PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Sucraid (sacrosidase) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Pediatric Gastroenterologist or Specialist in Genetic Disorders

  2. Individual is 5 months of age or older

  3. A confirmed diagnosis of congenital sucrase-isomaltase deficiency (CSID) in an individual having osmotic (watery) fermentative diarrhea, abdominal pain, cramps, bloating, gas

  4. Individual has been adherent with a sucrose free, low starch diet

  5. Individual has failure, contraindication or intolerance to Lyophilized Baker's yeast (*Saccharomyces cerevisiae*)

  6. Individual does not have secondary (acquired) disaccharidase deficiencies

  7. **ALL** of the following baseline tests have been completed before initiation of treatment:
     a. **ONE** of the following:
        i. Pathogenic or likely pathogenic mutation in the sucrose-isomaltase (SI) gene on chromosome 3 (3q25-q26)
        ii. Small bowel biopsy (See Definitions section for required results)
        iii. Decreased carbon-13 sucrose breath test
        iv. Normal lactose breath hydrogen test **AND** increased sucrose breath hydrogen test **AND** a stool pH of less than 6

  8. There are **NO** contraindications.
     a. Contraindications include:
        i. Hypersensitivity to yeast, yeast products, glycerin (glycerol), or papain

  Initial approval duration: 1 box (containing 2 bottles) per month x 3 months

- **Criteria for continuation of coverage (renewal request):** Sucraid (sacrosidase) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Pediatric Gastroenterologist or Specialist in Genetic Disorders

  2. **Medical record documentation of a routine re-evaluation of continued need for the medication, as affected individuals tend to experience spontaneous improvement of their symptoms with age, as colonic bacteria become able to metabolize non-absorbed carbohydrates into organic acids (lactic**

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acid and short chain fatty acids), most of which are then absorbed (*Documentation of re-evaluation must be sent with renewal requests*)

3. Individual's condition responded while on therapy
    a. Response is defined as at least a 50% reduction in **ALL** of the following:
        i. Symptoms of abdominal pain, cramps, bloating, gas
        ii. Number of stools per day
        iii. Watery, loose stool consistency
        iv. Number of symptomatic days

4. Individual has been adherent with the medication

5. Individual continues to be adherent with a sucrose free, low starch diet

6. Individual does not have secondary (acquired) disaccharidase deficiencies

7. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Severe wheezing

8. There are no significant interacting drugs

Renewal duration: 1 box (containing 2 bottles) per month x 6 months

Description:

Sucraid (sacrosidase) chemically is beta D-fructofuranoside fructohydrolase. Sacrosidase is derived from Baker's yeast (*Saccharomyces cerevisiae*) that hydrolyzes sucrose. Sucraid (sacrosidase) is indicated as oral replacement therapy of genetically determined sucrase deficiency, which is part of congenital sucrase-isomaltase deficiency (CSID). The effects of sacrosidase have not been evaluated in patients with secondary (acquired) disaccharidase deficiencies. Sucraid (sacrosidase) does not contain isomaltase.

CSID is a carbohydrate intolerance disorder characterized by malabsorption of oligosaccharides and disaccharides. It is also known as disaccharide intolerance I, congenital sucrase-isomaltose malabsorption, congenital sucrose-isomaltose malabsorption, SI deficiency, sucrose-isomaltase deficiency, sucrase-isomaltase deficiency, and congenital sucrose intolerance. It is an autosomal recessive disorder. Onset usually occurs during infancy after weaning from breast milk or lactose-only formula onto foods containing sucrose or starch. Clinical manifestations include osmotic-fermentative diarrhea, abdominal distension and discomfort, flatulence and vomiting. Severe symptoms may lead to failure to thrive, dehydration and malnutrition. The gastrointestinal symptoms associated with CSID are nonspecific; the diagnosis is often delayed and patients can be misdiagnosed with irritable bowel syndrome, cystic fibrosis, celiac disease or other causes of chronic diarrhea.

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With CSID there is complete or almost complete lack of endogenous sucrase activity, marked reduction in isomaltase activity, moderate decrease in maltase activity, and normal lactase levels. Sucrase is naturally produced in the brush border of the small intestine, primarily the distal duodenum and jejunum. Sucrase hydrolyzes sucrose (a disaccharide) into its component monosaccharides, glucose and fructose. Isomaltase breaks down disaccharides from starch into simple sugars.

In the absence of endogenous human sucrase, sucrose is not metabolized. Unhydrolyzed sucrose and starch are not absorbed from the intestine and their presence in the intestinal lumen leads to osmotic retention of water resulting in loose watery stools. Unabsorbed sucrose in the colon is fermented by bacterial flora to produce increased amounts of hydrogen, methane, and water resulting in excessive gas, bloating, abdominal cramps, nausea, and vomiting.

CSID is inherited as an autosomal recessive genetic trait. The faulty gene has been identified to chromosome 3 (3q25-q26). The *SI* gene provides instructions for producing the enzyme sucrase-isomaltase. Mutations that cause this condition alter the structure, disrupt the production, or impair the function of sucrase-isomaltase. More than 25 mutations within the human sucrase gene are responsible for these CSID phenotypes. Sucrase-isomaltase variants can occur on either sucrase or isomaltase subunits, resulting in varied effects on sucrase-isomaltase enzyme activity.

CSID is difficult to diagnose. Approximately 4-10% of pediatric patients with chronic diarrhea of unknown origin have CSID. Several tests can be used to diagnose CSID tests but when used alone may be inaccurate.

Stool pH < 6 is not always a reliable screening test for the diagnosis of sugar malabsorption as stools with a pH < 6 may not have sugar detected and stools with a pH > 6 may have substantial amount of sugar present.

A hydrogen breath test or a sucrose hydrogen breath test showing an increase in breath hydrogen after a sucrose challenge is not specific for CSID; the test may have a high incidence of false-positive results due to villous injury, dumping syndrome, and the presence of small bowel bacterial overgrowth (SIBO) where unabsorbed sugar is converted to hydrogen gas by colonic bacteria.

Use of a differential urinary disaccharide ratio of sucrose to lactulose relies on obtaining an accurate 10-hour urine collection.

A sucrose breath test for screening and confirmation of CSID using a novel non-invasive ^{13}C-sucrose labeled substrate has been developed and validated, and is said to be accurate and specific for CSID, however getting breath samples may be difficult in small children. ^{13}C-sucrose breath testing with infrared spectrophotometry, requires 2 breath tests (one with labeled ^{13}C-sucrose and another with labeled ^{13}C-glucose) $^{13}CO_2$-enriched breath samples are collected for each. The results are expressed as a coefficient of glucose oxidation (CGO) and using a cutoff of < 79% CGO, it yields 100% sensitivity and specificity for CSID. But secondary sucrase deficiency cannot be excluded without clinical evaluations and biopsy.

The definitive test for diagnosis of CSID is the measurement of intestinal disaccharidases following small bowel biopsy. The small bowel biopsy should show normal villous architecture. The biopsy specimens should be assessed for lactase, sucrase, isomaltase (palatinase) & maltase activities. The activity assay should show complete or almost complete lack of endogenous sucrase activity, variable isomaltase activity that ranges from no activity to full activity, decrease in maltase activity, and normal lactase levels (within 1 standard deviation of the

mean) or a sucrase:lactase ratio of < 1 in the setting of reduced lactase. In addition, there should be a normal lactose breath hydrogen test to rule out a diagnose lactose intolerance. It is important to rule out secondary (or acquired) forms of disaccharidase deficiencies as the effects of Sucraid (sacrosidase) have not been evaluated in these patients with secondary (acquired) disaccharidase deficiencies.

Treatment of CSID involves following a strict sucrose- and starch-restricted diet, and an oral solution of Baker's yeast-derived enzyme replacement.

Potential causes of secondary or acquired sucrose-isomaltase deficiency or malabsorption:

Villous atrophy or alteration	Celiac disease Non-tropical sprue Chemotherapy and radiation therapy Crohn's disease Allergic enteropathy Immunodeficiency Malnutrition
Infection	Acute gastroenteritis Giardiasis Tropical sprue HIV enteropathy SIBO
Rapid transit	Rapid gastric emptying Chronic non-specific diarrhea Dumping syndrome Ulcerative, microscopic, and lymphocytic colitis

Definitions:

Small bowel biopsy shows ALL of the following:

- Normal villous architecture
- Absent or markedly reduced sucrase activity
- Isomaltase (palatinase) activity ranging from no to full activity
- Normal or reduced maltase activity
- Normal lactase activity or a sucrase:lactase ratio of < 1 if have reduced lactase

Resources:

Sucraid (sacrosidase) product information, revised by manufacturer QOL Medical LLC 04-2020, at DailyMed http://dailymed.nlm.nih.gov. Accessed September 28, 2020.

International Foundation for Gastrointestinal Disorders, Inc (IFFGD). Congenital Sucrase-Isomaltase Deficiency (CSID) Update October 02, 2019 at https://www.iffgd.org/other-disorders/congenital-sucrase-isomaltase-deficiency-csid.html?showall=1. Accessed September 28, 2020.

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