

Oral nutritional supplements

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Coverage policy

For this policy, prescribed oral nutritional supplements are defined as either nutritionally complete formulas used as the sole source of nutrition, or nutritionally incomplete amino acid-based elemental formulas or hydrolyzed semi-elemental nonstandard formulas designed to meet the unique nutritional needs of a specific medical condition (Cederholm, 2017).

Oral nutritional supplements are clinically proven and, therefore, may be medically necessary to increase body mass index or weight or to prevent other complications of malnutrition for members who are not meeting their energy or nutrient needs or are at risk of malnutrition, when diet alone is insufficient to meet daily nutritional requirements and when the following general criteria and age-specific criteria are met:

General criteria (Arvanitakis, 2020; Bischoff, 2020a, 2020b; Burgos, 2018; Cuerda, 2021; Freeman, 2021; Iyer, 2022; Muscaritoli, 2021):

- The oral nutritional supplement is specially formulated to address a medical need.
- The oral nutritional supplement is prescribed for the treatment of the member's medical needs.
- The member has either:

- A limited or impaired capacity to ingest, digest, absorb, or metabolize ordinary foodstuffs or certain nutrients.
- Other special medically determined nutrient requirements that are different from those of healthy people.
- Reversible causes have been ruled out.
- Nutritional assessment with justification is provided.

For members younger than age 21, oral nutritional supplements are clinically proven and, therefore, may be medically necessary for any of the following conditions:

- Metabolic diseases or inborn errors of metabolism, to prevent complications resulting in severe intellectual disability and death (Genetic Metabolic Dietitians International and the Southeast Regional Newborn Screening and Genetics Collaborative, 2020).
- Severe food allergies refractory to dietary and other treatments, which if left untreated, will cause malnourishment, chronic physical disability, intellectual disability, or death (National Institute of Allergy and Infectious Diseases, 2010):
 - IgE-mediated food protein allergies.
 - Food protein-induced enterocolitis syndrome.
 - Eosinophilic esophagitis, gastroenteritis, or colitis.
- Cystic fibrosis with failure to achieve optimal growth rates and nutritional status with oral dietary intake and pancreatic enzyme replacement therapy alone (Turck, 2016).
- As the sole source of nutrition for disorders of gross anatomy impeding or obstructing passage of nutrition through the alimentary canal and the absorption of macronutrients, e.g., short bowel syndrome, intestinal fistula, intestinal dysmotility, mechanical obstruction, or extensive small bowel mucosal disease (Cuerda, 2021; Freeman, 2021; Iyer, 2022).
- Other state-mandated indications.
- Other indications determined on a case-by-case basis.

For members younger than age 21, oral nutritional supplements are investigational/not clinically proven and, therefore, not medically necessary for the following conditions :

- When prescribed in the absence of a clear medical justification.
- Based on food preference or member convenience.
- For the treatment of mild to moderate food allergies or food intolerance that can be addressed by diet modification (National Institute of Allergy and Infectious Diseases, 2010).

For members 21 years or older, oral nutritional supplements are clinically proven and, therefore, may be medically necessary to treat any of the following conditions:

- Metabolic diseases or inborn errors of metabolism to prevent complications resulting in severe intellectual disability and death (Genetic Metabolic Dietitians International and the Southeast Regional Newborn Screening and Genetics Collaborative, 2020).
- As the sole source of nutrition for disorders of gross anatomy impeding or obstructing passage of nutrition through the alimentary canal and the absorption of macronutrients, e.g., short bowel syndrome, intestinal fistula, intestinal dysmotility, mechanical obstruction, or extensive small bowel mucosal disease (Cuerda, 2021; Freeman, 2021; Iyer, 2022).
- Cystic fibrosis with failure to achieve optimal growth rates and nutritional status with oral dietary intake and pancreatic enzyme replacement therapy alone (Turck, 2016).

- Other state-mandated indications.
- Other indications determined on a case-by-case basis.

For members 21 years or older, oral nutritional supplements are investigational/not clinically proven and, therefore, not medically necessary:

- For members with dementia to improve cognitive performance or prevent cognitive decline (Volkert, 2015).
- When prescribed in the absence of a clear medical justification.
- Based on food preference or member convenience.
- For the treatment of mild to moderate food allergies or food intolerance that can be addressed by diet modification (National Institute of Allergy and Infectious Diseases, 2010).

For any determinations of medical necessity for medications, refer to the applicable state-approved pharmacy policy.

Limitations

The following nutritional products are not medically necessary as medical foods:

- Oral polymeric standard formulas (e.g., Boost, Ensure, NeoSure, PediaSure) in the absence of a medical justification.
- Oral polymeric or oligomeric (hydrolyzed) formulas to support a low-ketogenic diet.
- Oral organic formulas.
- Elemental semisolid foods
- Self-blenderized formulas.
- Oral additives and food thickeners.
- Gluten-free foods.
- Individual vitamin or mineral supplements.
- High-protein powders or nutritional drinks.
- Low-carbohydrate dietary supplements.
- Non-prescription weight loss or weight gain products.
- Fluid and electrolyte replacements.

Alternative covered services

- Guideline-directed standard of care.
- Enteral nutrition.
- Parenteral nutrition.
- Nutritional counseling.

Background

The American Society for Parenteral and Enteral Nutrition (undated) has adapted the following definition of malnutrition (undernutrition) from Soeters (2009): “An acute, subacute or chronic state of nutrition, in which a combination of varying degrees of overnutrition or undernutrition with or without inflammatory activity have led to a change in body composition and diminished function.”

Following this definition, malnutrition may be disease-related with an inflammatory component (e.g., cachexia or acute disease or injury-related), disease-related without an inflammatory component (e.g.,

cognitive dysfunction or malabsorption conditions), or nondisease-related (e.g., hunger or frailty). In affluent societies, disease-related causes are the principal forms of nutrient deficiency, while socioeconomic or psychologic related malnutrition are the main causes in less affluent communities; hunger remains the principal cause in developing countries (Cederholm, 2017).

Disease-related causes of malnutrition include genetic diseases, chronic conditions, and treatment interventions, for which medical nutritional therapy is essential to ameliorating the clinical manifestations of the disease (Cederholm, 2017). Among those with disease-related malnutrition, inflammation is often a key cause and may mitigate the response to routine nutritional support (Merker, 2020).

Oral nutritional supplements provide essential nutrients and calories to patients who cannot meet their nutritional requirements by usual food alone. They are available as ready-to-drink liquids, cremes, or powder supplements that can be added to drinks and foods in nutritionally complete or incomplete forms (Cederholm, 2017).

The first commercially available formulation was for dietary treatment of phenylketonuria in the 1950s. Since then, special formulations have been developed to address nutritional deficiencies caused by other inborn errors of metabolism, Crohn's disease, ulcerative colitis, cancer treatment, surgery, and other conditions that limit the ability to ingest, digest, or absorb regular food (Li, 2021).

Nutritionally complete products contain a balanced nutritional composition of macro- and micronutrients that reflect the dietary recommendations for healthy people. They may supplement insufficient intake or may be used as the sole source of nourishment for prolonged periods. Nutritionally incomplete products may contain specific nutrients in higher amounts or omit other nutrients, and are not suitable for use as the sole source of nutrients. Disease-specific oral nutritional supplements often fall into this category, as they are modified to meet specific nutritional and metabolic demands of certain diseases (Cederholm, 2017). When provided under medical supervision as part of a therapeutic regimen, oral nutritional supplements are considered medical foods, as defined below.

Regulatory considerations

The U.S. Food and Drug Administration defines a medical food as a "food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation." (FDA section 5(b) of the Orphan Drug Act (21 U.S.C. 360ee (b) (3)). The regulatory definition of medical foods encompasses these key attributes (U.S. Food and Drug Administration, 2016):

- Medical foods are specially formulated and processed; they are not naturally occurring foodstuffs used in a natural state.
- Medical foods are intended for the dietary management of patients' therapeutic or chronic medical needs.
- Medical foods must be consumed or administered enterally (orally or tube feeding) under active and ongoing medical supervision. They are not simply recommended by a physician as part of an overall diet to manage symptoms or reduce the risk of a disease or condition.
- The patient either:
 - Requires use of the product as a major component of a disease or condition's specific dietary management.
 - Has limited or impaired capacity to ingest, digest, absorb, or metabolize ordinary foodstuffs or certain nutrients.

- Has other special medically determined nutrient requirements that are different from those of healthy people.
- Obtaining or maintaining essential nutrient requirements (e.g., essential amino acids, essential fatty acids) cannot be achieved by modification of the normal diet alone.

“Foods for special dietary use” and “dietary supplements” are other regulatory classifications of foodstuffs developed for medical or health needs. Foods for special dietary use supplement or fortify the ordinary or usual diet with any vitamin, mineral, or other dietary property for particular dietary needs that exist by reason of a physical, physiological, pathological or other condition (e.g., diseases, convalescence, pregnancy, lactation, allergic hypersensitivity to food, underweight, overweight), or age. Dietary supplements provide nutrients intended to meet ordinary nutritional requirements of healthy people, but do not address medical issues or a particular nutritional problem. Unlike medical foods, neither requires medical supervision for use nor may they lawfully make disease-related claims on labelling (Markowitz, 2020).

Findings

This policy includes evidence of the efficacy of oral nutritional supplements as treatment for, or to prevent, malnutrition or the manifestations of malnutrition, ideally provided in community-based populations. The definition of oral nutritional supplements in the research was variable. Evidence was included if the research clearly described oral nutritional supplements as a prescribed multinutrient formula taken orally (i.e., not individual nutrient supplements), although the supplements may have been prescribed along with other dietary interventions.

Causes of undernutrition or malnutrition are due to inadequate intake, inadequate nutrient absorption, increased metabolic demands, or a combination. Despite the wide availability of nutritional formula, including those marketed for specific disease conditions, there is limited evidence supporting their efficacy and use in clinical practice.

Current guideline recommendations below are based largely on expert consensus, reflecting the limited evidence for many indications. There is greater certainty of the benefit of oral nutritional supplements for populations whose underlying disease has nutrient requirements that are different from those of healthy people than for populations whose oral intake is inadequate but share similar nutritional requirements with normal, healthy individuals.

Guidelines recommend oral nutritional supplements to increase body mass index or weight gain or to prevent other complications of malnutrition for patients who are not meeting their energy or nutrient needs or are at risk of malnutrition, when diet alone is insufficient to meet daily nutritional requirements. The evidence for an effect on other functional improvements, mortality, or quality of life is less certain or absent for many disease states other than inborn errors of metabolism.

The European Society for Clinical Nutrition and Metabolism guidelines recommend oral nutritional supplements for the following populations:

- Dementia: As sole source of nutrition or as a supplement to the usual diet, for patients with insufficient oral nutritional intake from normal food to improve body weight/body mass index, but not to address cognitive impairment or prevent further cognitive decline (Volkert, 2015).
- Cystic fibrosis: For children and adults who fail to achieve optimal growth rates and nutritional status with oral dietary intake and pancreatic enzyme replacement therapy alone, with regular reevaluation for continued use (Turck, 2016).

- Inflammatory bowel disease: To supplement normal food intake in patients with active disease or for perioperative patients to reduce the negative impact of undernutrition post-operatively (Bischoff, 2020a).
- Neurology: To supplement normal food intake in patients with amyotrophic lateral sclerosis with progressive weight loss, multiple sclerosis, or stroke, who are malnourished or at risk of malnutrition, but insufficient evidence for Parkinson's disease (Burgos, 2018).
- Mild hepatic encephalopathy: For patients with intact cough and swallow reflexes when feeding goals cannot be attained by oral nutrition alone (Bischoff, 2020b).
- Acute/chronic pancreatitis if oral nutrition is insufficient for reaching the calorie and protein goals (Arvanitakis, 2020).
- Chronic intestinal failure due to nonmalignant disease: Defined as the reduction of gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes, such that intravenous supplementation is required to maintain health and/or growth, e.g., short bowel, intestinal fistula, intestinal dysmotility, mechanical obstruction, and extensive small bowel mucosal disease; suggest oral isotonic nutritional supplements in borderline cases at risk of malnutrition (Cuerda, 2021).
- Cancer: If able to eat but not adequately (e.g., less than 50% of the requirement for more than one week or only 50% to 75% of the requirement for more than two weeks) (Muscaritoli, 2021).
- Geriatric patients with malnutrition or at risk of malnutrition with chronic conditions when dietary counseling and food fortification are not sufficient to reach nutritional goals (Volkert, 2022).

The Genetic Metabolic Dietitians International and the Southeast Regional Newborn Screening and Genetics Collaborative (2020) developed joint evidence-based nutrition management guidelines for several inherited metabolic disorders, in which diet management is an integral treatment for individuals at all ages. The inherited metabolic diseases addressed in their guidelines are phenylketonuria, maple syrup urine disease, propionic acidemia, very-long-chain acyl-CoA dehydrogenase deficiency, and medium-chain acyl-CoA dehydrogenase deficiency. The evidence for medical nutrition therapy for these conditions is based primarily on expert opinion and limited case series, many of which reported outcomes for patients diagnosed prior to newborn screening.

The National Institute of Allergy and Infectious Diseases (2010) recommends avoidance of specific food allergens in managing individuals with documented or proven IgE-mediated or non-IgE-mediated food allergy with or without other related comorbidities such as atopic dermatitis, asthma, or eosinophilic esophagitis. Since these individuals are at risk for nutritional deficiencies and growth deficits, the Institute stresses the importance of properly diagnosing the food allergy and consuming an allergen-free yet nutritionally adequate diet. They do not specifically mention use of oral nutritional supplements.

The American Gastroenterological Association recommends oral nutritional supplements to treat refractory celiac disease to correct deficiencies in macro- and micronutrients (Green, 2022) and to supplement parenteral nutrition in patients with short bowel syndrome at risk for micronutrient deficiencies (Iyer, 2022).

The Kidney Disease Outcomes Quality Initiative suggests a minimum of a three-month trial of oral nutritional supplements to improve nutritional status if dietary counseling alone does not achieve sufficient energy and protein intake to meet nutritional requirements in adults with chronic kidney disease stages 3 to 5 or post-transplantation who have or are at risk of protein energy wasting (Ikizler, 2020).

The American Society of Clinical Oncology issued no recommendation for or against dietary supplements in patients with cancer cachexia based on inconclusive low-quality evidence of benefit (Roeland, 2020).

The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition recommends following growth parameters and providing adequate nutrition by oral diet, or when necessary, by enteral feeding, for children with chronic pancreatitis to address macro- and micronutrient deficiencies (Freeman, 2021).

The North American Mitochondrial Disease Consortium recommends individual dietary supplements such as CoQ10, alpha-lipoic acid, and riboflavin for most patients with mitochondrial disorders. They recommend folinic acid and L-carnitine for patients with documented deficiencies or clinical manifestations associated with these deficiencies. There were no recommendations for prescribed oral nutritional supplements, other than when beginning supplement therapy, a “cocktail approach” should be avoided, deferring to administering one supplement at a time. There is a need for evidence-based guidelines for individual dietary supplements as well as other nutritional interventions, including special diets (Camp, 2016).

The following systematic reviews and meta-analyses provide additional evidence of effectiveness. Although much of the research is conducted in inpatient populations, we included analyses of prescribed multinutrient oral nutritional supplements in community-dwelling populations, where available. The research is of low quality, of short duration, and heterogeneous, reflecting the lack of consensus within the nutritional sciences with respect to defining the underlying causes of malnutrition/undernutrition, oral nutritional interventions, and outcome measures. This lack of consensus hampers research on health and economic outcomes in the management of disease- and condition-related nutrition therapy (Freijer, 2019). Adverse effects were reported inadequately.

Head and neck cancer

A systematic review of five registry studies and 10 randomized trials (n = 695) examined outcomes related to oral nutritional supplements, defined in this study as protein and calorie-rich enteral food supplements used to manage disease-related malnutrition. Compared with nutritional counseling alone, nutritional counseling plus oral nutritional supplements may result in a large increase in mortality, some increase in treatment tolerance, uncertain increases in quality of life and functional status, and potential adverse effects (e.g., nausea, vomiting and feeling of fullness). A meta-analysis of four of the trials found nutritional counseling plus oral nutritional supplements probably increased body weight slightly compared to nutritional counseling alone. The evidence was rated as very-low to low quality with an overall high risk of bias (Mello, 2021).

Cardiovascular disease

In adult patients with heart failure who are malnourished or at risk of malnutrition or cachexia, a systematic review of five low-quality randomized controlled trials (n = 275) found limited evidence of benefit on body weight and potentially on mortality and hospital readmission, with oral nutritional supplements administered alone or in combination with other nutritional interventions (Habaybeh, 2021).

Chronic obstructive pulmonary disease

A systematic review of ten randomized controlled trials examined the effects of oral nutritional supplements in 448 participants with stable disease. Meta-analysis of the changes induced by intervention found that respiratory function (forced expiratory volume in 1 s, lung capacity, blood gases) was unresponsive to nutritional support, but both inspiratory and expiratory muscle strength ($P = .041$)

and handgrip strength ($P = .05$) were significantly improved and associated with weight gains of ≥ 2 kg (Collins, 2013).

Chronic pancreatitis

Limited evidence suggested improved body weight and pain control from nutritional intervention, whether it consisted of dietary advice, dose escalation of pancreatic enzymes, oral nutritional supplements, or enteral feeding, compared to those who received no intervention. Additional higher quality research is needed to assess the effects of specific interventions on body composition and functional outcomes or the optimal nutritional treatment (Phillips, 2022; Wiese, 2021).

Older adults

A Cochrane review of 94 randomized controlled trials ($n = 10,284$) compared dietary advice to no dietary advice, and dietary advice with and without oral nutritional supplements, in groups of mostly older participants in hospital, residential care, and the community. There was low-certainty evidence that neither intervention had a significant effect on mortality at any time point or in hospitalizations at three months, but oral nutritional supplements may reduce hospitalizations up to six months. Low-certainty evidence suggests both dietary advice with or without oral nutritional supplements may result in weight gain in the short term, but the magnitude of the gain and length of intervention and follow-up required for benefits to emerge were inconsistent for all other outcomes (Baldwin, 2021).

Mixed-quality and limited evidence from 11 randomized and comparative nonrandomized studies ($n = 822$) suggests that oral nutritional supplements had a significant effect on reducing malnutrition or its adverse outcomes in frail older adults who were at risk of malnutrition or were malnourished living in care homes, hospitals, or the community (Thomson, 2022).

Another systematic review and meta-analysis of 17 studies ($n = 1,564$; follow-up: seven to 96 weeks) of mostly low to very low degrees of certainty found statistically insignificant effects of nutritional supplements in any of the measured outcomes (mortality, body mass index, weight, frailty status, muscle strength, gait speed, body composition, and cognitive function) (Moraes, 2021).

Eosinophilic esophagitis

There is moderate certainty evidence that an elemental diet is effective in achieving histopathologic remission. In six observational studies, 6.4% of subjects on an elemental diet failed to achieve histopathologic remission compared to 86.7% in a historical comparison group (risk ratio = .07, 95% confidence interval .05 to .12) (Rank, 2020).

On dialysis

For patients receiving maintenance dialysis therapy, very low-quality evidence from 15 studies ($n = 589$) suggests that short-term oral energy or protein/amino acid supplements may improve nutritional status by increasing serum albumin levels ($P = 0.003$) and body mass index ($P = 0.01$), without influence on serum potassium levels. Their effects on mortality and quality of life require further study (Liu, 2018).

In 16 low-quality randomized controlled trials ($n = 910$), oral nutritional supplements consisting of a mixture of macronutrients (mean difference = 2.36 kg, 95% confidence interval 0.45 to 4.26), administered for 48 weeks (mean difference 4.05 kg, 95% confidence interval 1.43 to 6.67) had some effects on increasing lean body mass but not on muscle strength or physical performance (Lu, 2021).

Wound healing

For patients in a long-term care setting with moderate-to-severe pressure ulcers (stage II, III, and IV) and an impaired nutritional status, a systematic review of three high-quality randomized controlled trials (n

= 273 total) found oral or enteral formulas enriched with arginine, zinc, and antioxidants resulted in improved pressure ulcer healing at eight weeks compared with standard formulas (Cereda, 2017).

In another systematic review of 21 randomized controlled trials and seven other prospective studies (n = 1,696 total), evidence of the effects of oral nutritional supplements on wound healing rates in different types of wounds was inconclusive. Oral nutritional supplements in the included studies comprised protein and amino acids (10 studies), mineral, vitamin, and antioxidants (nine), probiotics (one), and mixed nutrients (eight). Vitamin E, vitamin D, and omega-3 supplementation may be most beneficial in accelerating healing of various types of wounds, but more research is needed to examine the effects of these supplements on healing surgical wounds, in particular, and on which combinations of nutrients may be most beneficial in accelerating healing of various types of wounds (Daher, 2022).

A Cochrane review of nine randomized controlled trials (629 participants) found inconclusive evidence supporting the impact of nutritional interventions on the healing of diabetic foot ulcers compared to either no nutritional supplementation or different dosages of nutritional supplementation (Moore, 2020).

References

On January 23, 2023, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “malnutrition/therapy” (MeSH), “sarcopenia,” “failure to thrive,” “malnutrition,” “frailty,” “medical nutrition therapy” (MeSH), “medical nutrition therapy,” and “oral nutritional supplement.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

3/2023: initial review date and clinical policy effective date: 3/2023