

Order information

REF	CONTENT	Analyzer(s) on which cobas c pack(s) can be used
03183807 190	Uric Acid ver.2 (400 tests)	System-ID 07 6615 1 COBAS INTEGRA 400 plus COBAS INTEGRA 800
10759350 190	Calibrator f.a.s. (12 × 3 mL)	System-ID 07 3718 6
10759350 360	Calibrator f.a.s. (12 × 3 mL, for USA)	System-ID 07 3718 6
12149435 122	Precinorm U plus (10 × 3 mL)	System-ID 07 7999 7
12149435 160	Precinorm U plus (10 × 3 mL, for USA)	System-ID 07 7999 7
12149443 122	Precipath U plus (10 × 3 mL)	System-ID 07 8000 6
12149443 160	Precipath U plus (10 × 3 mL, for USA)	System-ID 07 8000 6
10171743 122	Precinorm U (20 × 5 mL)	System-ID 07 7997 0
10171735 122	Precinorm U (4 × 5 mL)	System-ID 07 7997 0
10171778 122	Precipath U (20 × 5 mL)	System-ID 07 7998 9
10171760 122	Precipath U (4 × 5 mL)	System-ID 07 7998 9
05117003 190	PreciControl ClinChem Multi 1 (20 × 5 mL)	System-ID 07 7469 3
05947626 190	PreciControl ClinChem Multi 1 (4 × 5 mL)	System-ID 07 7469 3
05947626 160	PreciControl ClinChem Multi 1 (4 × 5 mL, for USA)	System-ID 07 7469 3
05117216 190	PreciControl ClinChem Multi 2 (20 × 5 mL)	System-ID 07 7470 7
05947774 190	PreciControl ClinChem Multi 2 (4 × 5 mL)	System-ID 07 7470 7
05947774 160	PreciControl ClinChem Multi 2 (4 × 5 mL, for USA)	System-ID 07 7470 7

English

System information

Test UA2, test ID 0-615 (serum, plasma)

Test UAU2, test ID 0-515 (urine)

Intended use

In vitro test for the quantitative determination of the uric acid concentration in serum, plasma, and urine on COBAS INTEGRA systems.

Summary^{1,2,3,4,5,6,7,8,9,10,11,12,13,14}

Uric acid is the final product of purine metabolism in the human organism. Uric acid measurements are used in the diagnosis and treatment of numerous renal and metabolic disorders, including renal failure, gout, leukemia, psoriasis, starvation or other wasting conditions, and of patients receiving cytotoxic drugs.

The oxidation of uric acid provides the basis for two approaches to the quantitative determination of this purine metabolite. One approach is the reduction of phosphotungstic acid in an alkaline solution to tungsten blue, which is measured photometrically. The method is, however, subject to interferences from drugs and reducing substances other than uric acid.

A second approach, described by Praetorius and Poulson, utilizes the enzyme uricase to oxidize uric acid; this method eliminates the interferences intrinsic to chemical oxidation. Uricase can be employed in methods that involve the UV measurement of the consumption of uric acid or in combination with other enzymes to provide a colorimetric assay.

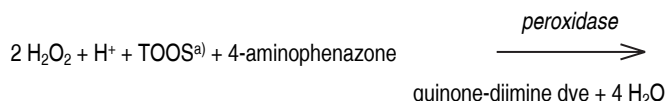
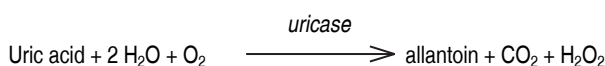
Another method is the colorimetric method developed by Town, et al. The sample is initially incubated with a reagent mixture containing ascorbate oxidase and a clearing system. In this test system it is important that any ascorbic acid present in the sample is eliminated in the preliminary reaction; this precludes any ascorbic acid interference with the subsequent POD indicator reaction. Upon addition of the starter reagent, oxidation of uric acid by uricase begins.

The Roche assay described here is a slight modification of the colorimetric method described above. In this reaction, the peroxide reacts in the presence of peroxidase (POD), TOOS, and 4-aminophenazone to form a quinoneimine dye. The intensity of the red color formed is proportional to the uric acid concentration and is determined photometrically.

Test principle

Enzymatic colorimetric test

Uricase cleaves uric acid to form allantoin and hydrogen peroxide.



a) N-ethyl-N-(2-hydroxy-3-sulfopropyl)-3-methylaniline

The color intensity of the quinone-diimine formed is directly proportional to the uric acid concentration and is determined by measuring the increase in absorbance at 552 nm.

Reagents - working solutions

- R1 Phosphate buffer: 0.05 mol/L, pH 7.8; TOOS: 7 mmol/L; fatty alcohol polyglycol ether: 4.8 %; ascorbate oxidase (EC 1.10.3.3; Zucchini) ≥ 83.5 µkat/L (25 °C); stabilizers
- SR Phosphate buffer: 0.1 mol/L, pH 7.8; potassium hexacyanoferrate (II): 0.3 mmol/L; 4-aminophenazone ≥ 3 mmol/L; uricase (EC 1.7.3.3; Arthrobacter protophormiae) ≥ 83.4 µkat/L (25 °C); peroxidase (POD) (EC 1.11.1.7; horseradish) ≥ 50 µkat/L (25 °C); stabilizers

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

Precautions and warnings

Pay attention to all precautions and warnings listed in Section 1 / Introduction of this Method Manual.

For USA: For prescription use only.

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



Danger

H318 Causes serious eye damage.

Prevention

P280 Wear eye protection/ face protection.

Response

P305 + P351 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do.
+ P338
+ P310 Continue rinsing. Immediately call a POISON CENTER or doctor/ physician.

Product safety labeling primarily follows EU GHS guidance.

Contact phone: all countries: +49-621-7590, USA: 1-800-428-2336

Reagent handling

Ready for use

Storage and stability

Shelf life at 2-8 °C See expiration date on
cobas c pack label

COBAS INTEGRA 400 plus system

On-board in use at 10-15 °C 12 weeks

COBAS INTEGRA 800 system

On-board in use at 8 °C 8 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: Heparin (Li-, Na-, NH₄⁺-) or EDTA (K₂-, K₃-) plasma

EDTA plasma values are approximately 8 % lower than serum values.

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: Assay urinary uric acid as soon as possible. Do not refrigerate. To prevent ureate precipitation in urine samples, add sodium hydroxide to keep the urine alkaline (pH > 8.0). To achieve stated uric acid stability, add NaOH prior to sample collection.

Urine samples are automatically prediluted 1:11 (1+10) with water by the instrument.

Centrifuge samples containing precipitates before performing the assay.

Stability in *serum/plasma*:¹⁵ 5 days at 2-8 °C
6 months at (-15)-(-25) °C

Stability in *urine*:¹⁶ 4 days at 15-25 °C
(upon NaOH addition):

Materials provided

See "Reagents – working solutions" section for reagents.

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.

Application for serum, plasma and urine

COBAS INTEGRA 400 plus test definition

Measuring mode	Absorbance
Abs. calculation mode	Endpoint
Reaction direction	Increase
Wavelength A/B	552/659 nm
Calc. first/last	33/39
Unit	µmol/L
<i>Serum, plasma</i>	

Reaction mode	R1-S-SR
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Urine

Reaction mode	D-R1-S-SR
Predilution factor	11

Pipetting parameters

<i>Serum, plasma, urine</i>		Diluent (H ₂ O)
R1	72 µL	
Sample	3 µL	45 µL
SR	14 µL	
Total volume	134 µL	

COBAS INTEGRA 800 test definition

Measuring mode	Absorbance
Abs. calculation mode	Endpoint
Reaction direction	Increase
Wavelength A/B	552/659 nm
Calc. first/last	44/55
Unit	µmol/L

Serum, plasma

Reaction mode	R1-S-SR
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Urine

Reaction mode	D-R1-S-SR
Predilution factor	11

Pipetting parameters

<i>Serum, plasma, urine</i>		Diluent (H ₂ O)
R1	72 µL	
Sample	3 µL	45 µL
SR	14 µL	
Total volume	134 µL	

Calibration

Calibrator	Calibrator f.a.s. Use deionized water as zero calibrator.
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Calibration mode	Linear regression
Calibration replicate	Duplicate recommended
Calibration interval	COBAS INTEGRA 400 plus system: Each cobas c pack, every 6 weeks, and as required following quality control procedures

COBAS INTEGRA 800 system:
Each lot and as required following quality control procedures

Traceability: This method has been standardized against ID-MS.

Quality control

Quality control <i>serum, plasma</i>	Precinorm U, Precinorm U plus or PreciControl ClinChem Multi 1 Precipath U, Precipath U plus or PreciControl ClinChem Multi 2
Quality control <i>urine</i>	Quantitative urine controls are recommended for routine quality control.
Control interval	24 hours recommended

Control sequence	User defined
Control after calibration	Recommended

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. 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 INTEGRA analyzers automatically calculate the analyte concentration of each sample. For more details, please refer to Data Analysis in the Online Help (COBAS INTEGRA 400 plus/800 analyzers).

Conversion factor: $\mu\text{mol/L} \times 0.0168 = \text{mg/dL}$

Limitations - interference

Criterion: Recovery within $\pm 10\%$ of initial value.

Serum, plasma

Icterus:¹⁷ No significant interference up to an I index of 39 for conjugated bilirubin and 33 for unconjugated bilirubin (approximate conjugated bilirubin concentration: 667 $\mu\text{mol/L}$ or 39 mg/dL ; approximate unconjugated bilirubin concentration: 564 $\mu\text{mol/L}$ or 33 mg/dL).

Hemolysis:¹⁷ No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 $\mu\text{mol/L}$ or 1000 mg/dL).

Lipemia (Intralipid):¹⁷ No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Ascorbic acid: No significant interference up to an ascorbic acid level of 1.7 mmol/L (30 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.^{18,19} Exceptions: Calcium dobesilate (e.g. Dexium) causes interference at therapeutic concentrations (uric acid level artificially low). Dicynone (Etamsylate) at therapeutic concentrations may lead to false-low results.²⁰

Acetaminophen intoxications are frequently treated with N-Acetylcysteine. N-Acetylcysteine at the therapeutic concentration when used as an antidote and the Acetaminophen metabolite N-acetyl-p-benzoquinone imine (NAPQI) independently may cause falsely low results.

Venipuncture should be performed prior to the administration of Metamizole. Venipuncture immediately after or during the administration of Metamizole may lead to falsely low results.

Uricase reacts specifically with uric acid. Other purine derivatives can inhibit the uric acid reaction.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.²¹

Urine

Ascorbic acid: No significant interference up to an ascorbic acid level of 1.7 mmol/L (30 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.¹⁹ Exceptions: Levodopa and methyldopa cause interference at therapeutic concentrations (uric acid level artificially low). Dicynone (Etamsylate) at therapeutic concentrations may lead to false-low results.

Acetaminophen, Acetylcysteine and Metamizole are metabolized quickly. Therefore, interference from these substances is unlikely but cannot be excluded.

High homogenetic acid concentrations lead to false results.

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 INTEGRA analyzers. Refer to the CLEAN Method Sheet for further instructions and for the latest version of the Extra wash cycle list.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Limits and ranges

Measuring range

Serum/plasma

11.9-1500 $\mu\text{mol/L}$ (0.20-25 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:10 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 10.

Urine

131-16000 $\mu\text{mol/L}$ (2.20-269 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:10 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 10.

Lower limits of measurement

Serum/plasma

Lower detection limit of the test:

11.9 $\mu\text{mol/L}$ (0.20 mg/dL)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 3 standard deviations above that of a zero sample (zero sample + 3 SD, repeatability, $n = 21$).

Urine

Lower detection limit of the test:

131 $\mu\text{mol/L}$ (2.20 mg/dL)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 3 standard deviations above that of a zero sample (zero sample + 3 SD, repeatability, $n = 21$).

Expected values

Serum, plasma²²

Males	202.3-416.5 $\mu\text{mol/L}$	(3.4-7.0 mg/dL)
Females	142.8-339.2 $\mu\text{mol/L}$	(2.4-5.7 mg/dL)

Urine (reference range according to Krieg and Colombo)

1st morning urine ²³	2200-5475 $\mu\text{mol/L}$	(37-92 mg/dL)
24 hours urine ²⁴	1200-5900 $\mu\text{mol/day}$	(200-1000 mg/day)
corresponding to	773-3986 $\mu\text{mol/L}^{b)}$	(13-67 mg/dL)

^{b)} calculated from a urine volume of 1.5 L/24 hours

Urine (reference range according Tietz)¹⁵

Average diet 250-750 mg/24 hours

Low purine diet

Males	< 480 mg/24 hours
Females	< 400 mg/24 hours

High purine diet < 1000 mg/24 hours

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. Results obtained in individual laboratories may differ.

Precision

Precision was determined using human samples and controls in an internal protocol with repeatability ($n = 21$) and intermediate precision (1 aliquot per run, 1 run per day, 21 days). The following results were obtained:

Serum, plasma

Repeatability	Level 1	Level 2
Mean	257 $\mu\text{mol/L}$ (4.32 mg/dL)	634 $\mu\text{mol/L}$ (10.7 mg/dL)

Repeatability	Level 1	Level 2
CV	1.1 %	1.0 %

Intermediate precision	Level 1	Level 2
Mean	259 µmol/L (4.35 mg/dL)	658 µmol/L (11.1 mg/dL)
CV	1.8 %	1.9 %

Urine

Repeatability	Level 1	Level 2
Mean	807 µmol/L (13.6 mg/dL)	1506 µmol/L (25.3 mg/dL)
CV	1.0 %	0.9 %

Intermediate precision	Level 1	Level 2
Mean	728 µmol/L (12.2 mg/dL)	1381 µmol/L (23.2 mg/dL)
CV intermediate precision	1.7 %	1.6 %

Method comparison

Uric acid values for human serum, plasma and urine samples obtained on a COBAS INTEGRA 700 analyzer using the COBAS INTEGRA Uric Acid ver.2 (UA2) reagent (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x) and with those determined using the previous reagent (UA) on a COBAS INTEGRA 700 analyzer (x).

Serum, plasma

Roche/Hitachi 917 analyzer	Sample size (n) = 55
Passing/Bablok ²⁵	Linear regression
$y = 0.978x + 5.95 \text{ µmol/L}$	$y = 0.962x + 10.7 \text{ µmol/L}$
$r = 0.990$	$r = 1.00$
SD (md 95) = 20.5	Sy.x = 8.32

The sample concentrations were between 57 and 1548 µmol/L (0.958 and 26.0 mg/dL).

COBAS INTEGRA 700 analyzer	Sample size (n) = 43
Passing/Bablok ²⁵	Linear regression
$y = 0.998x + 2.28 \text{ µmol/L}$	$y = 0.989x + 3.96 \text{ µmol/L}$
$r = 0.979$	$r = 1.00$
SD (md 95) = 6.14	Sy.x = 3.83

The sample concentrations were between 56 and 875 µmol/L (0.941 and 14.7 mg/dL).

Urine

Roche/Hitachi 917 analyzer	Sample size (n) = 89
Passing/Bablok ²⁵	Linear regression
$y = 0.960x - 0.339 \text{ µmol/L}$	$y = 0.959x + 9.68 \text{ µmol/L}$
$r = 0.968$	$r = 0.998$
SD (md 95) = 100.2	Sy.x = 46.9

The sample concentrations were between 45 and 3978 µmol/L (0.756 and 66.8 mg/dL).

COBAS INTEGRA 700 analyzer	Sample size (n) = 54
Passing/Bablok ²⁵	Linear regression
$y = 0.979x - 19.1 \text{ µmol/L}$	$y = 0.977x - 19.3 \text{ µmol/L}$
$r = 0.983$	$r = 1.00$
SD (md 95) = 34.9	Sy.x = 20.8

The sample concentrations were between 91 and 3802 µmol/L (1.53 and 63.9 mg/dL).

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UA2

Uric Acid ver.2**cobas®**
Substrates

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.

Symbols

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

	Contents of kit
	Volume after reconstitution or mixing
	Global Trade Item Number

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