

Resource Guide For Health Care Providers

Infant Formulas and Child/Adult Medical Foods

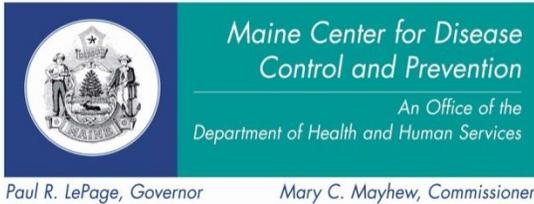


*Department of Health
and Human Services*

*Maine People Living
Safe, Healthy and Productive Lives*

Paul R. LePage, Governor

Mary C. Mayhew, Commissioner



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Dear Health Care Provider,

This letter is meant to inform you of some important changes to the Maine WIC Nutrition Program, which affects you and your patients.

The USDA Food and Nutrition Service Interim Rule 7 CFR Part 246 implements the first comprehensive revision to the WIC food benefits since 1980 and was developed to reflect current nutrition science and dietary recommendations. The USDA reminds us that WIC provides supplemental foods designed to address the nutritional needs of low-income pregnant, breastfeeding and non-breastfeeding postpartum women and infants and children up to 5 years of age. The interim rule states, "WIC was never intended to be a primary source of food, nor of general food assistance... The nutrition education provided by WIC enables participants to make informed decisions in choosing foods that, together with the supplemental foods contained in the WIC food packages, can meet their total dietary needs. The intent is to help participants continue healthful dietary practices after leaving the program."

USDA rules specify specific food benefits in seven "food packages," with each food package addressing the nutritional needs of a category of participants (infants, children, women). Food Packages I, II and III are the ones that impact WIC's provision of standard as well as medical formulas:

- Infants from birth to 6 months receive WIC supplemental foods as specified in Food Package I.
- Infants from 6 months to 1 year receive WIC supplemental foods as specified in Food Package II.
- Women, Infants and Children **with a qualifying medical condition** receive WIC supplemental foods as specified in Food Package III.

WIC eligible medical foods in Food Package III must serve the purpose of a food, meal or diet and provide a source of calories and one or more nutrients. These foods can only be provided when a licensed medical provider with prescriptive privileges in Maine authorizes their use. Close medical supervision is essential for individuals receiving these special medical foods and the responsibility for medical oversight and instruction lies with the participant's health care provider.

WIC participants needing a medical formula who have MaineCare insurance coverage may have the cost of the formula covered by MaineCare if the patient needs:

- An elemental formula
- A metabolic formula
- A tube feeding formula

For WIC participants who also have MaineCare insurance, the Maine WIC Nutrition Program will provide one month of formula vouchers when a medical formula prescription is initiated, allowing for a smooth transition through MaineCare's Prior Authorization process. A completed WIC prescription form is required for prior authorization for the family to receive the medical formula through MaineCare. WIC will continue to provide medical formula benefits, if necessary, for families experiencing a delay in MaineCare's Prior Authorization process. **Please be aware that the Maine WIC Nutrition Program will continue to provide medical formulas to WIC-enrolled participants that are not MaineCare eligible.**

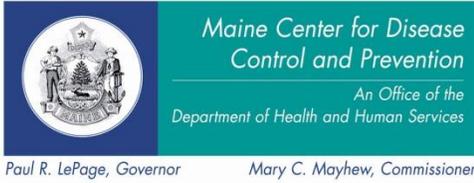
MaineCare members that also participate in WIC will continue to receive all other WIC services including nutrition counseling and WIC food benefits appropriate to their nutritional and medical needs. Medical documentation is required for the prescription of any medical formula or medical food as well as all regular foods for those participants with special health needs. The local WIC clinic must have written documentation of the:

- qualifying condition, including diagnosis
- amount needed per day
- length of time the medical formula/medical food will be required
- name of the authorized formula or supplemental food

The information required documenting medical need for the prescription of a medical formula or food is found on the *Medical Documentation for WIC Medical Formula or Medical Food/MaineCare Prior Authorization Form*. These forms can be obtained from any local WIC office, the State WIC Agency office or on the Maine CDC WIC Nutrition Program's website. According to the Food and Nutrition Service rules, documentation of a WIC participant's medical need for a medical formula must be kept on file at the WIC office.

The Food and Nutrition Service Rules and Regulations identify specific conditions that qualify for exempt medical/prescription formulas or foods. In infants 0 to 12 months of age these conditions include: premature birth, low birth weight, failure to thrive, inborn errors of metabolism and metabolic disorders, gastrointestinal disorders, malabsorption syndromes, immune system disorders, severe food allergies that require an elemental formula, and life threatening disorders, diseases and medical conditions that impair the infant's ability to utilize the nutrients. ***Food Package III is not authorized for infants diagnosed with formula intolerance or intolerance to lactose, sucrose, or milk or soy protein. Colic or fussiness are not medical conditions that qualify as justification for medical prescription formulas.***

The Maine WIC Nutrition Program is required by USDA to have a sole-source standard infant formula contract agreement. Currently, Enfamil Newborn, Enfamil Infant, Enfamil ProSobee and Enfamil Gentlease are the standard contract infant formulas for Maine. Non-contract soy or cow's milk protein formulas do not qualify as medically exempt prescription formulas.



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To Community Health Care Providers,

The Maine CDC WIC Nutrition Program would like to share with you the following information regarding medical formula and our newest contract formula, Enfamil PREMIUM® Newborn.

Infants Needing Medical Formula at time of Hospital Discharge

- WIC recommends that babies being discharged on any kind of **medical formula** item be given a minimum of a **3 business day** supply at discharge. If a weekend is involved, add the weekend days to the supply.
- WIC does not have medical formula on hand at its clinics. It is unlikely that a family could receive medical formula from WIC the day they are discharged from the hospital. Many medical formulas, such as nursettes and elemental products, must be ordered directly from the manufacturer.
- WIC has had many instances of babies going home with very little formula and the parent(s)/guardian(s) are told to “call WIC to get more.”

Enfamil PREMIUM® Newborn

- **Beginning 1/1/2013**, the Maine CDC WIC Nutrition Program began to provide Enfamil PREMIUM Newborn powder upon request from parents or health care providers for infants enrolled in the program.
- Enfamil Newborn powder is available to infants from birth through 3 months of age
- Partially breastfed babies (those who are breastfed most feedings) may receive up to one can of Enfamil PREMIUM® Newborn in the first 30 days of life to meet supplementation needs and to encourage establishment of full breastfeeding.
- Powdered Enfamil PREMIUM® Newborn is provided in 12.5 ounce cans; can yield = 90 ounces
- WIC maximum monthly issuance of Enfamil PREMIUM® Newborn is 9 cans per month for nonbreastfed babies as well as babies receiving minimal amounts of breastmilk.
- Babies who continue to breastfeed beyond 1 month of age and need continued supplementation can receive a maximum of 4 cans of Enfamil PREMIUM® Newborn from 1 through 3 months of age.
- Infants receiving Enfamil PREMIUM® Newborn powder through the WIC Program will be transitioned to Enfamil PREMIUM® Infant formula at the age of 4 months

Please call 1-800-437-9300 or send an email to wic.maine@maine.gov if you have any questions concerning this addition to the Maine CDC WIC formulary.

Medical Conditions That May Require Prescription of Medical Formula

Section:

Preterm Birth or Low Birth Weight



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PRETERM OR LOW BIRTH WEIGHT

Preterm and low birth weight infants are frequently discharged from the hospital growth retarded and show reduced growth throughout childhood. Considerable attention has been directed toward improving the nutrition of these infants while they are in the hospital, including the development of special nutrient-enriched formulas and multinutrient fortifiers, which can be added to human milk. Low birth weight is defined as an infant weighing less than 5 lbs 8 oz or 2500 gms. Preterm birth is any infant born less than 37 weeks gestational age.

Extremely preterm infants frequently experience impaired neurodevelopment, and poor growth is associated with impaired neurodevelopment. Long-term outcome data now show the neonatal period to be a critical one in terms of the effects of nutrition on later health and developmental outcomes.

Infants born with low birth weight, which were breastfed, had significantly higher developmental scores at 9 months of age than did formula fed infants.¹

Preterm infants are commonly discharged weighing little more than half the appropriate weight for a term infant at the equivalent postmenstrual age. Of more concern, more than 30% of these infants remained below the tenth percentile for weight at age 18 months, and more than 20% were below the tenth percentile at 7 to 8 year follow-up. The use of a nutrient-enriched formula in preterm infants has been associated with improved short-term growth. The American Academy of Pediatrics recognized the importance of nutrient enriched formula in the first 9 months in these infants. The use of preterm formulas to a postnatal age of 9 months results in greater linear growth and weight gain.

- 1) Infants born small for gestational age fare better developmentally if fed human breast milk. Every effort should be made to support breast feeding in these infants.²
- 2) In the case when a mother is unable to exclusively breast feed, preterm or low birth weight infants served by the Special Supplemental Nutrition Program for Women, Infants and Children (WIC) should receive a prescription for Enfacare or Neosure (22 calorie formulas) noting the qualifying diagnosis (prematurity or low birth weight) and the duration of treatment (9 months post natal age).³
- 3) Human milk fortifiers should only be used in the NICU setting. Since fortifiers are not readily available outside of the hospital setting, when premature infants are discharged, fortification of human milk may be accomplished with the use of powdered transition formula (Enfacare, Neosure) if necessary.

¹ Morley, R et al. Neurodevelopment in Children Born Small for Gestational Age: A Randomized Trial of Nutrient-Enriched Versus Standard Formula and Comparison with a Reference Breastfed Group. *Pediatrics*. 2004;Vol 113, No3:515-521.

² Morley, R. et al. Neurodevelopment in children born small for gestational age: a randomized trial of nutrient-enriched

³ Lucas, A., et. Al. Randomized trial of nutrient-enriched formula versus standard formula for post-discharge preterm infants. *Pediatrics*. 2001: Vol. 108, 703-711.

Medical Conditions That May Require Prescription of Medical Formula

Section:

**Gastroesophageal
Reflux**



GASTROESOPHAGEAL REFLUX ⁴

Gastroesophageal reflux (GER), defined as passage of gastric contents into the esophagus, and GER disease (GERD), defined as symptoms or complications of GER, are common pediatric problems encountered by both primary and specialty medical providers. Clinical manifestations of GERD in children include vomiting, poor weight gain, dysphagia, abdominal or substernal pain, esophagitis and respiratory disorders. During infancy GER is common and is most often manifest as vomiting. Recurrent vomiting occurs in 50% of infants in the first three months of life, in 67% of four month old infants, and in 5% of 10 to 12 month old infants. Vomiting resolves spontaneously in nearly all of these infants. Parents do not usually perceive vomiting as a problem when it occurs no more often than once daily, but they are more likely to be concerned when vomiting is more frequent, the volume of vomitus is large, or when the infant cries frequently with vomiting.

A small minority of infants develop GERD with symptoms including anorexia, dysphagia (difficulty swallowing), odynophagia (painful swallowing), arching of the back during feedings, irritability, hematemesis, anemia or failure to thrive. GER is one of the causes of apparent life-threatening events (ALTE) in infants and has been associated with chronic respiratory disorders including reactive airways disease, recurrent stridor, chronic cough and recurrent pneumonia in infants.

1- The Infant with Recurrent Vomiting:

In most infants, symptoms of GER do not decrease when there is a change from one milk formula to another. However, a subset of infants with vomiting has cow's milk protein allergy. In these infants, elimination of cow's milk protein from the diet resulted in decreased vomiting within 24 hours. Two successive, blind challenges corroborated the diagnosis of cow's milk protein allergy induced vomiting in infants. There is, therefore, evidence to support a one to two week trial of a hypoallergenic formula in formula fed infants with vomiting.

2- Infants with Recurrent Vomiting Unresponsive to Hypoallergenic Formula:

Milk-thickening agents do not improve reflux index scores but do decrease the number of episodes of vomiting. Use of thickened formulas compared with standard formula significantly increased the percentage of infants with no regurgitation, slightly reduced the number of episodes of regurgitation and vomiting per day (assessed jointly or separately), and increased weight gain per day; it had no effect on the reflux index, number of acid gastroesophageal reflux episodes per hour, or number of reflux episodes lasting >5 minutes but significantly reduced the duration of the longest reflux episode of pH <4. No definitive data showed that one particular thickening agent is more effective than another.⁵ The primary care provider should complete a medical documentation form for WIC and include instructions for mixing cereal with formula for the purpose of thickening.⁶ Some parents may have difficulty adding the appropriate amount of cereal and mixing the thickened formula. In these special cases a pre-prepared starch added formula may be substituted.

3- The Infant with Recurrent Vomiting and Poor Weight Gain, Irritability, Apnea or Apparent Life-threatening Events (ALTE), Asthma or Pneumonia:

Currently there is insufficient pediatric evidence to establish the optimal medical therapy in patients with significant complications of GER disease. Infants who are underweight due to GERD may gain weight when the caloric density of their feedings is increased. Antireflux surgery is considered in patients with persistent asthma and recurrent pneumonia, patients requiring prolonged medical therapy and patients

⁴ Pediatric GE Reflux Clinical Practice Guidelines. *Journal of Pediatric Gastroenterology and Nutrition*, 2001, Vol. 32, Suppl. 2. S1-S31

⁵ [Horvath A](#), [Dziechciarz P](#), [Szajewska H](#). The effect of thickened-feed interventions on gastroesophageal reflux in infants: systematic review and meta-analysis of randomized, controlled trials. *Pediatrics*. 2008 Vol 122, No 6:e1268-77.

⁶ Pediatric GE Reflux Clinical Practice Guidelines. *Journal of Pediatric Gastroenterology and Nutrition*, 2001, Vol. 32, Suppl. 2. S7-S8

with nonrespiratory complications of GER such as persistent vomiting, vomiting with growth retardation and severe esophagitis.

Formula Thickening Recipe

1 Tablespoon rice cereal added to 2 ounces formula = 27 calories/ounce

Medical Conditions That May Require Prescription of Medical Formula

Section:

Use of Soy Formulas



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Use of Soy Formulas

WIC contract soy formulas can be provided through the WIC office without prescription. According to the American Academy of Pediatrics Policy on Soy Protein-based Formulas: Recommendations for use in Infant Feeding, the Committee on Nutrition recommended the following:⁷

- 1- Isolated soy protein-based formula has no advantage over cow milk protein-based formula as a supplement for the breastfed infant.
- 2- Soy protein based formulas are lactose free and thus are appropriate for use in infants with galactosemia and the very rare hereditary lactase deficiency.
- 3- Isolated soy protein formula may be suitable for parents seeking a vegetarian diet for their term infant.
- 4- Previously well infants with acute gastroenteritis can usually be managed after rehydration with continued use of breast milk or cow milk based formula. WIC contract soy protein lactose free formula may be indicated when a young infant (typically under 3 months of age) has severe recalcitrant gastroenteritis.⁸ Some infants with severe gastroenteritis may require evaluation by a pediatric gastroenterologist and management with an elemental formula.
- 5- Congenital lactase deficiency is an extremely rare disorder manifested by persistent diarrhea. When this disorder is considered, the child should be promptly referred to a pediatric gastroenterologist.
- 6- Soy protein formulas do not have a role in management of cow's milk allergic infants.
- 7- Soy protein formulas have no proven value in the management of infantile colic.
- 8- Soy protein formulas are not designed or recommended for preterm infants less than 9 months postnatal age due to the development of significant osteopenia in preterm infants fed soy formula. Cow milk protein-based formulas designed for preterm infants are clearly superior to soy protein-based formula for preterm infants.
- 9- There is **no conclusive evidence** that soy protein formula adversely affects human development, reproduction or endocrine function.⁹
- 10- WIC Programs may authorize non-contract brand infant formulas without medical documentation in order to meet the requirements of family's religious eating patterns. Since Nestle Good Start Soy Plus is certified as both Kosher and Halal, this contract formula may be considered for families with these religious eating preferences. Likewise, WIC contract soy formula may be substituted for cow's milk protein formula based on family preference.

⁷ Soy Protein-Based Formulas: Recommendations for Use in Infant Feedings. American Academy of Pediatrics Committee on Nutrition. Pediatrics. 1998:Vol 101. No 1:148-153.

⁸ AAP Committee on Nutrition. Lactose Intolerance in Infants, Children and Adolescents. Pediatrics. 2006:Vol 118. No 3:1279-1286.

⁹ Bhatia, J, Greer, F and the AAP Committee on Nutrition. Use of Soy Protein-Based Formulas in Infant Feeding. Pediatrics. 2008:Vol 121, No5:1062-1068.

Medical Conditions That May Require Prescription of Medical Formula

Section:

Use of Hypoallergenic Infant Formulas



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USE OF HYPOALLERGENIC INFANT FORMULAS:

The AAP Committee on Nutrition and Section on Allergy and Immunology clinical report published in Pediatrics in January, 2008, reviewed the impact of various foods in infancy that may precipitate allergic disease. The report found, "The documented benefits of nutritional intervention that may prevent or delay the onset of atopic disease are largely limited to infants at high risk of developing allergy (ie, infants with at least 1 first-degree relative [parent or sibling] with allergic disease). Current evidence does not support a major role for maternal dietary restrictions during pregnancy or lactation. There is evidence that breastfeeding for at least 4 months, compared with feeding formula made with intact cow milk protein, prevents or delays the occurrence of atopic dermatitis, cow milk allergy and wheezing in early childhood. In studies of infants at high risk of atopy and who are not exclusively breastfed for 4 to 6 months, there is modest evidence that the onset of atopic disease may be delayed or prevented by the use of hydrolyzed formulas compared with formula made with intact cow milk protein, particularly for atopic dermatitis. Comparative studies of the various hydrolyzed formulas also indicate that not all formulas have the same protective benefit. There is also little evidence that delaying the timing of the introduction of complementary foods beyond 4 to 6 months of age prevents the occurrence of atopic disease. At present, there are insufficient data to document a protective effect of any dietary intervention beyond 4 to 6 months of age for the development of atopic disease."¹⁰

Elsewhere, it has been reported that 2% to 5% of infants manifest a food allergy in the first 1 to 3 months of life, which typically resolves by 1 year of age.¹¹ Guidelines for use of protein hydrolysate or amino acid-based infant formulas for allergic indications are proposed below. These recommendations result from a literature and experience review by Drs. Bancroft and Chiltonczyk on July 13, 2009.

Proposal:

Most, but not all, infants whose diet is restricted to extensively hydrolyzed- or amino acid-based formulas are assigned these restrictions in response to allergic conditions. For those children, we recommend the following approach:

Patient < 1 year of age

An **extensively hydrolyzed formula** is indicated for:

- severe eczema
- bloody stools due to allergic enterocolitis
- anaphylaxis triggered by exposure to cow's milk or soy proteins
- elevated IgE RAST test to cow's milk and soy
- consultative recommendation of an allergist or pediatric gastroenterologist
- asthma in the first year of life

An **amino acid-based formula** is indicated for:

- preexisting diagnosis of Eosinophilic Esophagitis or Eosinophilic Enteropathy
- biopsy-confirmed Eosinophilic Esophagitis or Eosinophilic Enteropathy
- documented anaphylaxis (pending consultation with allergist)
- consultative recommendation of an allergist or pediatric gastroenterologist

WIC will provide the first month of **elemental formula**, but MaineCare Prior Authorization for **continued elemental formula** prescription by a primary care provider must be accompanied by a consultation with a pediatric gastroenterologist or pediatric allergist as appropriate to the condition (consultation may initially be by

¹⁰ The AAP Committee on Nutrition and Section on Allergy and Immunology. Effects of Early Nutritional Interventions on the Development of Atopic Disease in Infants and Children: The Role of Maternal Dietary Restriction, Breastfeeding, Timing of Introduction of Complementary Foods, and Hydrolyzed Formulas. Pediatrics. 2008;Vol 121, No1:183-191.

¹¹ AAP Committee on Nutrition. Lactose Intolerance in Infants, Children and Adolescents. Pediatrics. 2006;Vol 118. No 3:1279-1286.

telephone). Special formula requirements for the above indications, begun in the first year of life may be continued by the primary care provider up to 1 year of age. Continuation of a special formula beyond 1 year of age, for the above indications, requires reconsultation with a pediatric allergist or pediatric gastroenterologist.

Patient > 1 year of age

Consultation with an allergist or pediatric gastroenterologist is required to initiate either an extensively hydrolyzed formula or amino acid-based formula after 1 year of age.

Any child assigned to an extensively hydrolyzed or amino acid-based formula beyond 1 year of age should have reconsultation with an allergist or pediatric gastroenterologist every 12-18 months as a requirement for continuation of the formula.

Definitions:

Atopic disease: Clinical disease characterized by atopy; typically refers to atopic dermatitis, asthma, allergic rhinitis, and food allergy. This report will be limited to the discussion of conditions for which substantial information is available in the medical literature.

Atopic dermatitis (eczema): A pruritic, chronic inflammatory skin disease that commonly presents during early childhood and is often associated with a personal or family history of other atopic diseases.

Asthma: An allergic-mediated response in the bronchial airways that is verified by the variation in lung function (measured by spirometry) either spontaneously or after bronchodilating drugs.

Cow milk allergy: An immunologically mediated hypersensitivity reaction to cow milk, including IgE mediated and/or non—IgE-mediated allergic reactions.

Food allergy: An immunologically mediated hypersensitivity reaction to any food, including IgE-mediated and/or non—IgE-mediated allergic reactions.

1. At the present time, there is a lack of evidence that maternal dietary restrictions during pregnancy play a significant role in the prevention of atopic disease in infants. Similarly, antigen avoidance during lactation does not prevent atopic disease, with the possible exception of atopic eczema, although more data are needed to substantiate this conclusion.
2. For infants at high risk of developing atopic disease, there is evidence that **exclusive** breastfeeding for at least 4 months compared with feeding intact cow milk protein formula decreases the cumulative incidence of atopic dermatitis and cow milk allergy in the first 2 years of life.
3. There is evidence that **exclusive** breastfeeding for at least 3 months protects against wheezing in early life. However, in infants at risk of developing atopic disease, the current evidence that exclusive breastfeeding protects against allergic asthma occurring beyond 6 years of age is not convincing.
4. In studies of infants at high risk of developing atopic disease who are not breastfed exclusively for 4 to 6 months or are formula fed, there is modest evidence that atopic dermatitis may be delayed or prevented by the use of extensively or partially hydrolyzed formulas, compared with cow milk formula, in early childhood. Extensively hydrolyzed (protein hydrolysate) formulas may be more effective than partially hydrolyzed in the prevention of atopic disease. In addition, more research is needed to determine whether these benefits extend into late childhood and adolescence. To date, the use of amino acid-based formulas for atopy prevention has not been studied.
5. There is no convincing evidence for the use of soy protein-based infant formula for the purpose of allergy prevention.
6. A subset of infants with vomiting has cow's milk protein allergy. In these infants, elimination of cow's milk protein from the diet resulted in decreased vomiting within 24 hours. Two successive, blind challenges corroborated the diagnosis of cow's milk protein allergy induced vomiting in infants. There is, therefore, evidence to support a one to two week trial of a hypoallergenic (protein hydrolysate) formula in formula fed infants with vomiting.

Medical Conditions That May Require Prescription of Medical Formula

Section:

Failure to Thrive Congenital Heart or Renal Disease Infants with Malabsorption



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Mary C. Mayhew, Commissioner

FAILURE TO THRIVE (FTT)

Definition¹²: Traditionally, FTT was characterized as “organic failure to thrive” in which the child’s growth failure was ascribed to a major medical illness, and “nonorganic failure to thrive” which was attributed primarily to psychological neglect or “maternal deprivation”. We now recognize that in all cases of “nonorganic” FTT and in many cases of “organic” FTT, the cause of growth failure is malnutrition, whether primary or secondary. Malnutrition not only jeopardizes the child’s growth but also impairs the child’s immune system and contributes to concurrent and long-term deficits in development and behavior. Management of failure to thrive includes an assessment of and therapy for malnutrition as well as an evaluation of the social and medical context in which they occur. Situations that can lead to failure of a child to appropriately gain weight and grow include:

- 1- Inadequate caloric intake. These could include children that are hypersensitive to texture as in children with autistic disorders or children that are on severely restricted diets as in Dan diets, ketogenic diets or vegan diets. These children need to be followed closely for adequate nutrient (protein and vitamin) and micronutrient intake. Failure to thrive due to inadequate caloric intake also may be the result of neglect or abuse and if suspected must be reported to DHHS.
- 2- A hypermetabolic state requiring a higher than expected need for calories. Some of these disorders may require a lower volume of fluid intake as well as an increase in calories resulting in a higher caloric density.
 - a. Chronic respiratory disorders like bronchopulmonary dysplasia
 - b. Chronic infectious diseases like HIV disease
 - c. Cardiovascular disorders and renal diseases
- 3- Malabsorption of food resulting in inadequate energy retention.

CONGENITAL HEART DISEASE OR RENAL DISEASE

Many infants with congenital heart disease, chronic lung disease and/or kidney disease have the challenge of living in a catabolic state requiring more calories for growth than most other children. These children have the dual challenge of being easily overwhelmed by an increase in fluids, thus requiring a high density of calories in a low volume of fluid. Any child with a diagnosis of congenital heart disease, renal disease or chronic pulmonary disease should be approved for the use of Similac PM 60/40 if prescribed by their provider.

USE OF FORMULAS FOR INFANTS WITH MALABSORPTION:

Malabsorption can occur in infancy for a variety of reasons including injury to or congenital abnormalities of the intestinal mucosa or loss of significant intestinal surface area, such as in short gut syndrome, which may impair digestion and absorption. Decreased pancreatic enzyme production, as in cystic fibrosis, and cholestatic liver disease (biliary atresia, alpha-1-antitrypsin deficiency, etc.) particularly impair digestion and absorption of dietary fats and fat-soluble vitamins.

- 1- Infants with abnormalities of the intestinal mucosa or with shortened intestinal length may require an extensively hydrolyzed or amino acid-based formula with glucose polymers rather than disaccharides.
- 2- Infants with pancreatic insufficiency or cholestasis may require a medium chain triglyceride-enriched formula and supplemental fat soluble vitamins.

Care of children with malabsorption should proceed under the guidance of a pediatric gastroenterologist or pulmonologist.

¹² American Academy of Pediatrics Pediatric Nutrition Handbook, 6th Edition (2009), page 601

Medical Conditions That May Require Prescription of Medical Formula

Section:

WIC Provision of Ready to Feed (RTF) Formulas Or Pre-Prepared Added Rice Starch Formulas



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Mary C. Mayhew, Commissioner

WIC PROVISION OF READY TO FEED (RTF) FORMULAS OR PRE-PREPARED ADDED STARCH FORMULAS

The USDA Food and Nutrition Service determined that all WIC formulas must be issued in powder or concentrated liquid forms unless:

- 1- The participant's household has unsanitary or restricted water supply or poor refrigeration.
- 2- The person caring for the infant is unable to correctly dilute the concentrated or powder form.
- 3- The formula is only available in ready to feed form.

For **special medical /prescription formulas only**, RTF may also be used if:

- 1- It better accommodates the infant or child's condition.
- 2- It improves the likelihood that the infant/child will consume the formula.

Pre-prepared added starch formulas can be made available for infants with severe gastroesophageal reflux through Maine WIC in the special situation where a child's caregiver is unable to correctly mix and thicken the formula with cereal.

Medical Conditions That May Require Prescription of Medical Formula

Section:

Use of Formulas For Infants with Metabolic Disease



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USE OF FORMULAS FOR INFANTS WITH METABOLIC DISEASE ¹³

The following section provides information on several metabolic disorders along with typical treatment plans. This is an extensive, all-inclusive list. Care of children with any confirmed metabolic disorder should proceed under the guidance of the Maine Children's Genetic and Metabolic Disorders Clinics and Dr. Wendy Smith and Dr. Tom Brewster.

Type of Condition

I. Amino Acid Disorders – Metabolic disorders involving an inability to break down specific amino acids (components of protein).

HOMOCYSTINURIA

The term "homocystinuria" designates a biochemical abnormality, not a specific disease entity. There are many causes of homocystinuria. All result in the inability to break down the amino acid homocystine and affect one of the transsulfation pathways that convert the sulfur atom of methionine into the sulfur atom of cysteine. This pathway is the chief route of disposal of methionine. Clinical problems include multiple, recurrent thromboemboli. Death has been reported within the first year of life. Approximately 50% of untreated individuals die by 25 years of age; death is frequently a result of thromboembolic events. Developmental delay is reported in 65% to 80% of untreated individuals.

The survival rate may improve with early, effective treatment. Treatment seems to reduce the risk of thromboembolic episodes and the incidence of mental retardation or developmental delay may be prevented or reduced. For patients with classic (homozygous) homocystinuria, early treatment with good biochemical control (lifetime plasma-free homocystine <11 mol/L) seems to prevent mental retardation, ectopia lentis seems to be delayed, and the incidence of seizures is reduced.

Treatment consists of protein restricted diet, methionine-free formula (with added cysteine), betaine, and vitamins B6, folate, and vitamin B12 (in responsive individuals). Outcome: without treatment, developmental delay, intellectual disability, lens dislocation, cardiovascular disease. With treatment, there is a variable risk for above chronic conditions.

- 1- Treatment depends on the underlying cause of homocystinuria. As a first step, pyridoxine (vitamin B6) responsiveness should be ascertained, because approximately 50% of patients respond to large doses of this vitamin.
- 2- Nonresponsive patients with CBS (cystathionine beta-synthase) deficiency should be treated with a methionine-restricted, cysteine supplemented diet. Folic acid and betaine therapy may also be helpful with all patients.
- 3- Specialized care is required that includes the ability to monitor amino acids and provide nutritional assessment and planning. Care should proceed under the guidance of the Maine Children's Genetic and Metabolic Disorders Clinics and Dr. Wendy Smith and Dr. Tom Brewster.

PHENYLKETONURIA:

Phenylketonuria (PKU) is the inability to break down the amino acid phenylalanine. Disease severity is based on the inherited ability to metabolize phenylalanine. Treatment consists of phenylalanine restricted medical formula. Outcome: without treatment, classic PKU results in mental retardation. With treatment and good dietary compliance most individuals do well. There remains an increased risk of learning disabilities and behavior problems, most often related to dietary compliance.

PKU is rarely diagnosed before 6 months of age without newborn screening, because the most common manifestation without treatment is developmental delay followed by mental retardation. Untreated individuals may also develop microcephaly, delayed or absent speech, seizures, eczema, and behavioral abnormalities. Early treatment of PKU is associated with improved intellectual outcome. Therefore, an infant with a positive newborn screening result should receive the benefit of rapid diagnostic testing. Diagnostic testing includes

¹³ American Academy of Pediatrics Committee on Genetics. Newborn Screening Fact Sheets. 2006:Vol118. No 3:e934-963.

quantitative determination of plasma Phe and tyrosine concentrations. If the Phe concentration is increased, additional studies are indicated to determine if the infant has an abnormality in synthesis or recycling of cofactor tetrahydrobiopterin BH4.

- 1- Once the diagnosis of hyperphenylalaninemia is confirmed, metabolic control should be achieved as rapidly as possible. This is achieved through the use of medical foods, including medical protein sources that are low in Phe; small amounts of Phe must also be provided, which is achieved through the use of small amounts of natural protein.
- 2- The infant with PKU can be given breast milk along with Phe-free formula under the direction of a metabolic dietitian.
- 3- The response to dietary treatment is monitored through periodic measurement of blood Phe concentrations, assessment of growth parameters, and review of nutritional intake.
- 4- Most US centers recommend lifelong dietary treatment. This is particularly important for women, because fetuses exposed to increased concentrations of Phe are at significant risk of microcephaly, congenital heart disease, and reduced IQ.
- 5- Recent evidence suggests that some individuals with hyperphenylalaninemia and classic PKU may benefit from BH4 treatment in addition to dietary Phe restriction.
- 6- As noted previously, there is no national or international consensus regarding the optimal concentration of Phe across the life span. Similarly, there is no consensus regarding discontinuation of dietary therapy.

TYROSINEMIA:

Tyrosinemia Type 1 – Inability to break down the amino acid tyrosine. Treatment consists of phenylalanine and tyrosine restricted medical formula, NTBC medication, and liver transplant (in unresponsive individuals). Outcome: without treatment, failure to thrive, cirrhosis of the liver, clotting disorders, kidney disease, and cancer. With recently available NTBC drug treatment affected individuals are doing remarkably well. Long-term follow-up studies are in progress.

Tyrosinemia Type 2 – Inability to break down the amino acid tyrosine (different pathway than type 1). Treatment consists of dietary restriction. Outcome – without treatment, results in mental retardation and corneal ulcers. With dietary treatment most individuals do well.

An increased tyrosine concentration on newborn screening requires confirmation and additional testing, because it may be caused by other metabolic disorders (eg, fructose and galactose enzyme deficiencies), giant cell hepatitis, neonatal hemochromatosis, and neonatal infections. The optimal approach is complex and requires determination of the concentrations of tyrosine and other amino acids and metabolites in the blood and urine.

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| Type 1 | Treatment options for tyrosinemia include dietary therapy, liver transplantation, and use of the pharmacologic agent NTBC. Clinical signs and symptoms improve with NBTC therapy and diet. |
| Type II | Therapy with a diet low in tyrosine and phenylalanine is curative in type II tyrosinemia. Early diagnosis can help avoid the risk of mental retardation in these patients. |
| Neonatal | Most cases of neonatal tyrosinemia, especially those seen in small preterm infants, may be transient and controlled by reducing the protein intake to 2 to 3 g/kg per day or by breastfeeding. Some patients respond to ascorbic acid supplementation. |

II. Carbohydrate Disorders

GALACTOSEMIA

Lactose, or milk sugar, is broken down into its constituent simple sugars, glucose and galactose, before absorption in the intestine. Galactosemia: the inability to break down lactose (present in human and cow milk products) to sugars. Treatment consists of dietary restriction of milk products. Outcome: without treatment, infants present in the first few days of life with vomiting, poor feeding, liver disease, and life-threatening

infection. With treatment, individuals do well in early childhood but frequently develop neuropsychological and ovarian problems during teenage years.

The genetic disorders that cause galactosemia vary in severity from a benign condition to a life-threatening disorder of early infancy. Early diagnosis and treatment of the latter condition can be lifesaving; hence, newborn screening for this disease has been instituted in many states. Exclusion of galactose from the diet results in marked improvement of the life-threatening complications of classic galactosemia. However, this treatment has only limited efficacy in the prevention of long-term complications. All newborn infants with positive screening results should be evaluated rapidly by an experienced physician for feeding difficulty, signs of sepsis, jaundice, and hepatomegaly. Untreated classic galactosemia may progress very rapidly to hepatic toxicity, with death resulting from sepsis or bleeding. Immediate restriction of dietary galactose is critical and should not await diagnostic testing.

Galactose is a reducing substance, and the presence of reducing substances in the urine is sometimes suggested as a test for galactosemia. However, this test is neither sensitive nor specific, and it should not be used as a screening or diagnostic test for galactosemia.

Diagnostic studies for classic galactosemia include quantitative analysis of GALT and red blood cell galactose 1-phosphate. In states where the screening test measures GALT activity, these studies will establish or rule out classic galactosemia. When the screening results, including estimates of galactose and galactose 1-phosphate and quantitative GALT activity, are normal, quantitative analysis of GALK and GALE are required to identify these forms of galactosemia. Infants suspected of having galactosemia should be fed with a galactose-free formula until diagnostic testing confirms a specific diagnosis.

- 1- After dietary galactose has been eliminated, most infants improve rapidly. Milk and milk products are excluded from the diet indefinitely, because significant ingestion of galactose at any age can be toxic. WIC contract soy formula is lactose free and should be prescribed for these children.
- 2- Because medications may contain galactose, the pediatrician should instruct parents to ask the pharmacist if a medication is galactose free before administering it to the child.
- 3- Regular nutritional evaluation is necessary to ensure adequate calcium intake.
- 4- Regular developmental evaluation and early speech assessment are also required. Girls should be monitored frequently in late childhood and adolescence for pubertal development.
- 5- Regular measurement of galactose 1-phosphate in red cells is the most common method used to assess dietary compliance.

III. Fatty Acid Disorders

These disorders affect the body's ability to breakdown fat as an energy source. The clinical findings are similar among these disorders including life-threatening coma and hypoglycemia (low blood sugar) due to prolonged fasting, such as with viral illnesses. Treatment consists of preventing prolonged fasting through feeding and IV fluids as needed.

Medium-chain acyl-CoA dehydrogenase (MCAD)

Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency is a disorder of fatty acid oxidation (FAO) first described in 1982–1983. Altogether, 10 disorders affecting mitochondrial FAO and ketogenesis have been identified. Among these, MCAD deficiency seems to be the most important because it is the most common and it has been implicated in some cases of sudden infant death syndrome (SIDS) and Reye syndrome.

Infants identified through newborn screening and prevented from prolonged fasting and hypoglycemia have normal growth and development without chronic illness. The classic presentation is an episode of vomiting and lethargy after a period of fasting in a child between 3 and 15 months of age. The child may have had a previous viral infection (gastrointestinal or upper respiratory) resulting in decreased oral intake that would have little consequence in an unaffected child. The episode may result in coma, and the child may remain obtunded even after hours of treatment with intravenous glucose. Undiagnosed disease has a mortality rate of 20% to 25%, many times with death occurring during the initial episode. Most deaths would be preventable if dietary therapy and measures to prevent fasting were begun before the onset of symptoms.

Any child with an octanoylcarnitine concentration of 1.0 mol/L or greater will require definitive diagnostic testing. Follow-up testing will consist of plasma acylcarnitine analysis, urinary organic acid analysis, and

molecular testing. The plasma acylcarnitine analysis and urinary organic acid analysis will confirm the diagnosis.

- 1- Treatment for MCAD deficiency consists of avoidance of fasting and mildly decreased intake of dietary fat coupled with L-carnitine supplementation.
- 2- MCAD deficiency results in a secondary deficiency of carnitine, because carnitine couples with toxic intermediates, resulting in their excretion while depleting carnitine stores. Although it remains questionable how helpful supplemental carnitine is during periods when the patient with MCAD deficiency is healthy, there is no doubt that exogenous carnitine is recommended during times of illness.
- 3- Care should proceed under the guidance of the Maine Children's Genetic and Metabolic Disorders Clinics and Dr. Wendy Smith and Dr. Tom Brewster.

Short-Chain Acyl-CoA Dehydrogenase Deficiency (SCAD)

Infants diagnosed through newborn screening and prevented from having hypoglycemia are asymptomatic with normal growth and development. Infants diagnosed clinically prior to newborn screening exhibited failure to thrive, muscle weakness, and developmental delay.

Long-Chain Acyl-CoA Dehydrogenase Deficiency (LCAD)

Features include chronic problems such as muscle weakness and heart muscle enlargement and dysfunction.

Long-Chain Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD)

Many individuals have more severe disease with cardiomyopathy, progressive liver failure, and peripheral neuropathy.

Very-Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)

These children have a clinical presentation similar to LCHAD.

Glutaric Acidemia Type 2

Complete enzyme deficiencies result in severe illness in the newborn period with decreased muscle tone, low blood sugar, cardiomyopathy, and coma. Some infants are born with dysmorphic facial features and polycystic kidneys. Some mildly affected children benefit from riboflavin supplementation.

IV. Organic Acidemias

These disorders are due to errors in the breakdown of amino acids causing high levels of toxic acids in the blood. Fasting and illness can trigger serious complications. Common findings include refusal to feed, vomiting, acidosis, dehydration, and low blood sugar.

Glutaric Acidemia Type 1

Affected children may develop normally up to age 2. Hallmark of the disease is onset of a movement disorder similar to that seen in Huntington's disease. Other findings include macrocephaly (large head) and stroke. Acute episodes may include vomiting, seizures, and coma. Treatment consists of a low-protein diet and supplemental riboflavin and carnitine. Long-term outcomes on treatment are currently not known.

Maple Syrup Urine Disease (MSUD)

The most severe form results in poor feeding and vomiting in the first week of life followed by lethargy and coma. There may be severe muscle rigidity. Acute treatment involves removal of branched-chain amino acids through peritoneal dialysis. Treatment after recovery of acute events involves synthetic formulas devoid of leucine, isoleucine, and valine. Long-term prognosis of affected children remains guarded.

Maple syrup urine disease (MSUD), also known as branched-chain ketoaciduria, is caused by a deficiency in activity of the branched-chain keto acid dehydrogenase (BCKD) complex. Deficiency of the BCKD complex results in accumulation of the branched-chain amino acids (BCAAs) leucine, isoleucine, and valine and the corresponding branched-chain ketoacids (BCKAs). Classic MSUD (residual enzyme activity <2%) is the most

severe and most common form. Affected infants are normal at birth, with symptoms usually developing between 4 and 7 days of age; however, lower intake of protein, as in breastfeeding, can delay the onset of symptoms until the second week of life. Initial symptoms are lethargy and poor sucking with little interest in feeding. Weight loss follows with abnormal neurologic signs (alternating hypertonia and hypotonia; dystonic posturing of the arms) becoming more and more apparent. The characteristic odor of the urine, described as smelling like maple syrup, burnt sugar, or curry, is then noted. Finally, seizures and coma, leading to death (in untreated cases), occurs. Laboratory findings include increased concentrations of BCAAs, ketosis, acidosis, and occasionally hypoglycemia.

A blood leucine concentration greater than 4 mg/dL, or a concentration of 3 to 4 mg/dL (305 mmol) in the first 24 hours of life, requires immediate medical follow-up. Plasma amino acid analysis reveals findings diagnostic for MSUD: increased concentrations of BCAAs, low alanine concentrations, and the presence of alloisoleucine.

- 1- Treatment consists of a carefully regulated diet that provides sufficient BCAAs for normal growth and development without exceeding the patient's degradative enzyme capacity. Because natural protein must be limited, a medical food product (BCAA-free) supplement is necessary.
- 2- The goal of long-term dietary management is normalization of blood BCAA concentrations while providing nutrition adequate to sustain growth and development in children. Dietary therapy should be continued for life.
- 3- A metabolic team, including not only a metabolic specialist but also a metabolic nutritionist, is crucial. Care should proceed under the guidance of the Maine Children's Genetic and Metabolic Disorders Clinics and Dr. Wendy Smith and Dr. Tom Brewster.
- 4- MSUD has been treated since the early 1960s, and consequently, some neurologically intact MSUD-affected women have reached childbearing age and reproduced. As has been reported for other enzyme deficiencies, postpartum metabolic decompensation can be a problem.

3-Hydroxy-3 Methylglutaryl-CoA Lyase Deficiency

Clinical presentation includes vomiting, dehydration, seizures, and coma. Treatment of acute events includes hydration and IV glucose infusion. Long-term management includes dietary protein and fat restriction.

3-Methylcrotonyl-CoA Carboxylase Deficiency

This disorder has varied age of onset with difficulty feeding, breathing problems, skin rash, alopecia, delayed development, seizures, and coma. Long-term treatment consists of dietary leucine restriction and carnitine supplementation.

Beta-Ketothiolase Deficiency

Clinical presentation is quite variable ranging from no symptoms into adulthood to severe acidosis in the first year of life leading to coma and death. Affected children may be asymptomatic in between episodes. Development is normal.

Isovaleric Acidemia

Newborns with the severe form of this metabolic disorder develop vomiting and acidosis in the first few days of life followed by lethargy, seizures, coma, and death if therapy is not initiated. Long-term management consists of a low-protein formula and carnitine supplementation. Milder forms of IVA have been identified through newborn screening and have an excellent prognosis.

Methylmalonic Acidemia

Severely affected newborns have acidosis, elevated blood ammonia, low blood count, coma, and death. Children with later onset forms have failure to thrive, hypotonia, and developmental delay. Long-term treatment consists of low-protein diet and administration of carnitine and vitamin B12. Prognosis depends on the type of enzyme defect.

Propionic Acidemia

Acute symptoms usually begin in the early weeks of life with poor feeding, vomiting, lethargy, dehydration, progressing rapidly to coma and death. Long-term management consists of natural protein diet along with synthetic protein formula deficient in propionate precursors. Long-term prognosis is guarded.

V. Urea Cycle Disorders

These inborn errors of metabolism prevent the detoxification of free ammonia released by the breakdown of amino acids to urea. The ammonia is highly toxic to the central nervous system. Affected newborns present with signs and symptoms of brain dysfunction. Affected babies are normal at birth but become symptomatic after protein feedings. They refused to eat, followed by vomiting, rapid respirations, lethargy, and coma. Seizures are common. Acute management consists of removal of ammonia from the body including the use of peritoneal dialysis or hemodialysis if needed and provision of adequate calories and essential amino acids.

Argininemia

Clinical presentation is different than the other urea cycle disorders. Symptoms may not develop for several months to years. Choreoathetotic movements and loss of developmental milestones suggest a degenerative disease of the central nervous system. Mental retardation is progressive. Treatment consists of a low-protein diet devoid of arginine. Administration of a synthetic protein made of essential amino acids usually results in a dramatic decrease in plasma arginine and improvement in neurologic abnormalities. Intellectual disabilities persist despite treatment.

Argininosuccinic Aciduria

The severity of the clinical features varies from high blood ammonia in the first few days of life with high mortality to later onset forms with mental retardation associated with vomiting, failure to thrive, and hepatosplenomegaly. Treatment is similar to other urea cycle disorders.

Citrullinemia

The clinical spectrum ranges from severe to asymptomatic forms. Mild forms may have a gradual onset with failure to thrive, frequent vomiting, and developmental delay. Some patients may remain asymptomatic into adulthood. Prognosis is poor for symptomatic newborns. Children with mild disease usually do well on a protein-restricted diet. Mild to moderate intellectual disabilities are common even in well-treated patients.

Ornithine translocase deficiency, also called Hyperornithinemia-Hyperammonemia-Homocitrullinuria (HHH) Syndrome

Symptoms associated with elevated blood ammonia levels may develop shortly after birth or may be delayed into adulthood. Acute episodes may be associated with refusal to eat, vomiting, lethargy, and coma. Progressive neurologic findings include lower leg weakness, spasticity, seizures, and varying degrees of mental retardation if undiagnosed and untreated. Treatment consists of protein restriction.