09-J2000-89

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Reviewed: 07/10/19

Revised: 08/15/19

Subject: Sacrosidase (Sucraid®) Oral Solution

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Sacrosidase (Sucraid) is an oral enzyme produced as a by-product of the manufacture of baker's yeast (Saccharomyces cerevisiae). Sacrosidase was approved by the US Food and Drug Administration (FDA) in April 1998 “as oral replacement therapy of the genetically determined sucrase deficiency, which is part of congenital sucrase-isomaltase deficiency.” Before approval of sacrosidase, the only treatment available was a life-long sucrose-free diet. Although sacrosidase substitutes for deficient sucrase, it does not provide specific replacement therapy for deficient isomaltase; thus, it may still be necessary to restrict dietary starch. Consultation with a registered dietitian (RD) to review recommended dietary restrictions and receive guidance on identifying (and avoiding when reasonable) foods with sucrose and/or starches is an important component of treatment. Congenital sucrase-isomaltase deficiency (CSID) is a rare genetic disease (10,000 to 50,000 in the US) characterized by a complete or almost complete lack of endogenous sucrase activity, a very marked reduction in isomaltase activity, a moderate decrease in maltase activity and normal lactase levels. In the absence of endogenous human sucrase, as in CSID, sucrose is not metabolized. Unhydrolyzed sucrose and starch are not absorbed from the intestine and their presence in the intestinal lumen may lead to osmotic retention of water and loose stools. In addition, unabsorbed sucrose in the colon is fermented by bacterial flora to produce increased amounts of hydrogen, methane and water. As a consequence, excessive gas, bloating, abdominal cramps, nausea, and vomiting may occur. Chronic malabsorption of disaccharides may result in malnutrition. Undiagnosed/untreated CSID patients often fail to thrive and fall behind in their expected growth and development curves.

Two small studies were conducted that led to the FDA approval of sacrosidase. A two-phase (dose response preceded by a breath hydrogen phase) double-blind, multi-site, crossover trial was conducted in 28 patients (aged 4 months to 11.5 years) with confirmed CSID. During the dose response phase, the patients were challenged with an ordinary sucrose-containing diet while receiving each of four doses of sacrosidase: full strength (9000 IU/mL) and three dilutions (1:10 [900 IU/mL], 1:100 [90 I./mL], and 1:1000

[9 IU/mL]) in random order for a period of 10 days. Patients who weighed no more than 15 kg received 1 mL per meal; those weighing more than 15 kg received 2 mL per meal. The dose did not vary with age or sucrose intake. A dose-response relationship was shown between the two higher and the two lower doses. The two higher doses of sacrosidase were associated with significantly fewer total stools and higher proportions of patients having lower total symptom scores, the primary efficacy end-points. In addition, higher doses of sacrosidase were associated with a significantly greater number of hard and formed stools as well as with fewer watery and soft stools, the secondary efficacy end-points. Analysis of the overall symptomatic response as a function of age indicated that in CSID patients up to 3 years of age, 86% became asymptomatic. In patients over 3 years of age, 77% became asymptomatic. Thus, the therapeutic response did not differ significantly according to age. A second study of similar design and execution as the first used 4 different dilutions of sacrosidase 1:100 (90 IU/mL), 1:1000 (9 IU/mL), 1:10,000 (0.9 IU/mL), and 1:100,000 (0.09 IU/mL). There were inconsistent results with regards to the primary efficacy parameters. In both trials, however, patients showed a marked decrease in breath hydrogen output when they received sacrosidase in comparison to placebo.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of sacrosidase (Sucraid) oral solution **meets the definition of medical necessity** when **ALL** of the following criteria are met (“1”, “2”, “3”, “4”, “5”, and “6”):

1. The member has a confirmed diagnosis of congenital sucrose-isomaltase deficiency (CSID) as documented by **ANY** of the following (“a”, “b”, “c”):
    a. A small bowel biopsy with disaccharidase enzyme assay that is positive for sucrase deficiency [i.e., a sucrase level below the laboratory’s reference level, typically <25 mcM/min/g] - laboratory documentation must be submitted
    b. A positive genetic test for a pathogenetic mutation in the sucrose-isomaltose (SI) gene located on chromosome 3 (3q25-q26) - laboratory documentation must be submitted
    c. For members with a documented contraindication to upper GI endoscopy with small bowl biopsy [the specific contraindication(s) to the biopsy procedure must be provided], the diagnosis may alternatively be confirmed by meeting **BOTH** of the following (“i” and “ii”) - documentation of the results for all applicable tests must be submitted:
        i. **EITHER** of the following:
            - A negative lactose breath test **AND** a positive hydrogen breath test for sucrose intolerance (i.e., an increase in breath hydrogen of >10ppm when challenged with sucrose after fasting
            - A positive 13C-sucrose breath test (i.e., a mean percentage of glucose oxidation value of less than 85%)
        ii. A fecal pH test indicating an inappropriate stool pH (<6.0)

2. Sacrosidase is prescribed by, or in consultation with, a gastroenterologist, endocrinologist, or medical geneticist/genetic specialist
3. Prior to the initiation of sacrosidase therapy, the member and/or member's guardian/caretaker has met with a healthcare professional (e.g., prescriber, primary care provider, nurse, dietitian/nutritionist) to review recommended dietary restrictions and receive education on identifying (and avoiding when reasonable) foods with sucrose and/or starches
4. Sacrosidase therapy will be used in conjunction with dietary limitation of sucrose intake [i.e., used for meals or snacks when avoidance of sucrose is not possible or recommended]
5. Member is age 5 months or older
6. Dosage does not exceed the following:
    a. >15 kg (33 lbs.): 2 mL with each sucrose-containing meal or snack, but not to exceed 8 mL (4 doses) per day [one box with two 118 mL (4 oz) bottles equals a 29-day supply]
    b. ≤15 kg (33 lbs.): 1 mL with each sucrose-containing meal or snack, but not to exceed 8 mL per day [one box with two 118 mL (4 oz) bottles equals a 29-day supply]

Approval duration: 3 month

Continuation of sacrosidase (Sucraid) oral solution **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1", "2", "3", "4", and "5"):

1. An authorization or reauthorization has been previously approved by Florida Blue in the past 2 years for the treatment of congenital sucrose-isomaltase deficiency, **OR** the member has previously met **ALL** indication-specific initiation criteria.
2. The member has had a beneficial response to treatment as evidence by an improvement in the gastrointestinal symptoms associated with CSID
3. Sacrosidase is prescribed by, or in consultation with, a gastroenterologist, endocrinologist, or medical geneticist/genetic specialist
4. The member and/or member's guardian/caretaker has met with a healthcare professional (e.g., prescriber, primary care provider, nurse, dietitian/nutritionist) in the past 24 months to assess dietary compliance with low-sucrose or sucrose-free diet and/or a low-starch or starch-free diet
5. Dosage does not exceed the following:
    a. >15 kg (33 lbs.): 2 mL with each sucrose-containing meal or snack, but not to exceed 8 mL (4 doses) per day [one box with two 118 mL (4 oz) bottles equals a 29-day supply]
    b. ≤15 kg (33 lbs.): 1 mL with each sucrose-containing meal or snack, but not to exceed 8 mL per day [one box with two 118 mL (4 oz) bottles equals a 29-day supply]

Approval duration: 12 months

The administration of sacrosidase to aid in the diagnosis of congenital sucrose-isomaltase deficiency (CSID) is considered **experimental or investigational**, as there is insufficient clinical evidence to support this use.

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD

REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Indicated as oral replacement therapy of the genetically determined sucrase deficiency, which is part of congenital sucrase-isomaltase deficiency (CSID),
- The recommended dosage is 1 mL (up to 15 kg of body weight) or 2 mL (greater than 15 kg) taken orally with each meal or snack diluted with 2 to 4 ounces (60 to 120 mL) of water, milk, or infant formula. Half of the dosage should be taken at the beginning of the meal or snack and the remainder be taken during the meal or snack.
- The beverage or infant formula should be served cold or at room temperature. The beverage or infant formula should NOT be warmed or heated before or after addition of sacrosidase because heating is likely to decrease potency. Also, sacrosidase should not be reconstituted or consumed with fruit juice since its acidity may reduce the enzyme activity.
- The dosage may be measured with the 1 mL measuring scoop (provided) or by drop count method (1 mL equals 28 drops from the container tip).

Dose Adjustments

- Specific guidelines for dosage adjustments in renal or hepatic impairment are not available; it appears that no dosage adjustments are needed.

Drug Availability

- Each mL of Sucraid contains 8,500 International Units (IU) of the enzyme sacrosidase. The product is available in 4 fluid ounce (118 mL) see-through plastic bottles, packaged two bottles per box. A 1 mL measuring scoop is provided with each bottle. Store in a refrigerator at 36°F - 46°F (2°C - 8°C), and protect from heat and light.

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Patients known to be hypersensitive to yeast, yeast products, glycerin (glycerol), or papain

Precautions/Warnings

- Sucraid may cause a serious allergic reaction. If you notice any swelling or have difficulty breathing, get emergency help right away. Before taking your first and second doses, be sure that there are health professionals nearby (within a few minutes of travel) just in case there is an allergic reaction.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnosis Codes That Support Medical Necessity

E74.31	Sucrase-isomaltase deficiency

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of guideline creation.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

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13. U.S. National Library of Medicine: Genetics Home Reference. Congenital sucrase-isomaltase deficiency. Available at: https://ghr.nlm.nih.gov/condition/congenital-sucrase-isomaltase-deficiency. Accessed on: 6/14/19. COMMITTEE

APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 7/10/19.

GUIDELINE UPDATE INFORMATION:

09/15/17	New Medical Coverage Guideline.
08/15/18	Review and revision to guidelines consisting of updating the position statement and references.
08/15/19	Review and revision to guidelines consisting of updating the references.