i-STAT CREA Cartridge

Intended for use with the i-STAT Alinity Instrument

NAME

i-STAT CREA Cartridge – REF 03P84-25

INTENDED USE

The i-STAT Crea cartridge with the i-STAT Alinity System is intended for use in the *in vitro* quantification of creatinine in arterial, venous, or capillary whole blood.

Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.

SUMMARY AND EXPLANATION/CLINICAL SIGNIFICANCE

Measured:

Creatinine (Crea)

Elevated levels of creatinine are mainly associated with abnormal renal function and occur whenever there is a significant reduction in glomerular filtration rate or when urine elimination is obstructed. The concentration of creatinine is a better indicator of renal function than urea or uric acid because it is not affected by diet, exercise, or hormones.

The creatinine level has been used in combination with BUN to differentiate between prerenal and renal causes of an elevated urea/BUN.

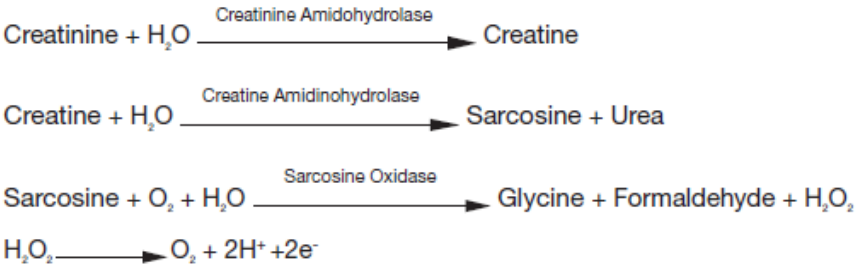
TEST PRINCIPLE

The i-STAT System uses direct (undiluted) electrochemical methods. Values obtained by direct methods may differ from those obtained by indirect (diluted) methods. [1]

Measured:

Creatinine (Crea)

Creatinine is measured amperometrically. It is hydrolyzed to creatine in a reaction catalyzed by the enzyme creatinine amidohydrolase. Creatine is then hydrolyzed to sarcosine by creatine amidinohydrolase. The oxidation of sarcosine, catalyzed by sarcosine oxidase, produces hydrogen peroxide (H_2O_2). The liberated hydrogen peroxide is oxidized at the platinum electrode to produce a current which is proportional to the sample creatinine concentration.



Calculated:

eGFR (estimated Glomerular Filtration Rate)

Estimated Glomerular filtration rate is an index of kidney function, used to screen for and detect early kidney damage, to help diagnose chronic kidney disease (CKD), and to monitor kidney status.

The i-STAT Alinity can report a calculated eGFR result when a creatinine test result is obtained. The two calculation options are:

- The Modification of Diet in Renal Disease (MDRD) Study equation [2]:
  - **eGFR = 175 x $[S_{cr}]^{-1.154}$ x $(Age)^{-0.203}$ x (0.742 if female) x (1.212 if African American)**, *where S_{cr} is serum creatinine (mg/dL), and age is expressed in years*.
- The Chronic Kidney Disease Epidemiology Collaboration formula (CKD-EPI):
  - **eGFR = 141 x $\min(S_{cr}/k, 1)^{\alpha}$ x $\max(S_{cr}/k, 1)^{-1.209}$ x 0.993^{Age} x 1.018 [if female] x 1.159 [if Black]**, *where S_{cr} is serum creatinine (mg/dL), k is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of S_{cr}/k or 1, and max indicates the maximum of S_{cr}/k or 1*.

Limitations of the Procedure:

The formula is valid for adults between the ages of 18 and 120 years.

Warnings and Precautions:

eGFR >60 mL/min/1.73m^2 does not exclude the possibility of mild renal disease. Further laboratory testing may be necessary to distinguish normal renal function from mild renal disease.

Creatinine-based estimating equations are not recommended for use with individuals with unstable creatinine concentrations, nor with persons with extremes in muscle mass and diet.

The MDRD eGFR equation has not been validated for those who are 70 years of age or older because muscle mass normally decreases with age. As a result, eGFR for patients older than 70 requires clinical correlation but is still regarded as a useful tool when caring for patients older than 70. [2]

See below for information on factors affecting results. Certain substances, such as drugs, may affect analyte levels in vivo.[3] If results appear inconsistent with the clinical assessment, the patient sample should be retested using another cartridge.

REAGENTS

Contents

Each i-STAT cartridge contains one reference electrode (when potentiometric sensors are included in the cartridge configuration), sensors for the measurement of specific analytes, and a buffered aqueous calibrant solution that contains known concentrations of analytes and preservatives. A list of reactive ingredients for the i-STAT Creatinine cartridge is shown below:

Sensor	Reactive Ingredient	Biological Source	Minimum Quantity
Crea	Creatinine	N/A	158.4 µmol/L
	Creatine Amidinohydrolase	Microbial	0.01 IU
	Creatinine Amidohydrolase	Microbial	0.02 IU
	Sarcosine Oxidase	Microbial	0.001 IU

Warnings and Precautions

- For *in vitro* diagnostic use.
- Cartridges are intended for single-use only. Do not reuse.
- Refer to the i-STAT Alinity System Operations Manual for all warnings and precautions.

Storage Conditions

- Refrigeration at 2–8 ºC (35–46 ºF) until expiration date.
- Room Temperature at 18–30 ºC (64–86 ºF). Refer to the cartridge box for room temperature storage requirements.

INSTRUMENTS

The i-STAT CREA cartridge is intended for use with the i-STAT Alinity Instrument (Model No. AN-500).

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Arterial, venous or capillary whole blood.
Sample volume: 65 µL

Blood Collection Options and Test Timing (time from collection to cartridge fill)

As higher heparin-to-blood ratios may affect results, fill blood collection tubes and syringes to capacity, following manufacturers' instructions.

CREA Sample Collection	
Syringe	**Without anticoagulant** · Mix sample immediately before filling cartridge. · Fill cartridge within 3 minutes of sample collection. **With balanced heparin anticoagulant** · Mix sample immediately before filling cartridge. · Fill cartridge within 30 minutes of sample collection.

CREA Sample Collection	
Evacuated Tube	**Without anticoagulant** · Mix sample immediately before filling cartridge. · Fill cartridge within 3 minutes of sample collection. **With lithium heparin anticoagulant** · Mix sample immediately before filling cartridge. · Fill cartridge within 30 minutes of sample collection.
Capillary Tube	**With balanced heparin anticoagulant** · Mix sample immediately before filling cartridge. · Fill cartridge within 3 minutes of sample collection. **With lithium heparin anticoagulant** - if labeled for measurement of electrolytes. · Mix sample immediately before filling cartridge. · Fill cartridge within 3 minutes of sample collection.
Fill cartridge directly from skin puncture	While a sample can be transferred directly from a skin puncture to a cartridge, a capillary tube is preferred.

PROCEDURE FOR CARTRIDGE TESTING

Preparation for Use:

1. Individual cartridges may be used after standing five minutes at room temperature. An entire box of cartridges should stand at room temperature for one hour.
2. All cartridges should be used immediately after opening pouch.
3. If the pouch has been punctured, the cartridge should not be used.
4. Do not return cartridges to the refrigerator after bringing them to room temperature.

How to Perform Patient Testing

1. From the Home screen, touch "**Perform Patient Test**". This initiates the patient testing pathway.
2. To begin, follow instructions on the screen to "**Scan or Enter OPERATOR ID**"
3. Follow instructions on the screen to "**Scan or Enter PATIENT ID**"
4. Continue to follow prompts on the screen to proceed with patient testing. "**Scan (CARTRIDGE POUCH) Barcode**", Scanning is required. Information cannot be entered manually.
5. The screen for selecting sample type will display if more than one sample type is applicable; select sample type if applicable.
6. Follow instructions on the screen to "**Close and Insert Filled Cartridge**". The action buttons at the bottom of the screen allow forward, backward and pause functionality.
7. Once the cartridge is inserted, "**Contacting Cartridge**" will display followed by the countdown bar. The following alerts are also displayed: **"Cartridge locked in instrument. Do not attempt to remove the Cartridge**" and "**Testing - Instrument Must Remain Level**".
8. When the test is complete, the test results are displayed.

Analysis Time

Approximately 130–200 seconds.

Quality Control

The i-STAT Alinity System quality control regimen comprises various aspects, with a system design that reduces the opportunity for error, including:

1. The i-STAT Alinity System automatically runs a comprehensive set of quality checks of analyzer and cartridge performance each time a sample is tested. This internal quality system will suppress results if the analyzer or cartridge does not meet certain internal specifications.
2. Aqueous-based control solutions are available for verifying the integrity of newly received cartridges.
3. In addition, the instrument performs internal electronic checks and calibration during each test cycle, and the Electronic Simulator test provides an independent check on the ability of the instrument to take accurate and sensitive measurements of voltage, current and resistance from the cartridge. The instrument will pass or fail this electronic test depending on whether or not it measures these signals within limits specified in the instrument software.

For additional information on Quality Control, refer to the i-STAT Alinity System Operations Manual located at www.pointofcare.abbott.

Calibration Verification

Standardization is the process by which a manufacturer establishes "true" values for representative samples. A multi-point calibration is derived for each sensor by this standardization process. These calibration curves are stable over many lots.

A one-point calibration is performed each time a cartridge requiring calibration is used. During the first part of the testing cycle, the calibrant solution is automatically released from its foil pack and is positioned over the sensors. The signals produced by the sensors' responses to the calibrant solution are measured. This one-point calibration adjusts the offset of the stored calibration curve. Next, the instrument automatically moves the sample over the sensors and the signals produced by the sensors' responses to the sample are measured. While coefficients are used rather than graphic calibration curves, the calculation of the result is equivalent to reading the sample's concentration from an adjusted calibration curve.

EXPECTED VALUES

TEST	UNITS *	REPORTABLE RANGE	REFERENCE RANGE *arterial*	REFERENCE RANGE *venous*
MEASURED				
Crea	mg/dL	0.2–20.0	0.6–1.3 [4]	
	µmol/L	18–1768	53–115	
CALCULATED				
estimated Glomerular Filtration Rate (eGFR)	mL/min/1.73m^2	0 – 60	>90	
estimated Glomerular Filtration Rate – Black/African American (eGFR-a)	mL/min/1.73m^2	0 – 60	>90	

* The i-STAT System can be configured with the preferred units. (See "Unit Conversion" below.)

Unit Conversion

- **Creatinine (Crea):** To convert mg/dL to µmol/L, multiply the mg/dL value by 88.4.

i-STAT Alinity does not have default reference ranges programmed into the instrument. The reference ranges shown above are intended to be used as guides for the interpretation of results. Since reference ranges may vary with demographic factors such as age, gender and heritage, it is recommended that reference ranges be determined for the population being tested.

METROLOGICAL TRACEABILITY

The measured analytes in the i-STAT CREA cartridge are traceable to the following reference materials or methods. The i-STAT System controls and calibration verification materials are validated for use only with the i-STAT System and assigned values may not be commutable with other methods.

Creatinine (Crea)
The i-STAT System test for creatinine measures creatinine amount-of-substance concentration in the plasma fraction of arterial, venous, or capillary whole blood (dimension µmol L^{-1}) for in vitro diagnostic use. Creatinine values assigned to i-STAT System controls and calibration verification materials are traceable to the U.S. National Institute of Standards and Technology (NIST) standard reference material SRM967.

Additional information regarding metrological traceability is available from Abbott Point of Care Inc.

PERFORMANCE CHARACTERISTICS

The performance data summarized below was collected at Abbott Point of Care. Representative cartridges were used to collect the data.

Precision*

A multiday precision study was performed with aqueous calibration verification materials in representative cartridges. Duplicates of each aqueous fluid were tested twice a day for 20 days.

Test	Units	Aqueous Cal Ver	n	Mean	SD (Standard Deviation)	CV (%) [Coefficient of Variation (%)]
Crea	mg/dL	Low Abnormal	80	0.27	0.028	10.3
		Normal	80	1.05	0.025	2.4
		High Abnormal	80	3.83	0.083	2.2
		Very High Abnormal	80	14.63	0.403	2.8

*Note: Representative data, individual laboratories may vary from these data.

Method Comparison

Method comparison was demonstrated in a study comparing the i-STAT Alinity to the i-STAT 1 Wireless (i-STAT 1W) using representative cartridges. The studies were based on CLSI guideline EP9-A3.[5] Whole blood samples anticoagulated with lithium heparin were evaluated. Samples were analyzed in duplicate on both systems. A weighted Deming regression analysis was performed using the first replicate result from the i-STAT Alinity versus the mean of the duplicates from the i-STAT 1W.

Test	Units		Comparative Method i-STAT 1W
Crea	mg/dL	n	194
		Slope	0.988
		r	0.999
		intercept	0.003
		Xmin	0.2
		Xmax	19.2

In the method comparison table, n is the number of specimens, and r is the correlation coefficient.

FACTORS AFFECTING RESULTS

The following substances were evaluated in plasma for relevant analyte at the test concentrations recommended in CLSI guideline EP7-A2[6] unless otherwise noted. For those identified as an interferant the interference is described.

Substance	Test Concentration (mmol/L)	Analyte	Interference (Yes/No)	Comment
Acetaldehyde	0.04[7]	Crea	No	
Acetaminophen	1.32	Crea	Yes	Increased results

Substance	Test Concentration (mmol/L)	Analyte	Interference (Yes/No)	Comment
Acetaminophen (therapeutic)	0.132 [7]	Crea	No	
Acetylcysteine	10.2	Crea	Yes	Increased results
Acetylcysteine (therapeutic)	0.3 [8 9]	Crea	No	
Ascorbate	0.34	Crea	Yes	Increased by up to 0.3 mg/dL
Bicarbonate	35.0	Crea	No	
Bilirubin	0.342	Crea	No	
Bromide (therapeutic)	2.5 [10 11 12]	Crea	Yes	Increased results
Calcium Chloride	5.0	Crea	No	
Creatine	0.382	Crea	Yes	Increased by up to 0.3 mg/dL. See Other Factors Affecting Results below for CO_2 dependence
Dopamine	0.006	Crea	No	
Formaldehyde	0.133 [7]	Crea	No	
β-Hydroxybutyrate	6.0 [13]	Crea	No	
Glycolic Acid	10.0	Crea	Yes	Decreased results. Use another method.
Hydroxyurea	0.92	Crea	Yes	Increased results. Use another method.
Lactate	6.6	Crea	No	
Methyldopa	0.071	Crea	No	
Nithiodote (Sodium thiosulfate)	16.7 [14]	Crea	Yes	Increased results
Pyruvate	0.31	Crea	No	
Salicylate	4.34	Crea	No	
Uric Acid	1.4	Crea	No	

The degree of interference at concentrations other than those reported above might not be predictable. It is possible that interfering substances other than those tested may be encountered.

Relevant comments regarding interference of Acetaminophen, Acetylcysteine, Bromide, Hydroxyurea and Nithiodote are noted below:

- Acetaminophen has been shown to interfere with i-STAT creatinine results at a 1.32 mmol/L, a toxic concentration that is proscribed by the CLSI guideline. Acetaminophen at 0.132 mmol/L, which represents the upper end of the therapeutic concentration range, has been shown not to significantly interfere with i-STAT creatinine results.
- Acetylcysteine has been tested at two levels: the CLSI recommended level of 10.2 mmol/L and a concentration of 0.30 mmol/L. The latter is 3 times the peak plasma therapeutic concentration associated with treatment to reverse acetaminophen poisoning. APOC has not identified a therapeutic condition that would lead to levels consistent with the CLSI recommended level. Acetylcysteine at a concentration of 10.2 mmol/L increased i-STAT creatinine results, while acetylcysteine at a concentration of 0.3 mmol/L did not significantly interfere with i-STAT creatinine results.
- Bromide has been tested at two levels: the CLSI recommended level and a therapeutic plasma concentration level of 2.5 mmol/L. The latter is the peak plasma concentration associated with halothane anesthesia, in which bromide is released. APOC has not identified a therapeutic condition that would lead to levels consistent with the CLSI recommended level. Bromide tested at concentrations of 2.5 and 37.5 mmol/L interfered with i-STAT creatinine results.

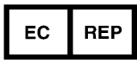
- Hydroxyurea is a DNA synthesis inhibitor used in the treatment of various forms of cancer, sickle cell anemia, and HIV infection. This drug is used to treat malignancies including melanoma, metastatic ovarian cancer, and chronic myelogenous leukemia. It is also used in the treatment of polycythemia vera, thrombocythemia, and psoriasis. At typical doses ranging from 500 mg to 2 g/day, concentrations of hydroxyurea in patients' blood may be sustained at approximately 100 to 500 µmol/L. Higher concentrations may be observed soon after dosing or at higher therapeutic doses.
- Nithiodote (sodium thiosulfate) is indicated for the treatment of acute cyanide poisoning. The journal article titled "Falsely increased chloride and missed anion gap elevation during treatment with sodium thiosulfate" indicated that sodium thiosulfate could be used in the treatment of calciphylaxis indicating that "the highest concentration likely to be seen in plasma [is] after infusion of a 12.5 g dose of sodium thiosulfate pentahydrate. Assuming that the 12.5 g dose of sodium thiosulfate pentahydrate is distributed in a typical blood volume of 5 L with a hematocrit of 40%, the peak sodium thiosulfate plasma concentration expected is 16.7 mmol/L." [14]

*It is possible that other interfering substance may be encountered. The degree of interference at concentrations other than those listed might not be predictable.

OTHER FACTORS AFFECTING RESULTS

Factor	Analyte	Effect
Creatine	Creatinine	The normal range of creatine concentration in plasma is 0.17–0.70 mg/dL (13 – 53 µmol/L) in males and 0.35 – 0.93 mg/dL (27 – 71 µmol/L) in females. [7] Creatine may be elevated in patients using creatine supplements, experiencing muscle trauma or other primary or secondary myopathies, taking statins for hyperlipidemia control, or in patients with hyperthyroidism or a rare genetic defect of the creatine transporter protein.
CO_2 dependence	Creatinine	The dependence of the i-STAT creatinine with respect to Carbon Dioxide (CO_2) is as follows: For creatinine results ≤ 2.0 mg/dL, no correction for $\boldsymbol{P}CO_2$ is required. For creatinine results > 2.0 mg/dL, the following correction applies: $\mathbf{Creatinine_{corrected} = creatinine * (1 + 0.0025 * (PCO_2 - 40))}$

KEY TO SYMBOLS

Symbol	Definition/Use
	14 days room temperature storage at 18–30 ^{0}C.
	Use by or expiration date. The expiration date, expressed as YYYY-MM-DD, indicates the last day the product may be used.
	Manufacturer's lot number or batch code. The lot number or batch code appears adjacent to this symbol.
	Sufficient for <n> tests.
	Authorized representative for Regulatory Affairs in the European Community.
	Temperature limitations. The upper and lower limits for storage are adjacent to upper and lower arms.
	Catalog number, list number, or reference.
	Do not reuse.
	Manufacturer.
	Consult instructions for use or see System Manual for instructions.
	*In vitro* diagnostic medical device.
	Compliance to the European directive on *in vitro* diagnostic devices (98/79/EC)
	For prescription use only.

Additional Information: to obtain additional product information and technical support, refer to the Abbott company website at www.pointofcare.abbott.

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