

Unresolved Gas, Bloating, Diarrhea...Could It Be CSID?

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QOL Medical, LLC

Financial Disclosures

- [Disclose financial relationships with manufacturers and medical organizations here (e.g., QOL Medical, LLC); if none, list “None.”]

COULD IT BE
CSID

CONGENITAL SUCRASE-ISOMALTASE DEFICIENCY



WHAT IS CSID?

CSID: Congenital Sucrase-Isomaltase Deficiency

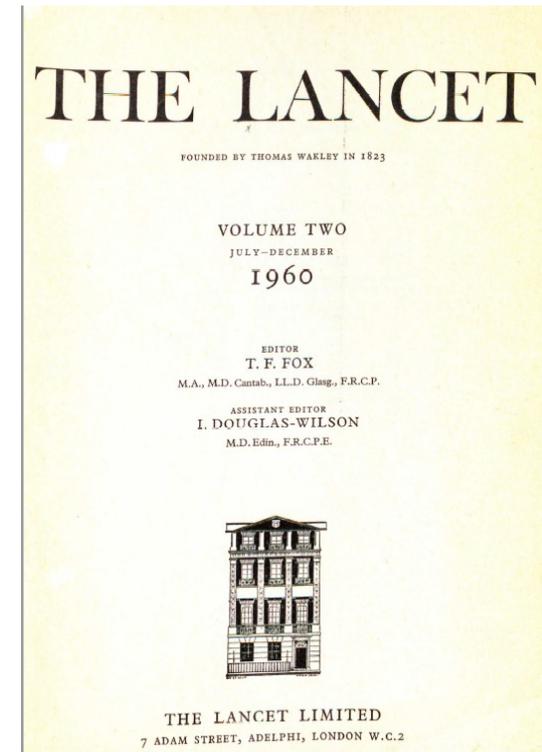
Sucrase-Isomaltase

- An enzyme that digests the majority of dietary carbohydrates
 - Table sugar (sucrose) and many starches (e.g., potatoes, bread)
- Expressed in the microvilli of the brush border membrane
- Releases glucose and fructose from sucrose (sugar) so they can be absorbed into the bloodstream

Congenital Sucrase-Isomaltase Deficiency

The first report of an autosomal recessive Congenital Sucrase-Isomaltase Deficiency (CSID) was published in 1960.

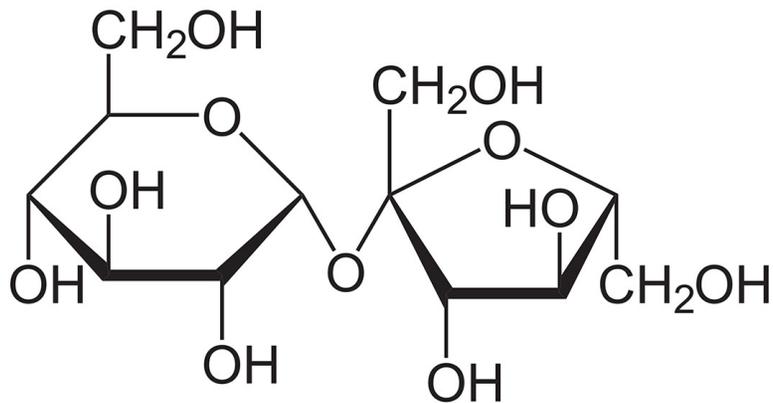
Diarrhoea Caused by Deficiency of Sugar-Splitting Enzymes



Weijers HA, Van De Kamer JH, Mossel DAA, Dicke WK. Diarrhoea Caused by Deficiency of Sugar-Splitting Enzymes. *Lancet*. 1960;276(7145):296-7.

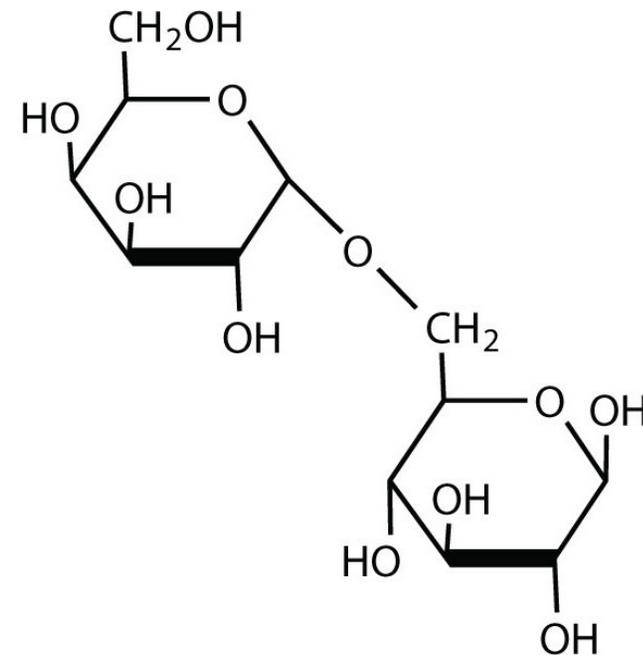
Sucrase-Isomaltase Substrates

Sucrose



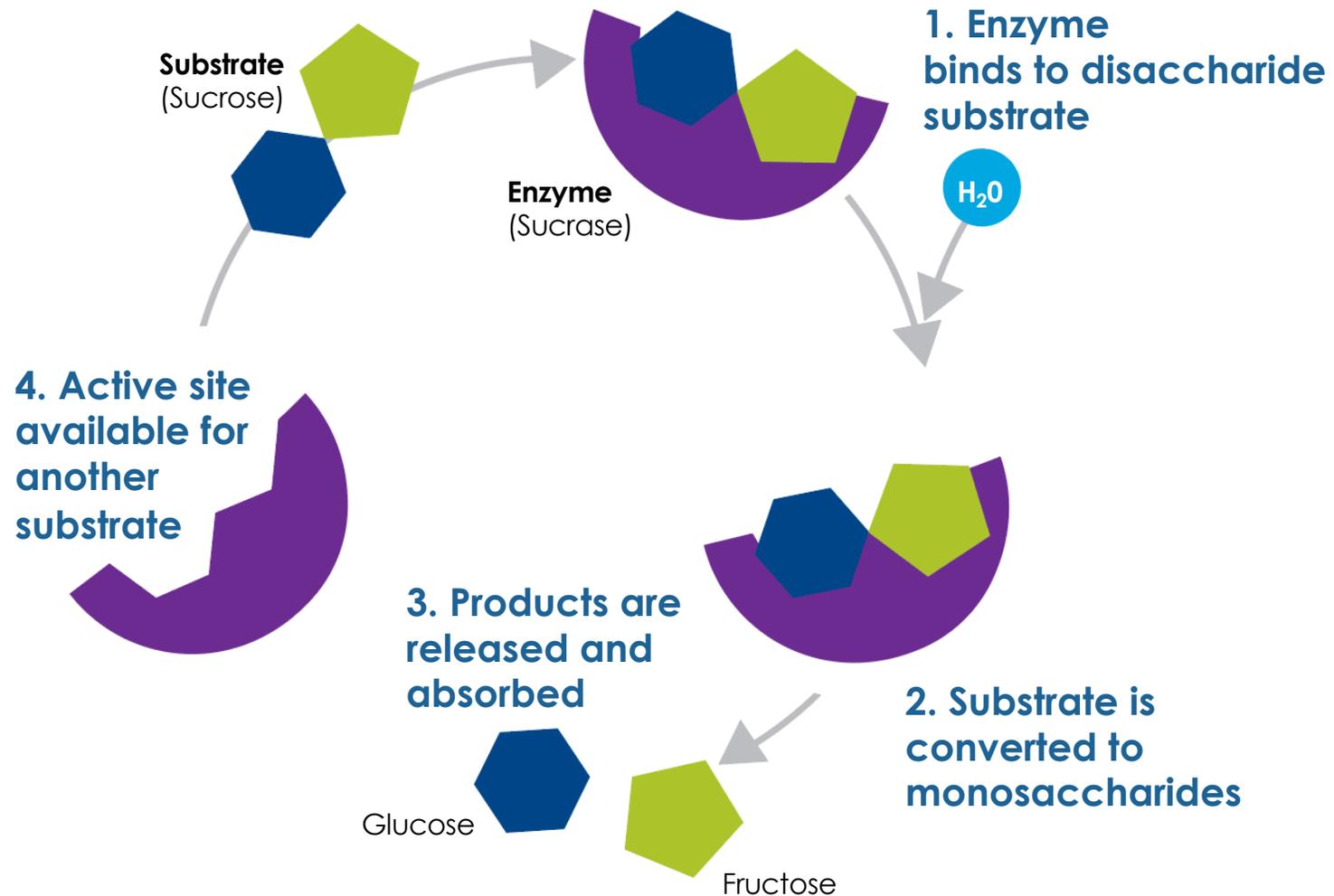
Glucose + Fructose
(α -1,2 glycosidic bond)

Isomaltose

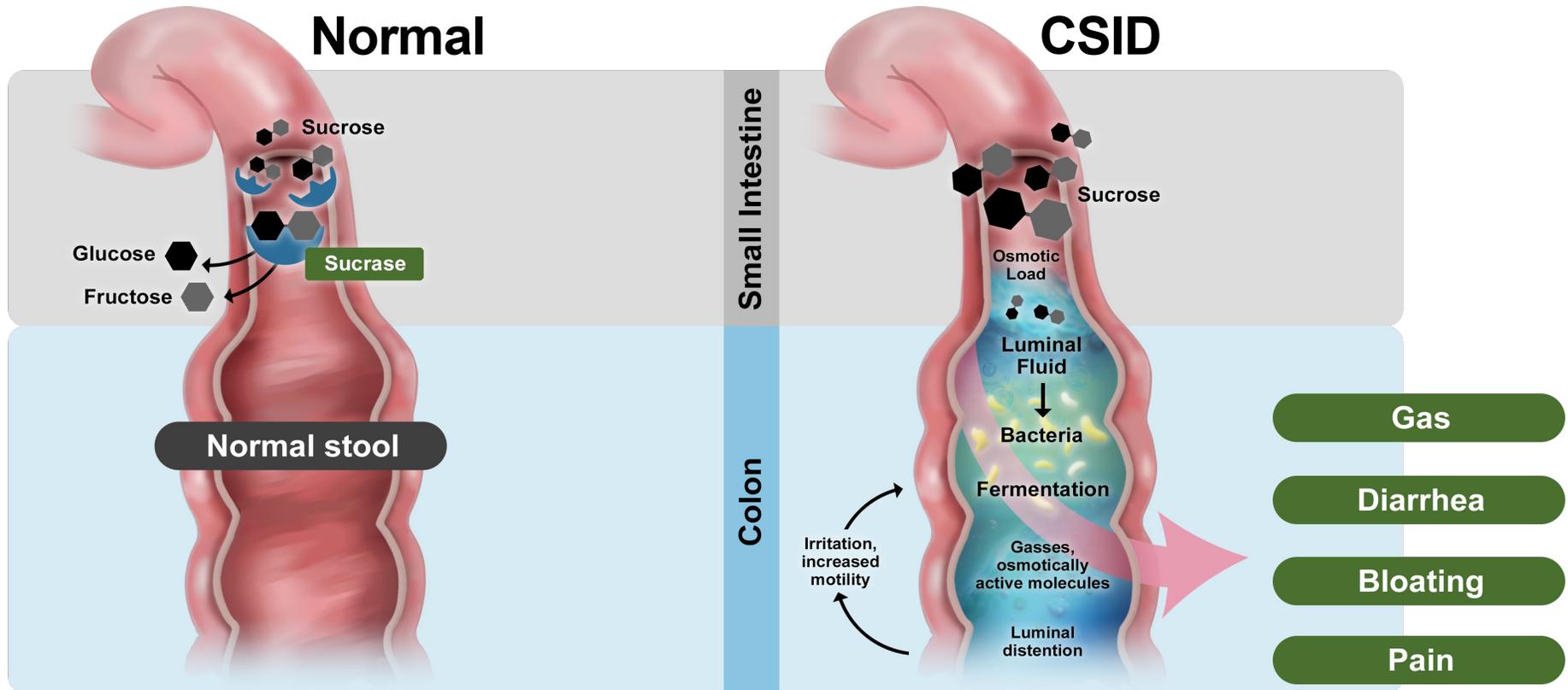


Glucose + Glucose
(α -1,6 glycosidic bond)

How Sucrase Works to Hydrolyze Sucrose



CSID Carb Maldigestion Pathophysiology



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HOW DO CSID PATIENTS PRESENT?

CSID Signs and Symptoms

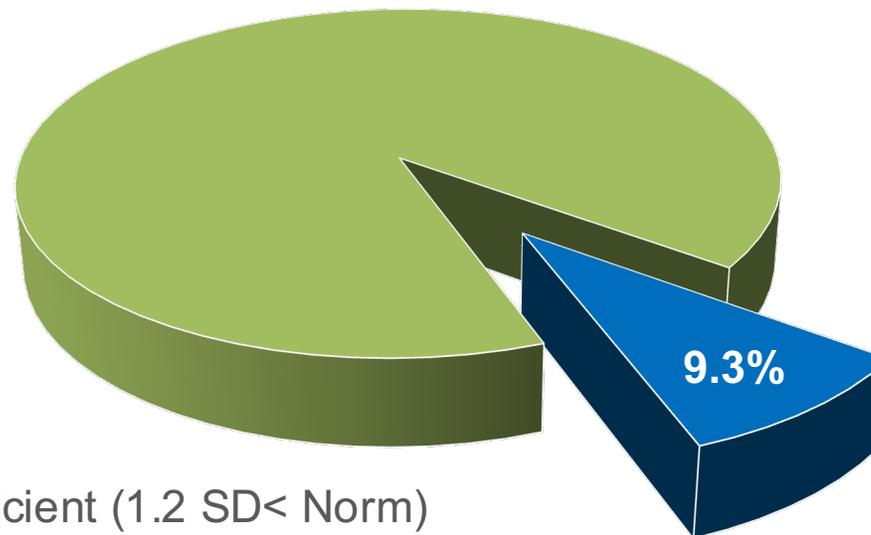
- Identifying the CSID Subset – FLiP
 - **F**requent: multiple events per day, multiple days per week (gas, bloating, diarrhea, abdominal pain, nausea, and vomiting)
 - **L**ifelong: truly chronic patients
 - **P**ostprandial: symptoms after eating
- Other Signs
 - High diarrhea frequency (CSID patients know where the bathrooms are throughout their daily routine)
 - Family history: likely relatives with chronic “IBS-D like” symptoms
 - Carb/sweet food avoidance: may report that very sugary desserts (birthday cake) cause more severe symptoms
 - Urgent need for bathroom

Diet Failures Can Help Identify CSID Patients

- Subset of gas/bloating/diarrhea patients who also report avoidance of sucrose and starch food items
- Low-FODMAP diet (does not exclude sucrose)
- Gluten-free diet (does not exclude sucrose or starches)

How Common Is Sucrase Deficiency?

Study of Idiopathic Sucrase Deficiency¹ N = 27,875*



- Sucrase Deficient (1.2 SD < Norm)
- Normal

*Based on disaccharidase analyses performed on small bowel biopsies.

1. Nichols BL Jr, Adams B, Roach CM, Ma CX, Baker SS. Frequency of Sucrase Deficiency in Mucosal Biopsies. *J Pediatr Gastroenterol Nutr.* 2012;55 (suppl 2):S28-30.

Incidence of Sucrase-Isomaltase Rare Pathogenic Variants (SI-RPV) in GI Patients

	Chronic Diarrhea ¹	IBS-D ²
Subjects (N)	308	952
CSID Variants (n)	14	40
Incidence	4.5%	4.2%

- SI-RPV does not always cause CSID, but highly correlated
- Data suggests a portion of CSID patients might be misdiagnosed with IBS-D
- IBS-D symptoms are very similar to CSID symptoms
- Consider CSID in your diagnostic algorithm *especially* if patient is unresponsive to low-FODMAP diet/IBS-D treatments

1. QOL Medical, LLC. Data on file. 2. Garcia-Etxebarria K, Zheng T, Bonfiglio F, et al. Increased Prevalence of Rare Sucrase-Isomaltase Pathogenic Variants in Irritable Bowel Syndrome Patients. *Clin Gastroenterol Hepatol.* 2018;16(10):1673-1676.

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HOW IS CSID DIAGNOSED?

Long-Term Symptoms, Combined With:

- EGD, biopsy, and disaccharidase assay
 - 2 extra distal duodenal biopsy samples
 - Send to specialty disaccharidase testing lab
- Other tests that aid in diagnosing sucrase deficiency include:
 - ^{13}C -Sucrose Breath Test
 - Sucrose Hydrogen-Methane Breath Test
 - Sucrose Challenge Symptoms Test (50 g)
 - Short therapeutic trial of Sucraid[®] (sacrosidase) Oral Solution for patients where CSID is suspected

Please see Sucraid[®] (sacrosidase) Oral Solution Important Safety Information within this presentation and full Prescribing Information provided with this presentation. Sucraid[®] may cause a serious allergic reaction.

Indication

- **Sucraid[®] (sacrosidase) Oral Solution** is an enzyme replacement therapy for the treatment of genetically determined sucrase deficiency, which is part of Congenital Sucrase-Isomaltase Deficiency (CSID).

Important Safety Information for Sucraid[®] (sacrosidase) Oral Solution

- **Sucraid[®] may cause a serious allergic reaction.** Patients should stop taking Sucraid[®] and get emergency help immediately if any of the following side effects occur: difficulty breathing, wheezing, or swelling of the face. Care should be taken when administering initial doses of Sucraid[®] to observe any signs of acute hypersensitivity reaction.
- Do not use Sucraid[®] with patients known to be hypersensitive to yeast, yeast products, papain, or glycerin (glycerol).
- Although Sucraid[®] provides replacement therapy for the deficient sucrase, it does not provide specific replacement therapy for the deficient isomaltase.

Please see additional Important Safety Information in this presentation.

Important Safety Information for Sucraid[®] (sacrosidase) Oral Solution (continued)

- Adverse reactions as a result of taking Sucraid[®] may include worse abdominal pain, vomiting, nausea, diarrhea, constipation, difficulty sleeping, headache, nervousness, and dehydration.
- Before prescribing Sucraid[®] to diabetic patients, the physician should consider that Sucraid[®] will enable sucrose hydrolysis and the absorption of those hydrolysis products, glucose and fructose.
- The effects of Sucraid[®] have not been evaluated in patients with secondary (acquired) disaccharidase deficiency.
- **DO NOT HEAT SOLUTIONS CONTAINING SUCRAID[®].** Do not put Sucraid[®] in warm or hot fluids. Do not reconstitute or consume Sucraid[®] with fruit juice since the acidity of the juice may reduce the enzyme activity of Sucraid[®]. Half of the reconstituted Sucraid[®] should be taken at the beginning of the meal or snack and the other half during the meal or snack.
- Sucraid[®] should be refrigerated at 36°F - 46°F (2°C - 8°C) and should be protected from heat and light; single-use containers can be removed from refrigeration and stored at 59°F-77°F (15°C-25°C) for up to 3 days (72 hours).

Full Prescribing Information can be accessed online at sucraidprescribinginformation.com and is available at this presentation.

Disaccharidase Assay - The Gold Standard

- Disaccharidase assays
 - Able to measure activity of 4 enzymes, depending on substrate used: lactase, sucrase, maltase, palatinase (isomaltase)
 - 2-3 extra distal duodenal biopsies (best near ampulla of Vater)
 - Freeze and dry ice ship to specialty lab (not path lab)
- Upper GI endoscopy (EGD) can be broadly helpful to:
 - Help rule in/out celiac disease or lactose intolerance
 - Assess small bowel health



Disaccharidase Assay Reference Intervals

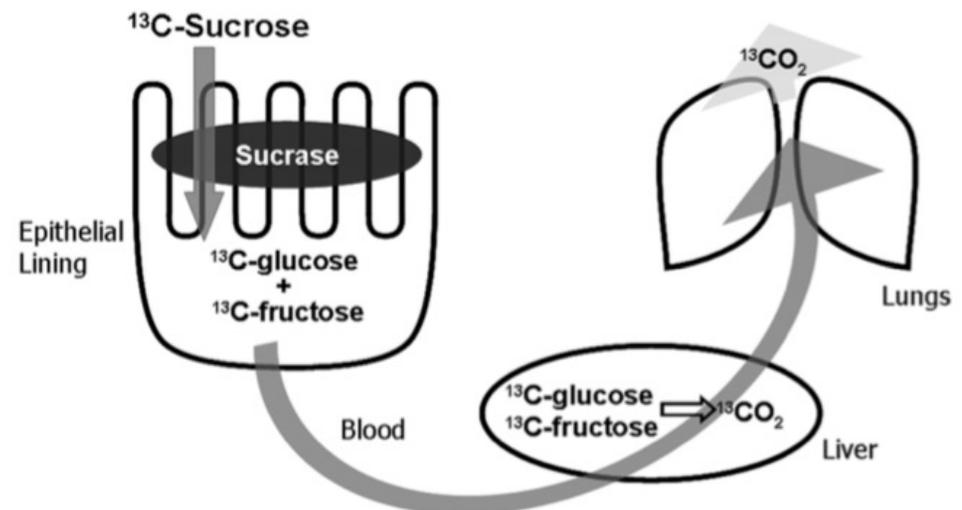
Disaccharidase	Normal Range*
Lactase	15 – 46 U/min/g protein
Sucrase	25 – 70 U/min/g protein
Maltase	100 – 224 U/min/g protein
Palatinase	5 – 26 U/min/g protein

*Subject to change following normal range studies conducted by the lab

Hackenmueller SA and Grenache DG. Reference Intervals for Intestinal Disaccharidase Activities Determined from a Non-Reference Population. *J Appl Lab Med*. 2016;1(2):172-80.

Sucrose Breath Test

- Test is noninvasive and can be administered by patient in the office or at home
- Patients with CSID may experience symptoms from the sucrose taken in the test
- For more information, or to order a test, call 1-800-705-1962



Principle of ^{13}C Breath Test

Sucrose Challenge Symptoms Test

Step 1:

Stir 4 tablespoons of ordinary table sugar into a 4-ounce glass of water. Mix until sugar is completely dissolved.

Step 2:

Drink it on an empty stomach.

Step 3:

See if symptoms such as bloating, gas, and diarrhea occur during the next 4-8 hours; such symptoms suggest that you might have sucrose intolerance.

Positives	Negatives
Simple and easy	No validation data
Cheap	Unknown negative and positive predictive value
Theoretically sensitive; high likelihood of symptoms in CSID	Likely severe symptoms in severe CSID patients

Therapeutic Trial When CSID Suspected

- For GI patients when:
 - Clinically inappropriate/difficult to perform biopsy for sucrase assay
 - Another putative diagnosis is in doubt
 - Clinical history/test results suggest possible CSID diagnosis
 - Short (e.g., one week) therapeutic trial for sucrase deficiency with enzyme replacement therapy
 - Significant symptom resolution supports CSID diagnosis

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TREATMENT

Sucraid® (sacrosidase) Oral Solution



- Sacrosidase is an enzyme derived from *Saccharomyces cerevisiae* (baker's yeast)
- Sucraid® helps CSID patients digest sucrose into fructose and glucose, which can then be absorbed into the bloodstream

Please see Sucraid® (sacrosidase) Oral Solution Important Safety Information within this presentation and full Prescribing Information provided with this presentation.

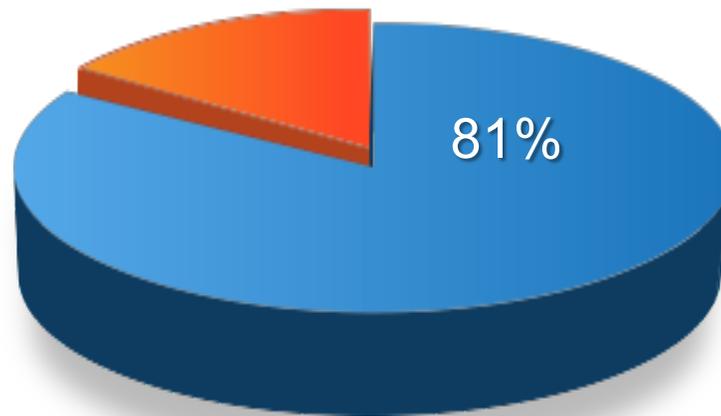
Sucraid® (sacrosidase) Oral Solution is an enzyme replacement therapy for the treatment of genetically determined sucrase deficiency, which is part of Congenital Sucrase-Isomaltase Deficiency (CSID).

Sucraid® may cause a serious allergic reaction. Sucraid® shouldn't be used by patients who are known to be hypersensitive to yeast, yeast products, papain, or glycerin (glycerol).

Sucraid[®] Overall Symptomatic Response

81% of patients became asymptomatic*
with Sucraid[®] in a 10-day clinical trial

N = 26



■ **Asymptomatic Patients with Sucraid[®]**

*Asymptomatic defined as symptom-free for at least 7 of the 10 study days.

Please see Sucraid[®] (sacrosidase) Oral Solution Important Safety Information within this presentation and full Prescribing Information provided with this presentation. Sucraid[®] may cause a serious allergic reaction.

Treem WR, McAdams L, Stanford L, Kastoff G, Justinich C, Hyams J. Sacrosidase Therapy for Congenital Sucrase-Isomaltase Deficiency. *J Pediatr Gastroenterol Nutr.* 1999;28(2):137-42.

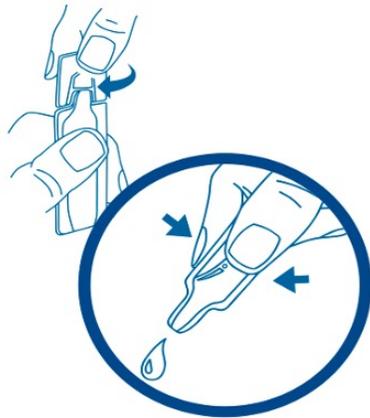
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HOW TO TAKE SUCRAID® (sacrosidase) ORAL SOLUTION

Administering Sucraid® Single-Use



Twist cap off single-use container. **Squeeze** contents into 4 oz of water, milk, or infant formula.



Mix your dose. Sucraid® should not be dissolved in or taken with fruit juice.



Half of your Sucraid® dosage should be taken at the beginning of each meal or snack and the remainder of your dosage should be taken during the meal or snack.

Sucraid® (sacrosidase) Oral Solution Single-Use dose is indicated for patients who are > 33 lbs. It should not be mixed with hot beverages, fruit juice, or other acidic beverages as this may reduce the efficacy of Sucraid®.

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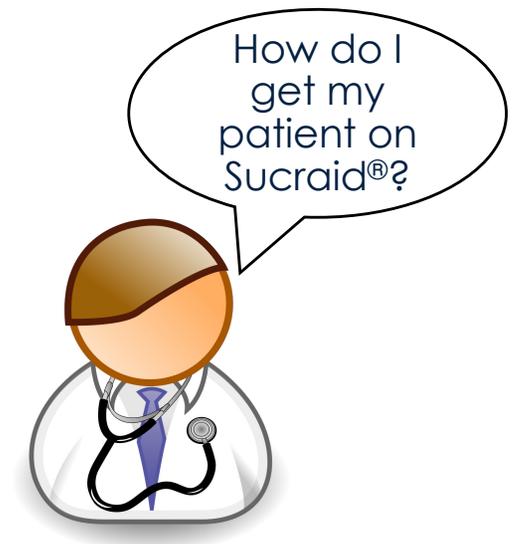
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**PRESCRIBE SUCRAID®
(sacrosidase) ORAL
SOLUTION**

A Positive CSID Patient: What Now?

- Frontier Therapies – Optum is the exclusive distributing specialty pharmacy for Sucraid[®] (sacrosidase) Oral Solution
- To prescribe Sucraid[®] and minimize treatment delays, prescribing healthcare providers should submit the following:
 - Valid prescription
 - Patient's pharmacy insurance information
 - Diagnostic test results
 - Supporting clinical documentation
 - ✓ ICD-10 diagnosis code
 - ✓ Progress notes
 - ✓ Tried and failed therapies
 - ✓ Diet modifications



Please see Sucraid[®] (sacrosidase) Oral Solution Important Safety Information within this presentation and full Prescribing Information provided with this presentation. Sucraid[®] may cause a serious allergic reaction.

How Do I Send in the Prescription?



Phone: 1-833-800-0122 Fax: 1-866-850-9155

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HOW TO GET SUCRAID[®] (sacrosidase) ORAL SOLUTION

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Sucraid[®] must be kept cold and is only available from one specialty pharmacy, Frontier Therapies – Optum . It cannot be ordered from retail pharmacies.

Please see Sucraid[®] (sacrosidase) Oral Solution Important Safety Information within this presentation and full Prescribing Information provided with this presentation. Sucraid[®] may cause a serious allergic reaction.

Helpful Information

For Product Information:

Frontier Therapies – Optum, Specialty Pharmacy

Phone: 1 (833) 800-0122

Fax: 1 (866) 850-9155

Sucraid.com

Please see Sucraid® (sacrosidase) Oral Solution Important Safety Information within this presentation and full Prescribing Information provided with this presentation. Sucraid® may cause a serious allergic reaction.

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QUESTIONS?

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THANK YOU

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Email@QOLMed.com]

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