B2MG

cobas®

Tina-quant β2-Microglobulin

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
08105529190	08105529500	Tina-quant β2-Microglobulin (150 tests)	System-ID 2025 001	**cobas c** 303, **cobas c** 503, **cobas c** 703

Materials required (but not provided):

08047545190	Calibrator β2-Microglobulin (2 × 1 mL)	Code 20474	
08362785190	Control Set β2-Microglobulin - Level I (2 × 1 mL) - Level II (2 × 1 mL)	 Code 20144 Code 20145	
08063494190	Diluent NaCl 9 % (123 mL)	System-ID 2906 001	

English

System information

B2MG: ACN 20250

B2MGU: ACN 20251

Intended use

Immunoturbidimetric assay for the quantitative in vitro determination of β2-microglobulin (B2MG) in human serum, plasma and urine on **cobas c** systems.

Summary

β2-microglobulin (B2MG) measurement, performed with this assay in human serum, plasma and urine can be used to aid in diagnosis of kidney diseases (such as glomerulopathies, tubulopathies, renal failure, and kidney-related amyloidosis), acute kidney allograft rejections, active rheumatoid arthritis and hematological diseases (including malignancies such as lymphoma and myeloma).

B2MG is a small globular peptide made up of 100 amino acid residues and with a molecular weight of 11800 D. It non-covalently associates with the major histocompatibility complex-I (MHC-I)/human leukocyte antigen-I (HLA-I) on the surfaces of all nucleated cells (exception: trophoblasts) and it is present in most biological fluids including serum, urine and synovial fluid.[1,2] Lymphocytes are the major location of synthesis. B2MG is constantly released into the blood in small quantities. B2MG is normally cleared by glomerular filtration in the kidneys. Thereafter, up to 99.9 % is reabsorbed by the proximal tubules.[1] The appearance of notable quantities of this protein in the urine reflects failure of the tubular resorptive mechanisms. Levels of serum and urinary B2MG reflect the functions of glomeruli and proximal tubules.[3]

Patients with renal dysfunction show high plasma concentrations of B2MG due to the impaired kidneys excretion.[2] Patients with acute kidney injury have a significantly higher serum B2MG concentration compared to healthy people.[4] In addition, serum B2MG levels are known to increase in renal diseases which disrupt glomerular filtration and tubular reabsorption.[1] B2MG clearance during dialysis treatment is clinically significant since B2MG can deposit as amyloid, leading to systemic amyloidosis in many patients on long-term dialysis and resulting in injury of many tissues, including kidneys, brain, heart and peripheral nerves, depending on the site of amyloid deposition.[2,5]

In urine, increased levels of B2MG are usually indicative of renal tubular injury.[3,6] In healthy patients only small amounts of B2MG can be detected. Drug nephrotoxicity causing severe, acute changes in tubular reabsorption and progressive renal diseases causing irreversible structural tubular defects impair tubular reabsorption of numerous smaller proteins including B2MG. Therefore, urinary B2MG is discussed as a marker for the diagnosis and monitoring of tubulointerstitial renal damage.[1,3] Excretion of B2MG is increased in Fanconi syndrome, a generalized dysfunction of the proximal tubules.[7] Causes for acquired Fanconi syndrome include exposure to toxins and drugs.[8] Elevated B2MG values may identify patients at higher risk of glomerular filtration rate (GFR) decline in other kidney diseases such as membranous nephropathy.[9] Furthermore, there is evidence that B2MG excretion is associated with acute allograft rejection in renal transplant recipients.[10]

B2MG serum concentration reflects the activation of the cellular immune system.[11] Increased serum B2MG levels have been shown in autoimmune diseases such as rheumatoid arthritis.[12,13,14,15]

In oncology increased serum B2MG levels are observed in patients with several malignancies, including lymphoma and multiple myeloma. In multiple myeloma, measurement of serum B2MG levels is considered essential for staging and recommended by the EHA-ESMO Clinical Practice Guidelines.[16,17,18] B2MG is also used as a prognostic factor for lymphoma malignancies and recommended as part of the initial workup in the ESMO guidelines (2013).[17,19,20,21,22,23,24,25,26,27,28] Furthermore, a prognostic index was created for patients with large B-cell lymphoma, comprising 4 factors: age, performance status, stage and B2MG. This was suggested as a useful risk model for categorising lymphoma patients into risk groups and predicting the various outcomes.[28]

Various assay methods are available for B2MG determination, such as radioimmunoassays (RIA), enzyme-linked immunosorbent assays (ELISA), nephelometric immunoassays, and turbidimetric methods.[29] The Roche B2MG assay is based on the principle of immunological agglutination with latex reaction enhancement.

Test principle

Immunoturbidimetric assay.

Latex-bound anti-β2-microglobulin antibodies react with antigen from the sample to form antigen/antibody complexes which are determined turbidimetrically after agglutination.[30]

Reagents - working solutions

R1 TRIS/HCl buffer: 23 g/L, pH 8.2; NaCl: 19 g/L; EDTA: 1.3 g/L; preservative

R3 Latex particles coated with polyclonal anti-human β2-microglobulin antibody (rabbit); preservative

R1 is in position B and R3 is in position C.

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317	May cause an allergic skin reaction.
H412	Harmful to aquatic life with long lasting effects.

Prevention:

P261	Avoid breathing mist or vapours.
P273	Avoid release to the environment.

P280	Wear protective gloves.

Response:

P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.

Disposal:

P501	Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

Reagent handling

Ready for use

Carefully invert reagent container several times prior to use to ensure that the reagent components are mixed.

Storage and stability

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	12 weeks

Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable.
Serum
Plasma: Li-heparin, K_2- and K_3-EDTA plasma

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Urine

Each urine sample must be centrifuged (10 minutes at approximately 3000 × g) prior to testing.[31]
B2MG is unstable in acidic conditions and degradation occurs at pH < 6 within 2 hours.[29,7] Thus, pre-analytical conditions are highly important. Since the degradation also takes place in the bladder, collection of a spot urine sample should not be performed in the morning due to a lower urine pH.[29]
A strict control of the urine pH after collection is required: urine samples must be adjusted to pH 7-9 by the addition of 1 N NaOH as soon as possible after receipt.[7]

Stability in serum and Li-heparin, K_2- and K_3-EDTA plasma:	3 days at 15-25 °C 3 days at 2-8 °C 6 months at -20 °C (± 5 °C) Freezing and thawing up to 2 times is allowed.
Stability in urine:	5 days at 15-25 °C 14 days at 2-8 °C 12 weeks at -20 °C (± 5 °C) Freezing and thawing up to 2 times is allowed.

Centrifuge samples containing precipitates before performing the assay.

See the limitations and interferences section for details about possible sample interferences.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

See "Order information" section

General laboratory equipment

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

Application for serum, plasma and urine

Test definition

Reporting time	10 min		
Wavelength (sub/main)	–/700 nm		
Reagent pipetting		Diluent (H_2O)	
R1	63 µL	–	
R3	63 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	1 µL	–	–
Decreased	1 µL	10 µL	100 µL
Increased	1 µL	–	–

For further information about the assay test definitions refer to the application parameters setting screen of the corresponding analyzer and assay.

Calibration

Application for serum/plasma (ACN 20250)

Calibrators	S1: H_2O S2: Calibrator β2-Microglobulin
Calibration mode	Linear
Calibration frequency	Full calibration - after reagent lot change - as required following quality control procedures

Application for urine (ACN 20251)
Transfer of calibration from serum/plasma application (ACN 20250)

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized against the WHO standard.

Quality control

For quality control, use control materials as listed in the "Order information" section. In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory's individual requirements. It is recommended to perform quality control always after lot calibration and subsequently at least every 12 weeks. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

cobas c systems automatically calculate the analyte concentration of each sample in the unit mg/L (nmol/L, µg/L).

Conversion factors:	mg/L × 84.7 = nmol/L mg/L × 1000 = µg/L

B2MG

Tina-quant β2-Microglobulin

cobas®

Limitations - interference

Serum/plasma

Criterion: Recovery within ± 0.22 mg/L of initial values at a β2-microglobulin concentration of ≤ 2.2 mg/L and within ± 10 % for samples > 2.2 mg/L.

Icterus:[32] No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[32] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[32] No significant interference up to an L index of 1000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

High-dose hook effect: No false result occurs up to a B2MG concentration of 240 mg/L.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[33,34]

Rheumatoid factors: No significant interference from rheumatoid factors up to a concentration of 1200 IU/mL.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[35]

Urine

Criterion: Recovery within ± 0.1 mg/L of initial values at a β2-microglobulin concentration of ≤ 1.0 mg/L and within ± 10 % for samples > 1.0 mg/L.

Hemolysis: No significant interference up to an H index of 1100 (approximate hemoglobin concentration: 1100 mg/dL).[32]

High-dose hook effect: No false result occurs up to a B2MG concentration of 240 mg/L.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[34]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[35]

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on **cobas c** systems. All special wash programming necessary for avoiding carry-over is available via the **cobas** link. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/SCCS Method Sheet. For further instructions, refer to the operator's manual.

Limits and ranges

Measuring range

Serum/plasma

0.2-8.0 mg/L (16.9-678 nmol/L)

Urine

0.2-5.8 mg/L (16.9-491 nmol/L)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:11 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 11.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank	= 0.1 mg/L (8.5 nmol/L)
Limit of Detection	= 0.15 mg/L (12.7 nmol/L)
Limit of Quantitation	= 0.2 mg/L (16.9 nmol/L)

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a total error of 20 %. It has been determined using low concentration human β2-microglobulin samples.

Expected values

Serum/plasma

< 60 years	0.8-2.4 mg/L	68-203 nmol/L[29]
> 60 years	≤ 3.0 mg/L	254 nmol/L[29]

Urine

male: ≤ 0.300 mg/L (25.4 nmol/L)[36]

female: ≤ 0.183 mg/L (15.5 nmol/L)[36]

B2MG/creatinine (urine): ≤ 2.46 nmol/mmol[36]

24 h urine: 2.80-30.7 nmol[7]

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

Precision

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP05-A3 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). Results for repeatability and intermediate precision were obtained on the **cobas c** 503 analyzer.

Serum/plasma

Repeatability	*Mean* mg/L	*SD* mg/L	*CV* %
CS B2MG1[a)]	2.53	0.0405	1.6
CS B2MG2[b)]	4.53	0.0303	0.7
Human serum 1	0.243	0.0247	10.2
Human serum 2	1.74	0.0273	1.6
Human serum 3	2.80	0.0191	0.7
Human serum 4	3.94	0.0393	1.0
Human serum 5	7.06	0.0300	0.4

Intermediate precision	*Mean* mg/L	*SD* mg/L	*CV* %
CS B2MG1[a)]	2.53	0.0459	1.8
CS B2MG2[b)]	4.51	0.0538	1.2
Human serum 1	0.243	0.0265	10.9
Human serum 2	1.74	0.0318	1.8
Human serum 3	2.81	0.0251	0.9
Human serum 4	3.94	0.0410	1.0
Human serum 5	7.06	0.0402	0.6

a) Control Set β2-Microglobulin, Level I

b) Control Set β2-Microglobulin, Level II

Urine

Repeatability	*Mean* mg/L	*SD* mg/L	*CV* %

CS B2MG1[a)]	2.54	0.0295	1.2
CS B2MG2[b)]	4.57	0.0355	0.8
Human urine 1	0.274	0.0373	13.6
Human urine 2	0.395	0.0385	9.8
Human urine 3	0.807	0.0457	5.7
Human urine 4	2.53	0.0425	1.7
Human urine 5	5.07	0.0389	0.8

Intermediate precision	*Mean mg/L*	*SD mg/L*	*CV %*
CS B2MG1[c)]	2.54	0.0385	1.5
CS B2MG2[d)]	4.57	0.0692	1.5
Human urine 1	0.274	0.0385	14.0
Human urine 2	0.395	0.0424	10.7
Human urine 3	0.807	0.0473	5.9
Human urine 4	2.53	0.0449	1.8
Human urine 5	5.06	0.0458	0.9

c) Control Set β2-Microglobulin Level I

d) Control Set β2-Microglobulin Level II

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

Method comparison

Serum/plasma

β2-Microglobulin values for human serum samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 64

Passing/Bablok[37]	Linear regression
y = 1.000x + 0.0150 mg/L	y = 1.001x + 0.00921 mg/L
τ = 0.991	r = 1.000

The sample concentrations were between 0.320 and 7.82 mg/L.

β2-Microglobulin values for human serum samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 67

Passing/Bablok[37]	Linear regression
y = 1.009x + 0.00991 mg/L	y = 1.004x + 0.0380 mg/L
τ = 0.976	r = 0.999

The sample concentrations were between 0.240 and 7.78 mg/L.

β2-Microglobulin values for human serum samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

Sample size (n) = 71

Passing/Bablok[37]	Linear regression
y = 1.019x - 0.0612 mg/L	y = 1.015x - 0.0528 mg/L
τ = 0.981	r = 0.999

The sample concentrations were between 0.484 and 7.65 mg/L.

Urine

β2-Microglobulin values for human urine samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 68

Passing/Bablok[37]	Linear regression
y = 1.000x + 0.00300 mg/L	y = 0.998x + 0.00986 mg/L
τ = 0.983	r = 1.000

The sample concentrations were between 0.260 and 5.52 mg/L.

β2-Microglobulin values for human urine samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 76

Passing/Bablok[37]	Linear regression
y = 1.021x - 0.00731 mg/L	y = 1.023x - 0.0105 mg/L
τ = 0.968	r = 0.999

The sample concentrations were between 0.200 and 5.39 mg/L.

β2-Microglobulin values for human urine samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

Sample size (n) = 73

Passing/Bablok[37]	Linear regression
y = 0.966x + 0.0129 mg/L	y = 0.969x + 0.00734 mg/L
τ = 0.975	r = 0.999

The sample concentrations were between 0.221 and 5.74 mg/L.

References

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A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard:

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

CE 0123

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