

# What is Congenital Sucrase-Isomaltase Deficiency?



Congenital Sucrase-Isomaltase Deficiency (CSID) is a rare, autosomal, inherited error of metabolism in which patients are born with absent or low levels of two digestive enzymes: sucrase and isomaltase.<sup>1</sup> Sucrase is the intestinal enzyme that aids in the breakdown of sucrose (simple table sugar) into glucose and fructose, which are used by the body as fuel. Isomaltase is one of several enzymes that helps digest starches.

By definition, congenital means it was “present at birth” and the deficiency is not acquired at any point due to infection or an outside source—that is called acquired sucrase-isomaltase deficiency. Both parents must carry the recessive gene for a child to be born with the disease.

All CSID patients lack sucrase activity, but the degree of isomaltase activity varies, suggesting the disease is not a consequence of a complete lack of SI gene expression. Therefore, CSID is considered a heterogeneous condition, or having great variability of severity between patients.

Because there is no way to amend the gene expression permanently, CSID is chronic and cannot be outgrown.

## Treatment of CSID

CSID is the result of the absence of sucrase, the enzyme that plays a role in the body’s breakdown

of sugar. Sucrase enzyme replacement therapy with Sucraid<sup>®</sup> acts as a substitute for the missing enzyme, and can reduce or eliminate the symptoms of this disease when taken as directed.<sup>2</sup>

It is important once a diagnosis of CSID has been made that the patient/caregiver works with a qualified nutritionist to review dietary restrictions, develops an understanding of food labels and ingredients (including alternative food and additive names), and is compliant with an individual outline of disease management, involving both dietary management and Sucraid<sup>®</sup> enzyme replacement therapy.

Although Sucraid<sup>®</sup> provides replacement therapy for deficient sucrase, it does not provide specific replacement therapy for any deficient isomaltase. Therefore, restricting starch in the diet may still be necessary to help reduce gastrointestinal symptoms as much as possible. The need for dietary starch restriction should be evaluated under a physician’s care.

**Sucraid<sup>®</sup>**  
(sacrosidase)  
oral solution

**A simple solution for a difficult disease**  
[www.sucraid.net](http://www.sucraid.net)

**SUCRAID<sup>®</sup> (sacrosidase) Oral Solution**

**DESCRIPTION**  
SUCRAID<sup>®</sup> (sacrosidase) oral solution is an enzyme replacement therapy for the treatment of genetically determined sucrose deficiency, which is part of congenital sucrose-isomaltase deficiency (CSID).

**CHEMISTRY**  
SUCRAID is a pale yellow, clear solution with a pleasant sweet taste. Each milliliter (mL) of SUCRAID contains 8,500 International Units (IU) of the enzyme sacrosidase, the active ingredient. The chemical name of this enzyme is β-D-fructofuranoside fructohydrolase. The enzyme is derived from baker's yeast (*Saccharomyces cerevisiae*).

It has been reported that the primary amino acid structure of this protein consists of 513 amino acids with an apparent molecular weight of 100,000 g/mole for the glycosylated monomer (Range 66,000-116,000 g/mole). Reports also suggest that the protein exists in solution as a monomer, dimer, tetramer, and octamer ranging from 100,000 g/mole to 800,000 g/mole. It has an isoelectric point of 4 (pI=4.093). SUCRAID may contain small amounts of papsin. Papsin is known to cause allergic reactions in some people. Papsin is a protein-cleaving enzyme that is introduced in the manufacturing process to digest the cell wall of the yeast and may not be completely removed during subsequent process steps.

SUCRAID also contains 50% glycerol (w/w) in an aqueous solution. Glycerol (glycerin) in the amount consumed in the recommended doses of SUCRAID has no expected toxicity. This enzyme preparation is fully soluble with water, milk, and infant formula (DO NOT HEAT SOLUTIONS CONTAINING SUCRAID). Do not put SUCRAID in warm or hot liquids.

**CLINICAL PHARMACOLOGY**

Congenital sucrose-isomaltase deficiency (CSID) is a chronic, autosomal recessive, inherited, phenotypically heterogeneous disease with very variable enzyme activity. CSID is usually characterized by a complete or almost complete lack of endogenous sucrose activity, a very marked reduction in isomaltase activity, a moderate decrease in maltase activity and normal lactase levels. Sucrose is naturally produced in the brush border of the small intestine, primarily the distal duodenum and jejunum. Sucrose hydrolyzes the disaccharide sucrose into its component monosaccharides, glucose and fructose. Isomaltase breaks down disaccharides from starch into simple sugars. SUCRAID does not contain isomaltase.

In the absence of endogenous human sucrose, 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. This may result in loose stools.

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. Previously, the treatment of CSID has required the continual use of a strict sucrose-free diet.

CSID is often difficult to diagnose. Approximately 4% to 10% of pediatric patients with chronic diarrhea of unknown origin have CSID. Measurement of expired breath hydrogen under controlled conditions following a sucrose challenge (a measurement of excess hydrogen excreted in exhalation) in CSID patients has shown levels as great as 6 times that in normal subjects.

A generally accepted clinical definition of CSID is a condition characterized by the following: stool pH <6, an increase in breath hydrogen of > 10ppm when challenged with sucrose after fasting

and a negative lactose breath test. However, because of the difficulties in diagnosing CSID, it may be warranted to conduct a short therapeutic trial (e.g. one week) to assess response in patients suspected of having CSID.

**CLINICAL STUDIES**

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 I.U./mL) and three dilutions (1:10 [900 I.U./mL], 1:100 [90 I.U./mL], and 1:1000 [9 I.U./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 endpoints. 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 endpoints.

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 I.U./mL), 1:1000 (9 I.U./mL), 1:10,000 (0.9 I.U./mL), and 1:100,000 (0.09 I.U./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.

**INDICATIONS AND USAGE**

SUCRAID (sacrosidase) oral solution is indicated as oral replacement therapy of the genetically determined sucrose deficiency, which is part of congenital sucrose isomaltase deficiency. (CSID)

**CONTRAINDICATIONS**

Patients known to be hypersensitive to yeast, yeast products, glycerin (glycerol), or papsin.

**WARNINGS**

Severe wheezing, 90 minutes after a second dose of sacrosidase, necessitated admission into the ICU for a 4-year old boy. The wheezing was probably caused by sacrosidase. He had asthma and was being treated with steroids. A skin test for sacrosidase was positive.

Other serious events have not been linked to SUCRAID.

**PRECAUTIONS**

Care should be taken to administer initial doses of SUCRAID near (within a few minutes' travel) a facility where acute hypersensitivity reactions can be adequately treated. Alternatively, the patient may be tested for hypersensitivity to SUCRAID through skin abrasion testing. Should symptoms of hypersensitivity appear, discontinue medication and initiate symptomatic and supportive therapy.

Skin testing as a rechallenge has been used to verify hypersensitivity in one asthmatic child who displayed wheezing after oral sacrosidase.

**GENERAL**

Although SUCRAID provides replacement therapy for the

deficient sucrose, it does not provide specific replacement therapy for the deficient isomaltase. Therefore, restricting starch in the diet may still be necessary to reduce symptoms as much as possible. The need for dietary starch restriction for patients using SUCRAID should be evaluated in each patient. It may sometimes be clinically inappropriate, difficult or inconvenient to perform a small bowel biopsy or breath hydrogen test to make a definitive diagnosis of CSID. If the diagnosis is in doubt, it may be warranted to conduct a short therapeutic trial (e.g. one week) with SUCRAID to assess response in a patient suspected of sucrose deficiency. The effects of SUCRAID have not been evaluated in patients with secondary (acquired) disaccharidase deficiencies.

**INFORMATION FOR PATIENTS:**

See Patient Package Insert. Patients should be instructed to discard bottles of SUCRAID 4 weeks after opening due to the potential for bacterial growth. For the same reason, patients should be advised to rinse the measuring scoop with water after each use.

SUCRAID is fully soluble with water, milk and infant formula, but it is important to note that this product is sensitive to heat. SUCRAID should not be reconstituted or consumed with fruit juice, since its acidity may reduce the enzyme activity.

**USE IN DIABETICS:**

The use of SUCRAID will enable the products of sucrose hydrolysis - glucose and fructose to be absorbed. This fact must be carefully considered in planning the diet of diabetic CSID patients using SUCRAID.

**LABORATORY TESTS:**

The definitive test for diagnosis of CSID is the measurement of intestinal disaccharidases following small bowel biopsy. Other tests used alone may be inaccurate: for example, the breath hydrogen test (high incidence of false-negatives) or oral sucrose tolerance test (high incidence of false positives). Differential urinary disaccharide testing has been reported to show good agreement with small intestinal biopsy for diagnosis of CSID.

**DRUG INTERACTIONS:**

Neither drug-drug nor drug-food interactions are expected or have been reported with the use of SUCRAID. However, SUCRAID should not be reconstituted or consumed with fruit juice, since its acidity may reduce the enzyme activity.

**CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY:**

Long-term studies in animals with SUCRAID have not been performed to evaluate the carcinogenic potential. Studies to evaluate the effect of SUCRAID on fertility or its mutagenic potential have not been performed.

**PREGNANCY:**

Teratogenic effects. Pregnancy Category C. Animal reproduction studies have not been conducted with SUCRAID. SUCRAID is not expected to cause fetal harm when administered to a pregnant woman or to affect reproductive capacity. SUCRAID should be given to a pregnant woman only if clearly needed.

**NURSING MOTHERS:**

The SUCRAID enzyme is broken down in the stomach and intestines and the component amino acids and peptides are then absorbed as nutrients.

**PEDIATRIC USE:**

SUCRAID has been used in patients as young as 5 months of age. Evidence in one controlled trial in primarily pediatric patients shows that SUCRAID is safe and effective for the treatment of

the genetically acquired sucrose deficiency, which is part of CSID.

**ADVERSE REACTIONS**

Adverse experiences with SUCRAID in clinical trials were generally minor and were frequently associated with the underlying disease.

In clinical studies of up to 54 months duration, physicians treated a total of 52 patients with SUCRAID. The adverse experiences and respective number of patients reporting each event (in parenthesis) were as follows: abdominal pain (4), vomiting (3), nausea (2), diarrhea (2), constipation (2), insomnia (1) headache (1) nervousness (1) and dehydration (1).

Note: diarrhea and abdominal pain can be a part of the clinical presentation of the **genetically determined sucrose deficiency**, which is part of congenital sucrose-isomaltase deficiency (CSID). One asthmatic child experienced a serious hypersensitivity reaction (wheezing) probably related to sacrosidase (see Warnings). The event resulted in withdrawal of the patient from the trial but resolved with no sequelae.

**OVERDOSAGE**

Over dosage with SUCRAID has not been reported.

**DOSAGE AND ADMINISTRATION**

The recommended dosage is 1 or 2 mL (8,500 to 17,000 I.U.) or 1 or 2 full measuring scoops (each full measuring scoop equals 1mL = 28 drops from the SUCRAID container tip equals 1mL) taken orally with each meal or snack diluted with 2 to 4 ounces of water, milk or infant formula. 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 SUCRAID because heating is likely to decrease potency. SUCRAID should not be reconstituted or consumed with fruit juice since its acidity may reduce the enzyme activity. It is recommended that approximately half of the dosage be taken at the beginning of the meal or snack and the remainder be taken during the meal or snack. The recommended dosage is as follows:

- 1 mL (8,500 I.U.) (one full measuring scoop or 28 drops) per meal or snack for patients up to 15 kg in body weight.
  - 2mL (17,000 I.U.) (two full measuring scoops or 56 drops) per meal or snack for patients over 15 kg in body weight.
- Dosage may be measured with the 1 mL measuring scoop (provided) or by drop count method (1mL equals 28 drops from the SUCRAID container tip).

**HOW SUPPLIED**

SUCRAID is available in 118 mL (4 fluid ounces) translucent plastic bottles, packaged two bottles per box. Each mL of solution contains 8,500 International Units (I.U.) of sacrosidase. A 1 mL measuring scoop is provided with each bottle. A full measuring scoop is 1 mL. Store in a refrigerator at 2° - 8° C (36° - 46°F). Discard four weeks after first opening due to the potential for bacterial growth. Protect from heat and light.

**RX only.**

Manufactured by PrimaPharm, Inc., San Diego, CA 92121

Distributed by QOL Medical, LLC, Kirkland, WA 98033

To order, or for any questions call 1-866-528-4750 or [www.sucraid.net](http://www.sucraid.net)

NDC# 67871-111-04

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**SUCRAID<sup>®</sup> (sacrosidase) Oral Solution**

Please read this leaflet carefully before you take SUCRAID<sup>®</sup> (sacrosidase) oral solution or give SUCRAID to a child. Please do not throw away this leaflet. You may need to read it again at a later date. This leaflet does not contain all the information on SUCRAID. For further information or advice, ask your doctor or pharmacist.

**Before taking SUCRAID:**

**WARNING:** 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 travel) just in case there is an allergic reaction.

**INFORMATION ABOUT YOUR MEDICINE**

The name of your medicine is SUCRAID (sacrosidase) oral solution. It can be obtained only with a prescription from your doctor.

**The purpose of your medicine:**

SUCRAID is an enzyme replacement therapy for the treatment of the genetically determined sucrose deficiency, which is part of congenital sucrose-isomaltase deficiency (CSID). CSID is a condition where your body lacks the enzymes needed to break down and absorb sucrose (table sugar) and other sugars from starch.

The symptoms of CSID often include frequent watery diarrhea, abdominal pain, bloating, and gas. In many cases, the symptoms of CSID are similar to other medical problems. Only your doctor can make a definite diagnosis of CSID. SUCRAID can help improve the breakdown and absorption of sucrose (table sugar) from the intestine and can help relieve

the gastrointestinal symptoms of CSID.

SUCRAID does not break down a type of starch called isomaltose. Therefore, you may need to restrict the amount of starch in your diet. Your doctor will tell you if you should restrict the amount of starch in your diet.

**Discuss the following important information with your doctor before you begin to take SUCRAID:**

Tell your doctor if you are allergic to, have ever had a reaction to, or have ever had difficulty taking yeast, yeast products, or glycerin (glycerol).

Tell your doctor if you have diabetes. With SUCRAID, sucrose (table sugar) can be absorbed from your diet and your blood glucose levels may change. Your doctor will tell you if your diet or diabetes medicines need to be changed.

**Side effects to watch for:**

Some patients may have worse abdominal pain, vomiting, nausea, or diarrhea. Constipation, difficulty sleeping, headache, nervousness, and dehydration have also occurred. Other side effects may also occur. If you notice these or any other side effects during treatment with SUCRAID, check with your doctor.

Stop taking SUCRAID and get emergency help immediately if any of the following side effects occur: difficulty breathing, wheezing, or swelling of the face.

**How to take your medicine:**

Each bottle of SUCRAID is supplied with a plastic screw cap which covers a dropper dispensing tip. Remove the outer cap and measure out the required dose. Reseal the bottle after each use by replacing and twisting the cap until tight.

Write down the date the sealed bottle is first opened in the space provided on the bottle label. Always throw away the bottle four weeks after first opening it because SUCRAID

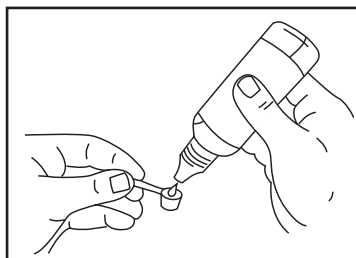
contains no preservatives. For the same reason, you should rinse the measuring scoop with water after each time you finish using it.

To get the full benefits of this medicine, it is very important to take SUCRAID as your doctor has prescribed. The usual dosage is 1 to 2 milliliters (mL) with each meal or snack: 1mL = 1 full measuring scoop (28 drops from the bottle tip) and 2 mL = 2 full measuring scoops (56 drops from the bottle tip). Measure your dose with the measuring scoop provided (see Figure 1). Do not use a kitchen teaspoon or other measuring device since it will not measure an accurate dose.

**Figure 1. Measure dose with measuring scoop.**

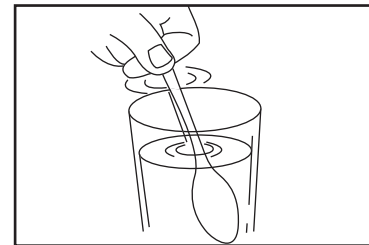
Mix your dose in 2 to 4 ounces of water, milk, or infant formula (see Figure 2). SUCRAID should not be dissolved in or taken with fruit juice.

**NEVER HEAT SUCRAID OR PUT IT IN WARM OR HOT BEVERAGES OR INFANT FORMULA.** Heating SUCRAID causes it to lose its effectiveness. The beverage or infant formula should be taken cold or at room temperature.



**Figure 2. Mix dose in beverage or infant formula.**

It is recommended that approximately half of your dosage be taken at the beginning of each meal or snack and the remainder of your dosage be taken during the meal or snack.



**Storing your medicine:**

SUCRAID 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. Always store SUCRAID in a refrigerator at 36°F - 46°F (2°C - 8°C). Protect SUCRAID from heat and light.

If your bottle of SUCRAID has expired (the expiration date is printed on the bottle label), throw it away. Keep this medicine in a safe place in your refrigerator where children cannot reach it.

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For questions call 1-866-528-4750

Rev 12/08

Part No. 0110

**References:**

1. Treem WR. Clinical heterogeneity in congenital sucrose-isomaltase deficiency. *J Pediatr*.1996;128:727-729. 2. Sucraid<sup>®</sup> Prescribing Information.