Overview

Useful For
Evaluation of patients with a clinical suspicion of inborn errors of creatine metabolism including arginine:glycine amidinotransferase deficiency, guanidinoacetate methyltransferase deficiency, and creatine transporter (SLC6A8) defect

Highlights
Depletion of cerebral creatine occurs in all 3 types of creatine deficiency syndromes (CDS): arginine:glycine amidinotransferase (AGAT) deficiency, guanidinoacetate methyltransferase (GAMT) deficiency, and creatine transporter (SLC6A8) deficiency.

Measurement of guanidinoacetate (GAA), creatine (Cr), and creatinine (Crn) in urine along with the Cr:Crn ratio distinguishes among the types of creatine deficiency syndromes.

Treatment with oral creatine supplementation is effective in some types of CDS.

Creatine supplementation may cause increased creatine values.

Additional Tests

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRBO</td>
<td>Creatine, (Bill Only), U</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>CRNBO</td>
<td>Creatinine, (Bill Only), U</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>GAABO</td>
<td>Guanidinoacetate, (Bill Only), U</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Testing Algorithm

CRDPU / Creatine Disorders Panel, Urine is a single test that carries the results for the panel. When the test is resulted, the following procedures are billed:

- CRBO / Creatine, Urine (Bill Only)
- CRNBO / Creatinine, Urine (Bill Only)
- GAABO / Guanidinoacetate, Urine (Bill Only)

For more information, see Newborn Screening Act Sheet Guanidinoacetate Methyltransferase Deficiency: Increased Guanidinoacetate in Special Instructions.

The following algorithms are available in Special Instructions:

- Newborn Screen Follow-up for Guanidinoacetate Methyltransferase Deficiency (GAMT)
- Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm

Special Instructions
Method Name
Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available
Yes

Specimen

Specimen Type
Urine

Specimen Required
Supplies: Urine Tubes, 10 mL (T068)

Specimen Volume: 1 mL

Collection Instructions:
1. Collect a random urine specimen.
2. Immediately freeze specimen.
3. If possible, do not send other tests ordered on same vial of urine. In doing so, the other tests may have increased turnaround time due to the strict frozen criteria of this assay.

Forms
If not ordering electronically, complete, print, and send an Inborn Errors of Metabolism Test Request (T798) with the specimen.

Specimen Minimum Volume
0.5 mL

Reject Due To
All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine</td>
<td>Frozen</td>
<td>29 days</td>
<td></td>
</tr>
</tbody>
</table>

Clinical and Interpretive
**Clinical Information**

Disorders of creatine synthesis (deficiency of arginine:glycine amidinotransferases: AGAT and guanidinoacetate methyltransferase: GAMT) and creatine transporter (SLC6A8) deficiency are collectively described as creatine deficiency syndromes (CDS). AGAT and GAMT deficiencies are inherited in an autosomal recessive manner, while the creatine transporter defect is X-linked. All 3 disorders result in a depletion of cerebral creatine and typically present with global developmental delays, intellectual disability, and severe speech delay. Commonly, patients with CDS develop seizures. Patients with GAMT and the creatine transporter deficiency exhibit behavioral problems and features of autism. Female carriers for the creatine transporter deficiency can have intellectual disability and behavioral problems, and some develop seizures.

Diagnosis is possible by measuring guanidinoacetate (GAA), creatine (Cr), and creatinine (Crn) in plasma and urine. The profiles are specific for each clinical entity. Patients with GAMT deficiency typically exhibit normal to low Cr, very elevated GAA, and low Crn. Patients with AGAT deficiency typically exhibit normal to low Cr, low GAA, and normal to low Crn. In comparison, elevated Cr, normal GAA, normal to low Crn, and an elevated Cr:Crn ratio characterize patients with creatine transporter defect.

Treatment with oral supplementation of creatine monohydrate is available and effective for the AGAT and GAMT deficiencies. Early treatment has been reported to prevent disease manifestations in affected but presymptomatic newborn siblings of individuals with GAMT or AGAT deficiencies. Creatine supplementation has not been shown to improve outcomes in males with the creatine transporter defect. Female carriers of creatine transporter deficiency who have symptoms, however, have been reported to benefit from creatine supplementation.

**Reference Values**

**Males**

<table>
<thead>
<tr>
<th>Age</th>
<th>Creatinine (nmol/mL)</th>
<th>Guanidinoacetate (nmol/mL)</th>
<th>Creatine (nmol/mL)</th>
<th>Creatine/Creatinine</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; or =31 days</td>
<td>430-5,240</td>
<td>9-210</td>
<td>12-2930</td>
<td>0.02-0.93</td>
</tr>
<tr>
<td>32 days-23 months</td>
<td>313-9,040</td>
<td>16-860</td>
<td>18-10,490</td>
<td>0.02-2.49</td>
</tr>
<tr>
<td>2-4 years</td>
<td>1,140-12,820</td>
<td>90-1,260</td>
<td>200-9,210</td>
<td>0.04-1.75</td>
</tr>
<tr>
<td>5-18 years</td>
<td>1,190-25,270</td>
<td>40-1,190</td>
<td>60-9,530</td>
<td>0.01-0.96</td>
</tr>
<tr>
<td>&gt;18 years (male)</td>
<td>3,854-23,340</td>
<td>30-710</td>
<td>7-470</td>
<td>0.00-0.04</td>
</tr>
</tbody>
</table>

**Females**

<table>
<thead>
<tr>
<th>Age</th>
<th>Creatinine (nmol/mL)</th>
<th>Guanidinoacetate (nmol/mL)</th>
<th>Creatine (nmol/mL)</th>
<th>Creatine/Creatinine</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; or =31 days</td>
<td>430-5,240</td>
<td>9-210</td>
<td>12-2930</td>
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<td>60-9,530</td>
<td>0.01-0.96</td>
</tr>
<tr>
<td>&gt;18 years</td>
<td>1,540-18,050</td>
<td>30-760</td>
<td>5-2810</td>
<td>0.00-0.46</td>
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**Interpretation**
Reports include concentrations of guanidinoacetate, creatine, and creatinine, and a calculated creatine:creatinine ratio. When no significant abnormalities are detected, a simple descriptive interpretation is provided. When abnormal results are detected, a detailed interpretation is given. This interpretation includes an overview of the results and their significance, a correlation to available clinical information, elements of differential diagnosis, and recommendations for additional biochemical testing.

**Cautions**
Correct specimen collection and handling are crucial to achieve reliable results.

Creatine supplementation will cause falsely elevated results.

**Clinical Reference**


**Performance**

**Method Description**

**PDF Report**
No

**Day(s) and Time(s) Test Performed**
Tuesday; 12 p.m.

**Analytic Time**
7 days

**Maximum Laboratory Time**
18 days

**Specimen Retention Time**
2 months
Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
82540-Creatine
82570-Creatinine
82542-Guanidinoacetate

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
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<tbody>
<tr>
<td>CRDPU</td>
<td>Creatine Disorders Panel, U</td>
<td>79290-3</td>
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<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
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<tr>
<td>23383</td>
<td>Creatine</td>
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<td>23384</td>
<td>Creatinine</td>
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<td>23385</td>
<td>Guanidinoacetate</td>
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<td>23268</td>
<td>Creatine/Creatinine Ratio</td>
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<td>23270</td>
<td>Creatine Disorders Panel Interp</td>
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<td>23272</td>
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