WISCONSIN NEWBORN SCREENING (NBS) PROGRAM – CONDITION NOMINATION

Nomination of a Condition to the Wisconsin Newborn Screening Panel

Date of Nomination

10/18/2024

NOMINATOR	
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Affiliation (i.e., health professional, researcher, clinician, advocate) Clinician /Metabolic Consultant for Wisconsin Newborn Screening Metabolic Subcommittee	
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CO-SPONSORING ORGANIZATION #1 (as appropriate, additional sponsors may be included on page 5)	
Name Roberto Mendez	Organization Wisconsin State Laboratory of Hygiene
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Condition	**STATEMENT**
Nominated Condition	Guanidinoacetate methyltransferase (GAMT) deficiency
Description of Disorder	Guanidinoacetate methyltransferase (GAMT) deficiency is one of three metabolic disorders related to cerebral creatine deficiency. It is an autosomal recessive disorder due to variants in the gene, GAMT, which encodes for the enzyme guanidinoacetate methyltransferase (OMIM #601240) . This enzyme converts Guanidinoacetate (GUAC) to creatine and a deficiency in this enzyme leads to a build-up of GUAC and low creatine levels. This disorder presents neurologic signs and symptoms including developmental delays particularly in speech, intellectual disability, behavioral issues including autism, seizures, and movement disorders like ataxia. Pre-symptomatic treatment with dietary interventions and supplements has shown significantly improved outcomes with most individuals being neurologically typical.
Screening Method	Determination of guanidinoacetate concentration and guanidinoacetate to creatine ratio in dried blood spots by non-derivatized tandem mass spectrometry
Gene	GAMT
OMIM or other names for condition	601240
Case Definition	Defect in creatine biosynthesis due to deficiency in guanidinoacetate methyltransferase leading to accumulation of guanidinoacetate (GUAC) and low creatine. Deficiency due to autosomal recessive inheritance of biallelic pathogenic variants in the gene GAMT.

NOTE: Please reference each statement/answer with the corresponding reference number listed in **Key References**.

CRITERION	
Criterion 1: Mandated testing should be limited to conditions that cause serious health risks in childhood that are unlikely to be detected and prevented in the absence of newborn screening.	
Timing of Clinical Onset	*Relevance of the timing of newborn screening to onset of clinical manifestations. Must cause serious health risks in childhood that are unlikely to be detected and prevented in the absence of newborn screening.* The clinical features of GAMT deficiency impact the central nervous system and become apparent in infancy or toddlerhood after a pre-symptomatic period.The developing affected fetus is protected because creatine transport across the placenta occurs during pregnancy (Ellery). The earliest symptoms are reported at 3-6 months of age (ACHDNC report). Clinical features include developmental delays particularly in speech development, intellectual disability, behavioral concerns including aggression, autism like features, hyperactivity and self-injury, seizures, hypotonia, movement disorders including ataxia and chorea (Mercimek-Andrews). Without detection by newborn screening, treatment would not start prior to clinical features observed and diagnostic evaluation makes the diagnosis.
Criterion 2: For each condition, there should be information about the incidence, morbidity and mortality, and the natural history of the disorder.	
Incidence	*Determined by what method(s): pilot screening or clinical identification?* GAMT deficiency is a rare disorder. In 2022, GeneReviews estimated that only 130 individuals have GAMT deficiency. The incidence, the number of newly identified cases over a specified timeframe, for GAMT deficiency is unknown Based on clinically reported cases, an incidence of <0.3/100,000 live births can be estimated. Several studies have estimated carrier frequency between from 1/250 to 1/812 to greater than 1/1475 newborns (Mercimek-Mahmutoglu, Desroches, Mercimek-Andrews). Based on this carrier frequency, the incidence would be calculated to be 1 in 250,000 to 1 in 2,640,0009 (Desroches). The incidence based on Utah and New York's newborn population (obtained during pilot's newborn screening of GAMT deficiency) is 1:405,6559 (Hart).
Severity of Disease	*Morbidity, disability, mortality, spectrum of severity, natural history.* GAMT deficiency is a rare disorder. Its pathophysiology is due to the lack of the product, creatine, as well as the buildup of GUAC. From the Advisory Committee on Heritable Disorders in Newborn and Children (ACHDNC) review, evidence indicates that the behavioral problems and intellectual disability are related to the creatine deficiency and intractable seizures and movement disorders are related to the elevated GUAC. Clinical features include developmental delays (DD) particularly in speech development, intellectual disability (ID), behavioral concerns including aggression, autism like features, hyperactivity and self-injury, seizures, hypotonia, movement disorders including ataxia and chorea. Intellectual disability can range from mild to severe, however most individuals (50 to 75%) have severe developmental delay (Mercimek-Andrews). There is variability in neurologic features. Outlined in the ACHDNC review are several studies with 20 to 48 subjects. Of note, patients overlap within these studies. The ACHDNC review accounts for this overlap in the reporting. From the ACHDNC review, decrease in life expectancy is not reported, but neurologic sequelae including epilepsy may be related to an increased risk of mortality See table for summary of studies of natural history .

Criterion 3: Conditions identified by newborn screening should be linked with interventions that have been shown in well-designed studies to be safe and effective in preventing serious health consequences.	
Urgency	How soon after birth must treatment be initiated to be effective? As stated above, GAMT deficiency impacts the central nervous system and become apparent in infancy or toddlerhood after a pre-symptomatic period. The earliest symptoms are reported at 3-6 months of age (ACHDNC).
Efficacy (Benefits)	Extent of prevention of mortality, morbidity, disability. Treatment limitations, such as difficulty with acceptance or adherence. The ACHDNC review concludes that case series suggesting pre-symptomatic or early initiation of treatment is associated with improved neurologic outcomes (ACHDNC review). These outcomes include reduced risk of intellectual disability and a decrease in seizures and movement disorders. There are no quantitative measures of developmental outcomes provided. See table for summary of studies of natural history.
Potential Harms	Potential medical or other ill effects from treatment. Potential harms from treatment include nutritional deficiencies. These deficiencies are likely due to the mild protein restriction needed as well as monitoring completed for patients on a protein restricted diet. Side effects for creatine can include water retention, muscle cramps, dehydration vomiting and diarrhea and liver dysfunction. Evidence based review of the literature has found creatine a safe supplement. There remains concerned about high dose creatine in individuals with preexisting renal disease and long term studies need to be completed (Holecek). Side effects for ornithine include gastrointestinal upset (Grimble)
Criterion 4: The interventions should be reasonably available to affected newborns.	

Modality	*Drug(s), diet, replacement therapy, transplant, surgery, other. Include information regarding regulatory status of treatment. .* Per the ACHDNC review, there are no current conference or committee or society guidelines for treatment. However, there are several articles that provide current treatment recommendations for arginine restriction and supplementation of creatine and ornithine, as well as monitoring guidelines. Current treatment involves dietary restriction of arginine as well as supplementation of creatine and ornithine. The goal of this treatment is to increase creatine levels and decrease GUAC levels. Recent recommendations include emphasis on oral creatine (typically 400 mg/kg daily) and ornithine (typically 100-800 mg/kg daily) (Stockler-Ipsiroglu 2022). Dietary protein restriction of arginine with arginine free medical formula and sodium benzoate (typically 100 mg/kg daily) may also be added to the treatment regimen. A note made by the TEP (Technical committee stated that protein restriction is less than other metabolic disorders (ACHDNC report). As part of dietary monitoring, regular blood GUAC and creatinine levels as well as plasma amino acids are obtained as frequently as every one to two months. Less frequent monitoring is needed as the individuals get older (Stockler-Ipsiroglu 2014) . As for evidence of treatment efficacy prior to 12 months of age, there are no controlled treatment trials, but available case series suggest better developmental outcomes for those who start treatment earlier. The ACHDNC review concludes that case series suggesting pre-symptomatic or early initiation of treatment is associated with improved neurologic outcomes (ACHDNC review). These outcomes include reduced risk of intellectual disability and a decrease in seizures and movement disorders. There are no quantitative measures of developmental outcomes provided. Table 6 summarizes this data from the ACHDNC. Future Treatments Per ACHDNC review, there are no targeted treatments available. Gene therapy has been tested in a mouse model and was shown to normalized GUAC levels (Khoja)
Availability	*Describe scope of availability and note any limitations. .* Treatment for GAMT deficiency is similar to treatment for other protein metabolism disorders already on the newborn screen like phenylketonuria. Therefore, the expertise to treatment including metabolic dietitians are available at the metabolic clinics at Children's Wisconsin and UW Waisman center. ACHDNC review does note that the treatments of creatine and orthinine are classified as dietary supplements; therefore, there is an increased risk of unknown substances in the manufacturing and distribution. The Association of Creatine Disorders (ACD) patient advocacy group has partnered with a laboratory to make high quality supplements. Sodium benzoate is available through compounding pharmacies. Medical metabolic formula is available through various companies.
Criterion 5: Appropriate follow-up should be available for newborns that have a false positive newborn screen.	

Follow-up for False Positives	*Define the follow-up process.* Consistent with existing Wisconsin NBS practices, the state NBS laboratory at WSLH will communicate the positive GAMT screening result to the primary care provider and the metabolic center designated to engage in confirmatory testing and short term follow-up. Confirmatory testing includes biochemical testing for elevation in GAA and molecular testing of GAMT gene. True positive testing will be started on treatment. False positive NBS, whose numbers should be limited, will receive appropriate counseling related to newborn screening process and the results of the confirmatory testing indicating the patient does not have the condition. Based on the current plan for testing, 10 false positives are expected per year.
Criterion 6: The characteristics of mandated tests in the newborn population should be known, including specificity, sensitivity, and predictive value.	
Screening test(s) to be used	*Description of the high volume method, instrumentation and if available as part of multi-analyte platform.* Determination of guanidinoacetate concentration and guanidinoacetate to creatine ratio in dried blood spots by non-derivatized tandem mass spectrometry. This analysis is performed in tandem with the Revvity NeoBase 2 method for acylcarnitine and amino acid measurement. This method consists of extraction of metabolites and 1 hour incubation before analysis using the QSight MD 210 mass spectrometer. Guanidinoacetate concentration and guanidinoacetate to creatine ratio will be used to determine the screening status
Modality of Screening	*Dried blood spot, physical or physiologic assessment, other* Dried Blood Spot
Does the screening algorithm include a second tier test? If so, what type of test and availability?	*Dried blood spot, physical or physiologic assessment, other* No
Clinical Validation	*Location, duration, size, preliminary results of past/ongoing pilot study for clinical validation, positive predictive value, false positive rate, analytical specificity, sensitivity.* Four pilot studies have been performed in Australia, Canada, New York, and Utah.See below for summary of results.

Analytic Validation	*Limit of detection/quantitation, detection rate, reportable range of test results, reference range. Include regulatory status of test, information about reference samples and controls required for testing and availability of or potential for external quality assurance system, e.g., QC and PT for both screening and confirmatory tests.* Method validation is currently underway. This method is a laboratory developed test that is not FDA approved. Lower limit of quantitation is 1.21 µM. The upper limit of quantitation is 34.30 µM. A population study of 4,175 newborn screening samples was performed. The mean guanidinoacetate concentration was 2.310 with a standard deviation of 0.6279 µM. The mean guanidinoacetate to creatine ratio was 0.005465 with a standard deviation of .002662. Prospective reference ranges were generated using nonparametric approaches. Prospective screen borderline reference ranges were set to 4 µM for guanidinoacetate and 0.015 for guanidinoacetate to creatine ratio, representing the 99th percentiles for each result. Prospective screen positive reference ranges were set to 4.3 µM for guanidinoacetate and 0.018 for guanidinoacetate to creatine ratio, representing the 99.5th percentiles for each result. A prospective screening algorithm was created. Screen borderline was prospectively defined as a sample that is above both borderline cutoffs, but below at least one positive cutoff. Screen positive was prospectively defined as a sample that is above both positive cutoffs. Using these definitions, the sample population of 4,175 samples produced 2 screen borderline results and no screen positive results. Reference materials including linearity material is available through the CDC. High and low concentration control materials are available commercially through Revvity (Part number: 4413-0010). Additional quality control and proficiency testing materials is included with the current NBS lab enrollment in the Newborn Screening Quality Assurance Program.
Potential Secondary Findings	*May other disorders be identified by the screening test for the nominated condition?* ☐ Yes ☒ No ***If yes:*** • *How should that identification be handled—should those screening results be disclosed to the physicians or parents?* • *Would that disorder(s) meet the outlined criteria?* ☐ Yes ☐ No o *If yes, please prepare a separate nomination form for the secondary disorder(s)* o *If no, what criteria does it not meet?*

Summary of Population-based Pilot Study(ies)

Location of Prospective Pilot	Study 1: Victoria, Australia Study 2: British Columbia, Canada Study 3: Utah, USA Study 4: New York, USA
Number of Newborns Screened	Study 1: 771,345 Study 2: 135,372 Study 3: 273,902 (195,425 derivatized method; 78,477 non-derivatized method) Study 4: 537,408

Number of Positive Results	*Positive by primary test versus 2nd tier test if applicable.* Study 1: 3 Study 2: 259 positve by first-tier, 3 positive by second-tier Study 3: 366 positive by first-tier (365 derivatized method, 1 non-derivatized method), 3 screen positive by second-tier Study 4: 4,178 positive by first-tier. 23 positive by second-tier
False Positive Rate; False Negative Rate (if known)	*False positive by primary test versus 2nd tier test if applicable.* Study 1: 3 false positives Study 2: 3 false positives Study 3: 2 false positives by second-tier test Study 4: 22 false positives by second-tier test
Number of Infants Confirmed with Diagnosis	*How are diagnosis confirmed [clinical, biochemical, molecular]?* Study 1: 0 Study 2: 0 Study 3: 1, confirmed by plasma/urine guanidinoacetate and creatine measurement and DNA sequencing. Study 4: 1, confirmed by DNA sequencing Confirmatory testing can include blood and urine testing to demonstrate elevated GUAC as well as genetic testing to support the diagnosis (Mercimek-Andrews). Magnetic resonance spectroscopy can identify low creatinine levels and elevated GUAC in the brain (ACHDNC) The American College of Medical Genetics and Genomics has completed a technical standards and guidelines for the laboratory diagnosis of creatine deficiency syndromes including GAMT deficiency (Stöckler-Ipsiroglu) . This report notes that typically GUAC elevations are significantly increased although levels can vary particularly with supplementation of creatine or ornithine (Sinclair GB). The report recommends, in general, follow up DNA testing to confirm biochemical findings. Molecular testing typically finds detectable pathogenic variants with sequence analysis of GAMT, listing approximately 100% detection by sequencing (Mercimek-Andrews).
Criterion 7: If a new sample collection system is needed to add a disorder, reliability and timeliness of sample collection must be demonstrated.	
Is this a new sample collection system?	*If yes, demonstrate reliability and timeliness of sample collection process, including data collection, analysis, and reporting of new results.* No
Criterion 8: Before a test is added to the panel, the details of reporting, follow-up, and management must be completely delineated, including development of standard instructions, identification of consultants, and identification of appropriate referral centers throughout the state/region.	
Considerations of Screening and Diagnostic Testing	*False positives, carrier detection, invasiveness of method, other* The described screening method is multiplexed with fatty acid oxidation disorders, aminoacidopathies, and organic acidurias currently on the Wisconsin newborn screening panel using the same dried blood spot currently used. In the event of a positive screen, the laboratory will contact the primary care provider, as well as appropriate metabolic consultants. Confirmatory testing will be coordinated between these healthcare providers. .

Is test FDA cleared/approved	*Include availability of information, sole source manufacturer, etc.* No
List all CLIA or CAP certified labs offering testing in the US	*Link to GeneTests, and Genetic Test Reference if applicable.* GTR Link: https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=C0574080[DISCUI]
Follow-up and management process	*Development of standard instructions, identification of consultants, identification of appropriate referral centers throughout the state/region, follow-up for results, management of ongoing care, education, and outreach.* Follow up and management processes would closely resemble practices for other inborn errors of metabolism on the Wisconsin newborn screen. Positive newborn screens would be reported to the infant's primary care physician (PCP) and metabolic consultants at Children's Wisconsin or UW Waisman Center. The metabolic consultants can direct PCP to complete confirmatory testing. If positive, patient can establish care in the metabolic clinic and start treatment. False positives can be counseled on their screening result. The metabolic center can provide ongoing metabolic management including patient education.
Criterion 9: Recommendations and decisions should include consideration of the costs of the screening test, confirmatory testing, accompanying treatment, counseling, and the consequences of false positives. The mechanism of funding those costs should be identified. Expertise in economic factors should be available to those responsible for recommendations and decisions.	
Screening test	Guanidinoacetate concentration and guanidinoacetate to creatine ratio. In order to measure guanidinoacetate and creatine, there is a need to replace the current MSMS multiplex assay with a commercially available assay. This change will require an estimated $10 increase per infant.
Confirmatory testing	Cost typically covered by medical insurance
Treatment	Cost of treatment that would be incurred by the state would include the cost of medical formula and supplements. Current recommendations for diet is restriction of protein intake to the Dietary Reference Intakes (DRI). This would not require that does not arginine-free formula, but may need a carbohydrate/fat formula (Duocal or prophree). Currrent cost of this formula is $140/case = $23/can; 1968kcal/can. Supplementation of creatine and ornithine based on current recommendations would vary by age as it is dose mg/kg. Estimates for supplementation in infancy is ~ $275 per year to ~$1900 per year for an adult. See table for calculations.
Counseling	Counseling can be performed at any of the regional centers
False positives	False positives would result in unnecessary confirmatory testing
Mechanism of funding	NBS for GAMT would need to be funded through the NBS fee.

Key References to support each criterion. Please list and attach as PDF(s). If mailing, include hard copies.	
#	**Criterion 1**
	Advisory Committee on Heritable Disorders in Newborn and Children. (06/2/2022) "Evidence-based Review of Newborn Screening for Guanidinoacetate Methyltransferase (GAMT) Deficiency: Final Report" Maternal and Child Health Bureau Ellery SJ, Della Gatta PA, Bruce CR, Kowalski GM, Davies-Tuck M, Mockler JC, et al. Creatine biosynthesis and transport by the term human placenta. Placenta. 2017 Apr;52:86–93..
	Mercimek-Andrews S, Salomons GS. Creatine Deficiency Disorders. 2009 Jan 15 [Updated 2022 Feb 10]. In: Adam MP, Mirzaa GM, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. In. Available from: https://www.ncbi.nlm.nih.gov/books/
	Criterion 2
	Mercimek-Andrews S, Salomons GS. Creatine Deficiency Disorders. 2009 Jan 15 [Updated 2022 Feb 10]. In: Adam MP, Mirzaa GM, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. In. Available from: https://www.ncbi.nlm.nih.gov/books/ Hart K, Rohrwasser A, Wallis H, Golsan H, Shao J, Anderson T, et al. Prospective identification by neonatal screening of patients with guanidinoacetate methyltransferase deficiency. Molecular Genetics and Metabolism. 2021 Sep;134(1–2):60–4. Mercimek-Andrews S, Sinclair G, van Dooren SJM, et al. Guanidinoacetate methyltransferase deficiency: First steps to newborn screening for a treatable neurometabolic disease. Molecular Genetics and Metabolism. 2012;107(3):433-437.12. Desroches CL, Patel J, Wang P, et al. Carrier frequency of guanidinoacetate methyltransferase deficiency in the general population by functional characterization of missense variants in the GAMT gene. Molecular Genetics and Genomics. 2015;290(6):2163-2171..
	Criterion 3
	Mercimek-Andrews S, Salomons GS. Creatine Deficiency Disorders. 2009 Jan 15 [Updated 2022 Feb 10]. In: Adam MP, Mirzaa GM, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. In. Available from: https://www.ncbi.nlm.nih.gov/books/.

	4Advisory Committee on Heritable Disorders in Newborn and Children. (06/2/2022) "Evidence-based Review of Newborn Screening for Guanidinoacetate Methyltransferase (GAMT) Deficiency: Final Report" Maternal and Child Health Bureau. Khaikin Y, Sidky S, Abdenur J, Anastasi A, Ballhausen D, Buoni S, et al. Treatment outcome of twenty-two patients with guanidinoacetate methyltransferase deficiency: An international retrospective cohort study. European Journal of Paediatric Neurology. 2018 May;22(3):369–79. Mercimek-Mahmutoglu S, Ndika J, Kanhai W, et al. Thirteen New Patients with Guanidinoacetate Methyltransferase Deficiency and Functional Characterization of Nineteen Novel Missense Variants in the GAMT Gene. Human Mutation. 2014;35(4):462-469. Mercimek-Mahmutoglu S, Pop A, Kanhai W, et al. A pilot study to estimate incidence of guanidinoacetate methyltransferase deficiency in newborns by direct sequencing of the GAMT gene. Gene. 2016;575(1):127-131 Yıldız Y, Ardıçlı D, Göçmen R, Yalnızoğlu D, Topçu M, Coşkun T, et al. Electro-clinical features and long-term outcomes in guanidinoacetate methyltransferase (GAMT) deficiency. European Journal of Paediatric Neurology. 2024 Mar;49:66–7 Dhar SU, Scaglia F, Li FY, Smith L, Barshop BA, Eng CM, et al. Expanded clinical and molecular spectrum of guanidinoacetate methyltransferase (GAMT) deficiency. Molecular Genetics and Metabolism. 2009 Jan;96(1):38–43. Schulze A, Hoffmann GF, Bachert P, Kirsch S, Salomons GS, Verhoeven NM, et al. Presymptomatic treatment of neonatal guanidinoacetate methyltransferase deficiency. Neurology. 2006 Aug 22;67(4):719–21. DeLuca, JM and SM McCandless. (05/12/2022) "Recommendations to the ACHDNC for Newborn Screening for Guanidinoacetate methyltransferase GAMT deficiency." Advisory Committee on Heritable Disorders in Newborn and Children meeting. www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/meetings/recommendations-gamt-deficiency-delua-mccandless.pdf. Farshidi S, Gaphari SR, Farokhi B, Hooshmand M. Creatine deficiency syndrome: Case report. Journal of Inherited Metabolic Disease. 2011;34:S125. Holeček M. Side effects of amino acid supplements. Physiol Res. 2022 Mar 25;71(1):29-45. doi: 10.33549/physiolres.934790. Epub 2022 Jan 19. PMID: 35043647; PMCID: PMC8997670. Grimble GK. Adverse gastrointestinal effects of arginine and related amino acids. J Nutr. 2007 Jun;137(6 Suppl 2):1693S-1701S. doi: 10.1093/jn/137.6.1693S. PMID: 17513449.
	Criterion 4
	Advisory Committee on Heritable Disorders in Newborn and Children. (06/2/2022) "Evidence-based Review of Newborn Screening for Guanidinoacetate Methyltransferase (GAMT) Deficiency: Final Report" Maternal and Child Health Bureau. Stöckler-Ipsiroglu S, Braissant O, Schulze A. Disorders of Creatine Metabolism. In: Physician's Guide to the Diagnosis, Treatment, and Follow-Up of Inherited Metabolic Diseases.2022:235-249.
	Khoja S, Lambert J, Nitzahn M, Eliav A, Zhang Y, Tamboline M, et al. Gene therapy for guanidinoacetate methyltransferase deficiency restores cerebral and myocardial creatine while resolving behavioral abnormalities. Molecular Therapy - Methods & Clinical Development. 2022 Jun;25:278–96
	Criterion 5
	Criterion 6
	Mercimek-Andrews S, Salomons GS. Creatine Deficiency Disorders. 2009 Jan 15 [Updated 2022 Feb 10]. In: Adam MP, Mirzaa GM, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. In. Available from: https://www.ncbi.nlm.nih.gov/books/ Advisory Committee on Heritable Disorders in Newborn and Children. (06/2/2022) "Evidence-based Review of Newborn Screening for Guanidinoacetate Methyltransferase (GAMT) Deficiency: Final Report" Maternal and Child Health Bureau.

	Sinclair GB, van Karnebeek CDM, Ester M, Boyd F, Nelson T, Stockler-Ipsiroglu S, et al. A three-tier algorithm for guanidinoacetate methyltransferase (GAMT) deficiency newborn screening. Molecular Genetics and Metabolism. 2016 Jul;118(3):173–7. Stöckler-Ipsiroglu S, Braissant O, Schulze A. Disorders of Creatine Metabolism. In: Physician's Guide to the Diagnosis, Treatment, and Follow-Up of Inherited Metabolic Diseases.2022:235-249.
	Criterion 7
	Criterion 8
	Criterion 9
	Cost estimates per Jess Kopesky, RD.

Additional Co-sponsoring Organizations

CO-SPONSORING ORGANIZATION #2	
Name	Organization
Affiliation (i.e., health professional, researcher, clinician, advocate)	
Address	
Email Address	Telephone Number

CO-SPONSORING ORGANIZATION #3	
Name	Organization
Affiliation (i.e., health professional, researcher, clinician, advocate)	
Address	
Email Address	Telephone Number

CO-SPONSORING ORGANIZATION #4	
Name	Organization
Affiliation (i.e., health professional, researcher, clinician, advocate)	
Address	
Email Address	Telephone Number

CO-SPONSORING ORGANIZATION #5	
Name	Organization
Affiliation (i.e., health professional, researcher, clinician, advocate)	
Address	
Email Address	Telephone Number

Submission Checklist	
☐	Nomination form
☐	Conflict of Interest Forms completed by Nominator and all Co-Sponsoring Organizations
☐	PDF(s) or hard copies of references

Contact information of Nominator:

Submit Nominations to: DHSWICongenitalDisorders@wisconsin.gov

Or mail to:

WI Division of Public Health
Newborn Screening Program
1 West Wilson Street – Room 233
Madison, WI 53703