use

Measurement of glycated albumin (GA) in serum or plasma

Glycated albumin (GA) is a glycation product of albumin (ALB), which is a protein that circulates in the blood. Because the blood half-life of ALB is approximately 17 days, GA assay results reflect the mean blood glucose level over a period of 2–4 weeks before blood collection. Therefore, GA is a useful index of glycemic control for patients with diabetes.

Assay Principle**

1. Assay Principle

1) Measurement of GA
In the first reaction, glycated amino acids are cut out from GA by a protease. In the second reaction, fructosyl amino acid oxidase (FAOD) acts on the glycated amino acids to produce hydrogen peroxide, which causes condensation of 4-aminoantipyrine and N,N-bis (4-sufobutyl)-m-toluidine disodium (DSBmT) in the presence of peroxidase (POD) to produce a purple-red pigment. The GA level is determined by measuring the absorbance of this purple-red pigment.

GA:
First reaction

$$\text{GA} \xrightarrow[\text{Protease}]{} \text{Glycated amino acids}$$

Second reaction

$$\text{Glycated amino acids} + O_2 + H_2O \xrightarrow{\text{FAOD}} \text{Glucosone} + \text{amino acids} + H_2O_2$$

$$H_2O_2 + \text{4-aminoantipyrine} + \text{DSBmT} \xrightarrow{\text{POD}} \text{Purple-red pigment}$$

2) Measurement of albumin
In the first reaction, reduced albumin is converted to oxidized albumin. In the second reaction, bromocresol purple (BCP) acts on oxidized albumin to produce an albumin-BCP conjugate. The albumin level is determined by measuring the absorbance of this conjugate.

Albumin:
First reaction

$$\text{Reduced albumin} \longrightarrow \text{Oxidized albumin}$$

Second reaction

$$\text{Oxidized albumin} \xrightarrow{\text{BCP}} \text{Albumin-BCP conjugate}$$

3) Calculation of the GA level (%)
The measured GA level is divided by the albumin level and then corrected by the following formula to ensure consistency with routine assay results (Lucica GA-L, Asahi Kasei Pharma Corporation).

Correction formula: (GA level/albumin level) × 48.9 + 1.9

2. Features

1) Ready-to-use liquid reagents.
2) Can be used with various automated analyzers.

Procedural Precautions**

1. Properties of Samples and Sampling Methods

1) Samples
Serum and plasma (EDTA plasma, heparin plasma and sodium fluoride-treated plasma) may be used.
2) Storage of Samples[1)]
- After separation of serum (plasma), specimens may be stored for up to 7 days in a refrigerator.
- If specimens cannot be measured within 7 days of serum (plasma) separation, store them frozen (−30°C or lower). Avoid repeated freezing and thawing.
Stored specimens should be brought to room temperature (15–30°C) before use.

3) The same specimen (serum or plasma) should be used for measurement of both GA and albumin.

2. Interfering Substances

1) Assay results are not affected by free bilirubin (up to 12.5 mg/dL), conjugated bilirubin (up to 12.5 mg/dL), hemoglobin (up to 80 mg/dL), formazin turbidity (up to 3000 FTU), or ascorbic acid (up to 50 mg/dL).
2) Hemolysis leads to slight negative errors.
3) Penicillin G may be administered intravenously at high doses for treatment of infective endocarditis, sepsis, purulent meningitis, etc. In the presence of high penicillin levels, albumin assay values may decrease[1] and this will cause the GA value (%) to become higher than the actual value.
4) Accurate GA values (%) may not be obtained in patients with hypoalbuminemia.
5) Specimens from patients receiving amino acid infusions should be measured with great care. In particular, specimens should not be measured from

patients receiving infusions containing glucose premixed with amino acids, because false high assay results may be obtained.[2]

3. Others

1) Calibration materials
Use NORUDIA GA Calibrator as the calibration material.

Dosage/Administration (Assay Procedure)**

1. Preparation of reagents

GA Reagent (1): GA Enzyme Solution 1 is ready to use.
GA Reagent (2): GA Enzyme Solution 2 is ready to use.
ALB Reagent (1): ALB Buffer Solution 1 is ready to use.
ALB Reagent (2): ALB Coloring Solution 2 is ready to use.

2. Method of calibrator preparation

1) Add exactly 1 mL of purified water to 1 vial of this product, and mix it by using a wave rotor for approximately 30 minutes or let it stand at room temperature for approximately 30 minutes and then mix gently by inversion.
2) When stored in a refrigerator, each calibrator is stable for 7 days after preparation (freezing is prohibited).
Stored calibrators should be brought to room temperature (15–30°C) before use.
3) See the Attached Table for GA and albumin concentrations. The albumin concentration varies with each lot.

3. Assay Procedure

This product is compatible with various types of automated analyzers. An example of the assay procedure is indicated below.

1) Measurement of GA

Specimen 3.2 µL + GA Reagent (1) 120 µL → (37°C, 5 min.) → Measurement (Absorbance I※1)

GA Reagent (2) 40 µL → (37°C, 5 min.) → Measurement (Absorbance II※1)

→ Calculation of concentration

2) Measurement of albumin

Specimen 1.6 µL + ALB Reagent (1) 120 µL → (37°C, 5 min.) → Measurement (Absorbance III※2)

ALB Reagent (2) 60 µL → (37°C, 5 min.) → Measurement (Absorbance IV※2)

→ Calculation of concentration

3) Calculation of the GA level (%)
The measured GA level is divided by the albumin level and then corrected by the following formula to ensure consistency with routine assay results (Lucica GA-L, Asahi Kasei Pharma Corporation).

Correction formula: (GA level/albumin level) × 48.9 + 1.9

※1 Absorbance I and II: The difference in absorbance between 546 nm and 700 nm.
※2 Absorbance III and IV: The difference in absorbance between 600 nm and 660 nm.

Calibration materials: NORUDIA GA Calibrator (Manufacture's assigned value)

Assessment of Assay Results**

1. Reference standard range

11–16%[3)]

2. There may be reactions or interfering reactions with non-target substances. If assay results appear to be unreliable, repeat the measurement (if necessary, after dilution) or try another analytical methods.

Performance**

1. Sensitivity

GA: 0.010–0.030 per 100 µmol/L
Albumin: 0.020–0.045 per 100 µmol/L

2. Accuracy

GA value (%): 95–105% of the expected assay value

3. Within-run Reproducibility

Coefficient of variation of GA value (%): ≤ 3%
(Test methods used for 1.–3. are in-house methods.)

4. **Measurement Range** (On Hitachi 7180 automated analyzer)
6.0–64.1%

5. Correlation

1) Serum
N = 110, r = 0.998, y = 1.00x + 0.04
Control method: Approved in vitro diagnostic (enzymatic method)
2) Plasma (sodium fluoride-treated plasma)
N = 100, r = 0.997, y = 0.99x – 0.26
Control method: Approved in vitro diagnostic (enzymatic method)

6. Standard Calibration Materials

Certificated Reference Material for Measurement of Glycated Albumin in Human Serum (JCCRM611)
Certified Reference Material for Measurement of Albumin in Human Serum (JCCRM613)

Precautions for Use or Handling**

1. Precautions for Handling (to Ensure Safety)

1) All specimens used in the test should be handled as a material possibly infected with HIV, HBV, HCV, or other viruses. To prevent infection, use disposable gloves and avoid mouth pipetting during the test.
2) Sodium azide is contained in GA Enzyme Solution 1, and ProClin 300 that may cause skin irritation, etc. is contained as the preservative in GA Enzyme Solution 1, ALB Buffer Solution 1, and ALB Coloring Solution 2. If any of these reagents are accidentally ingested or come into contact with the eyes or skin, immediately rinse the area with water and seek medical treatment, if necessary.
3) The calibrators are calibration materials designed exclusively for use with NORUDIA GA. Do not use them for other purposes.
4) It may be difficult to dissolve the calibrators in cold water. Therefore, dissolve calibrators in purified water at approximately 20°C.
5) The calibrators are prepared from human blood components that have been confirmed to be negative for HBs antigens, HCV antibodies, and HIV antibodies. However, wear gloves, etc., and handle the calibrators with great care, because there is a risk of infection, as there is with specimens.

2. Precautions for Use

1) This product should be kept in a tightly-stopped container and stored as directed. Avoid freezing. Do not use this product if it has been left open or if it has been frozen because freezing can cause deterioration of the reagents, leading to inaccurate results.
2) Do not use expired reagents. Use of such reagents cannot guarantee the reliability of measurement values.
3) Do not replenish the reagents.
4) Do not perform the assay under direct sunlight.

3. Precautions for Disposal

1) Before disposal, used specimens and their containers must be immersed in sodium hypochlorite solution at a concentration of 0.1% or greater for 1 hour or longer or autoclaved at 121°C for 20 minutes.
2) To prevent infections from spilled samples or solutions containing samples, wipe the spilled area

thoroughly with disinfectants such as sodium hypochlorite solution at a concentration of greater than 0.1%.

3) The reagents and treated samples should be discarded as medical waste or industrial waste according to the waste disposal regulations.
4) The reagents should be disposed of in accordance with the Water Pollution Control act or related regulations.
5) Sodium azide has been added as an antiseptic agent in the GA Enzyme Solution 1. It can react with lead or copper pipes to produce the highly explosive metal azide. Therefore, the reagent should be flushed with large amounts of water during disposal.

4. Other Precautions

Do not use the containers for other purposes.

Storage and Shelf Life*

1. Storage temperature: 2–10°C
2. Shelf life: 14 months from the date of manufacture
   (The expiration date is printed on the outer package.)

Packaging**

Name		Package contents
NORUDIA GA	GA Enzyme Solution 1	2 × 40 mL
	GA Enzyme Solution 2	2 × 13.4 mL
	ALB Buffer Solution 1	2 × 40 mL
	ALB Coloring Solution 2	2 × 20 mL
	L Set	GA R1：45.6mL×1 GA R2：15.2mL×1 ALB R1：45.6mL×1 ALB R2：22.8mL×1
	Calibrator 1	3 × For 1 mL
	Calibrator 2	3 × For 1 mL

References**

1) Ono M. et al.: Clinica Chimica Acta, 407, 75–76, 2009.
2) Kouzuma T. et al.: Clinica Chimica Acta, 346, 135–143, 2004.
3) The Japan Diabetes Society: Guidelines for the Treatment of Diabetes Mellitus in Japan 2014–2015, 9, Bunkodo, 2014.
4) In house data, SEKISUI MEDICAL CO., LTD.

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