

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

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QOL Medical, LLC

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## 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

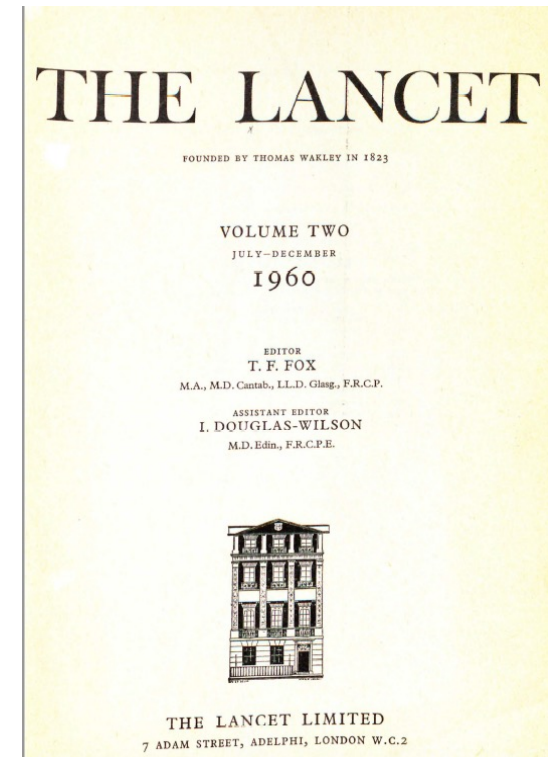
## Sucrase-Isomaltase

- 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.

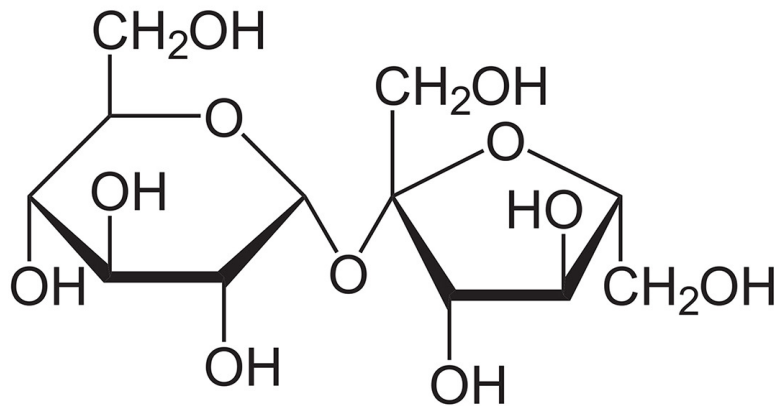
## Diarrhoea Caused by Deficiency of Sugar-Splitting Enzymes



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

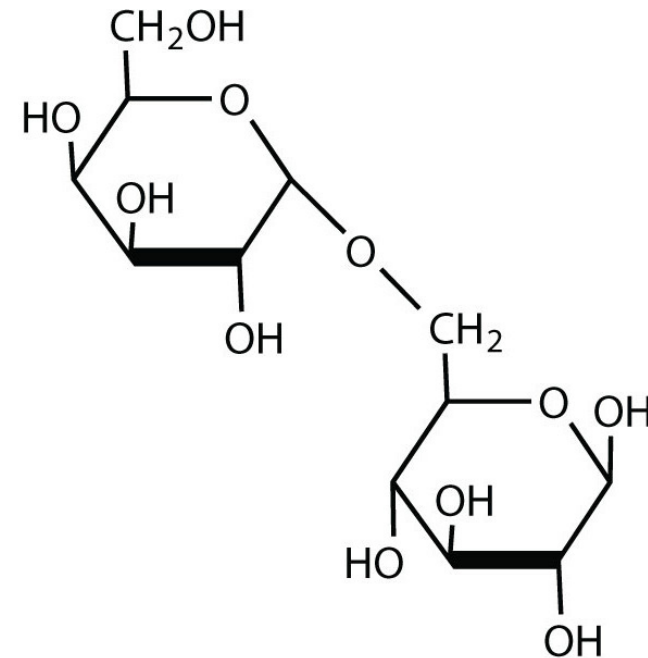
## Sucrase-Isomaltase Substrates

### Sucrose



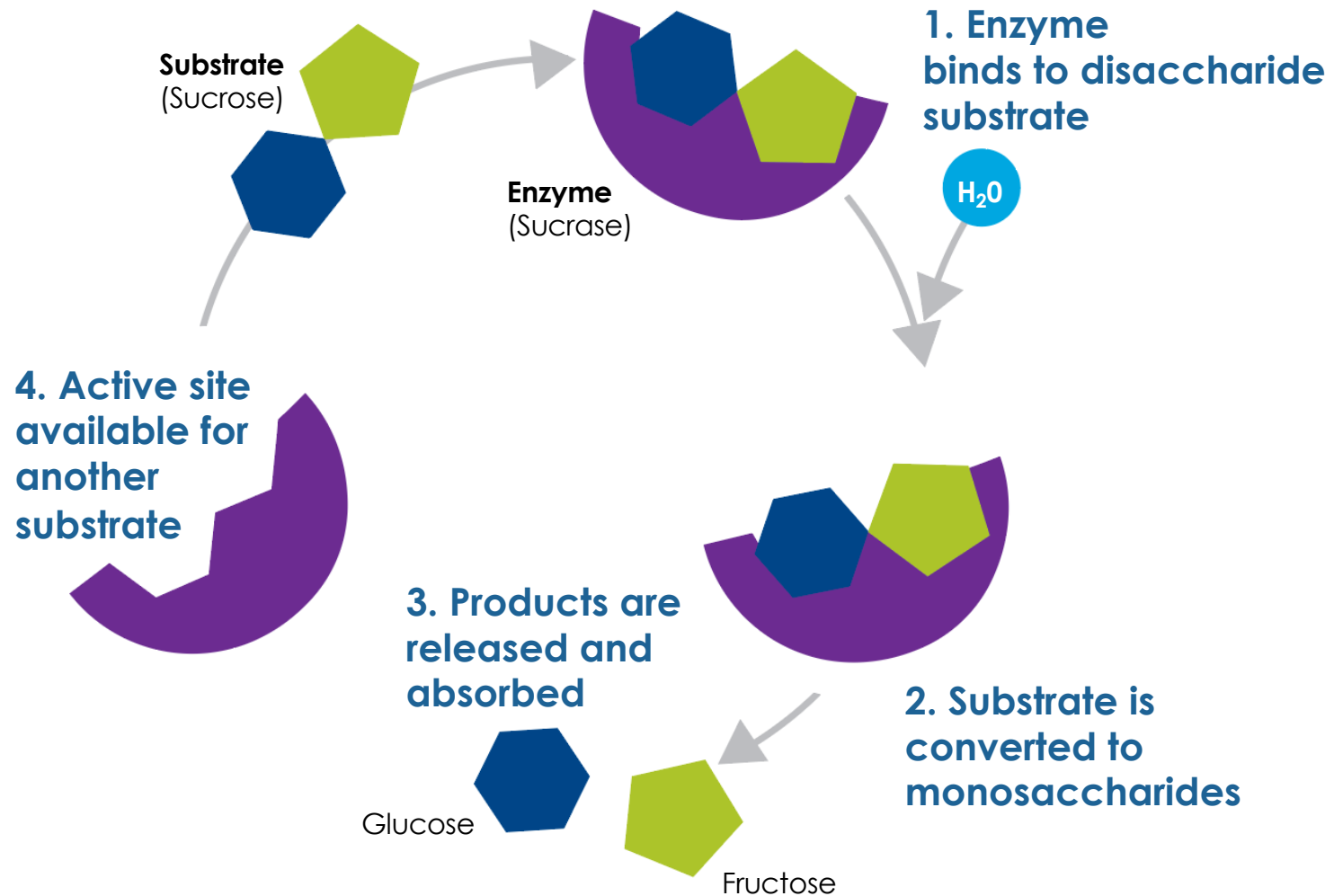
Glucose + Fructose  
( $\alpha$ -1,2 glycosidic bond)

### Isomaltose

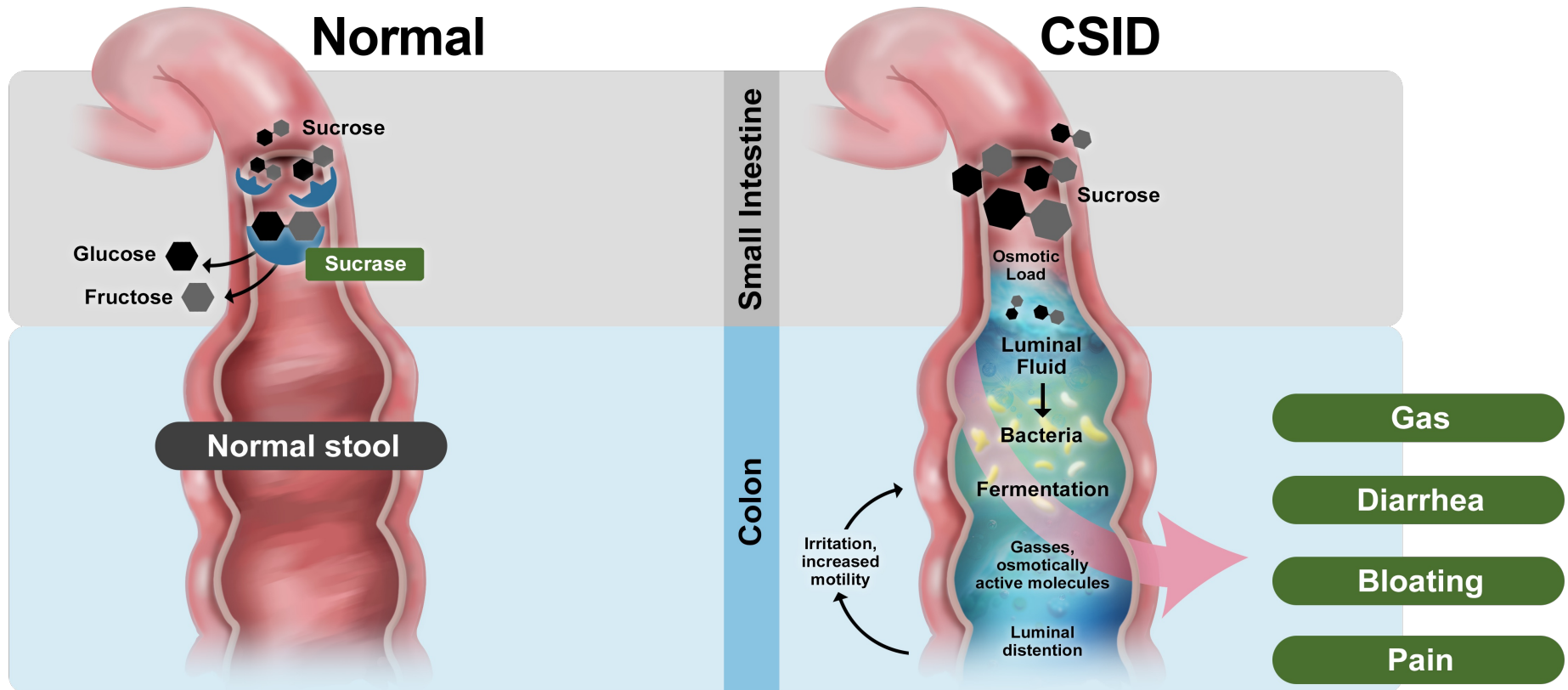


Glucose + Glucose  
( $\alpha$ -1,6 glycosidic bond)

# How Sucrase Works to Hydrolyze Sucrose



# CSID Carb Maldigestion Pathophysiology





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# HOW DO CSID PATIENTS PRESENT?

## CSID Signs and Symptoms

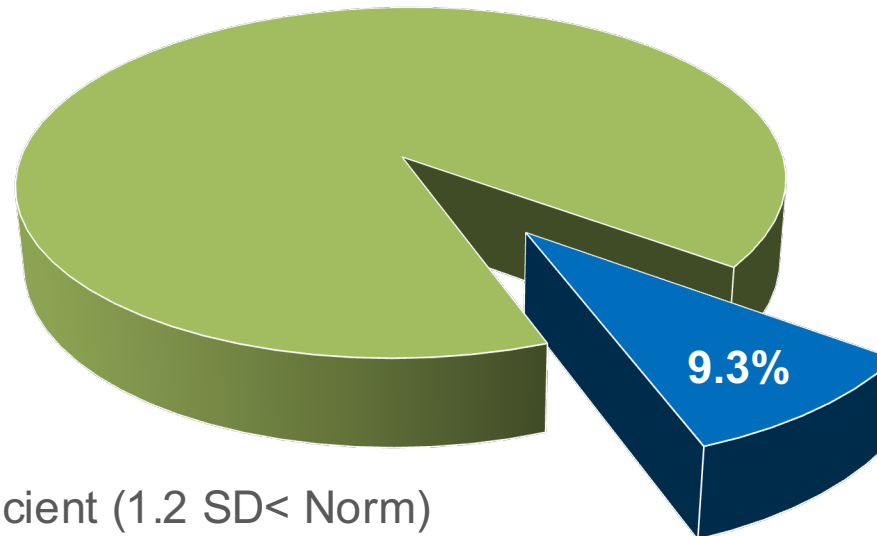
- Identifying the CSID Subset – FLiP
  - **F**requent: multiple events per day, multiple days per week (gas, bloating, diarrhea, abdominal pain, nausea, and vomiting)
  - **L**ifelong: truly chronic patients
  - **P**ostprandial: symptoms after eating
- Other Signs
  - High diarrhea frequency (CSID patients 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 Deficiency<sup>1</sup> 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 <sup>1</sup>	IBS-D <sup>2</sup>
Subjects (N)	308	952
CSID Variants (n)	14	40
<b>Incidence</b>	<b>4.5%</b>	<b>4.2%</b>

- 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:
  - $^{13}\text{C}$ -Sucrose Breath Test
  - Sucrose Hydrogen-Methane Breath Test
  - Sucrose Challenge Symptoms Test (50 g)
  - Short therapeutic trial of Sucraid<sup>®</sup> (sacrosidase) Oral Solution for patients where CSID is suspected

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



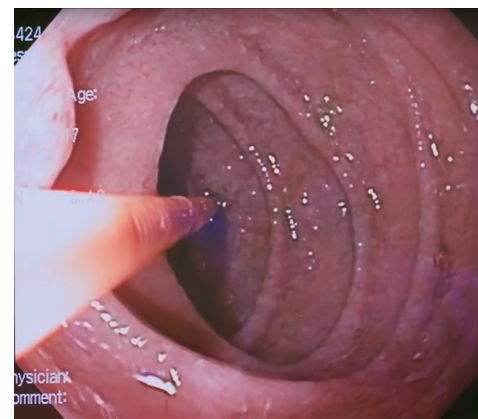
## Important Safety Information for Sucraid<sup>®</sup> (sacrosidase) Oral Solution (continued)

- Adverse reactions as a result of taking Sucraid<sup>®</sup> may include worse abdominal pain, vomiting, nausea, diarrhea, constipation, difficulty sleeping, headache, nervousness, and dehydration.
- Before prescribing Sucraid<sup>®</sup> to diabetic patients, the physician should consider that Sucraid<sup>®</sup> will enable sucrose hydrolysis and the absorption of those hydrolysis products, glucose and fructose.
- The effects of Sucraid<sup>®</sup> have not been evaluated in patients with secondary (acquired) disaccharidase deficiency.
- **DO NOT HEAT SOLUTIONS CONTAINING SUCRAID<sup>®</sup>.** Do not put Sucraid<sup>®</sup> in warm or hot fluids. Do not reconstitute or consume Sucraid<sup>®</sup> with fruit juice since the acidity of the juice may reduce the enzyme activity of Sucraid<sup>®</sup>. Half of the reconstituted Sucraid<sup>®</sup> should be taken at the beginning of the meal or snack and the other half during the meal or snack.
- Sucraid<sup>®</sup> 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](http://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

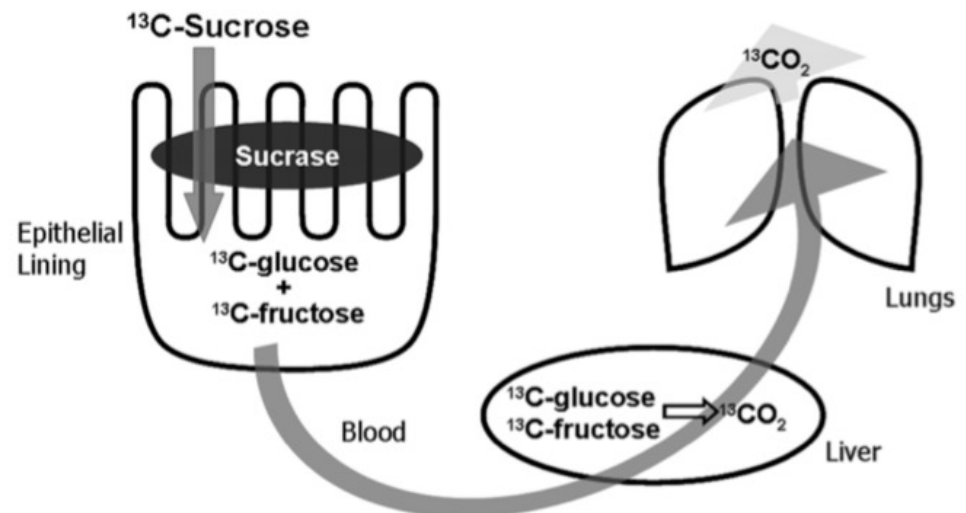
Disaccharidase	Normal Range*
Lactase	15 – 46 U/min/g protein
Sucrase	25 – 70 U/min/g protein
Maltase	100 – 224 U/min/g protein
Palatinase	5 – 26 U/min/g protein

\*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  $^{13}\text{C}$  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).

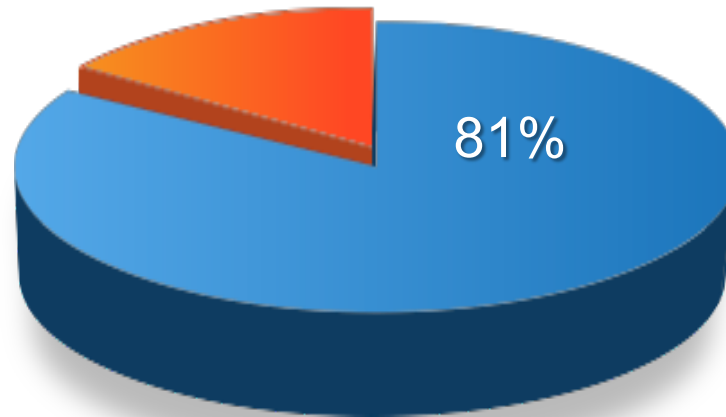
Sucraid® may cause a serious allergic reaction. Sucraid® shouldn't be used by patients who are known to be hypersensitive to yeast, yeast products, papain, or glycerin (glycerol).



## Sucraid<sup>®</sup> Overall Symptomatic Response

**81%** of patients became asymptomatic\*  
with Sucraid<sup>®</sup> in a 10-day clinical trial

N = 26



■ Asymptomatic Patients with Sucraid<sup>®</sup>

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

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

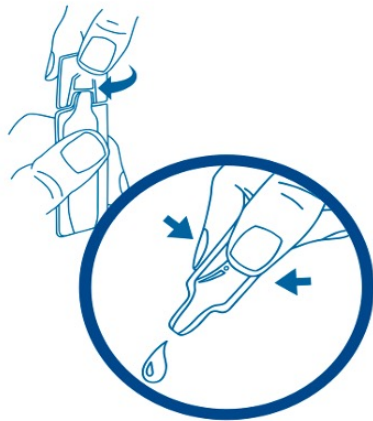
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# HOW TO TAKE SUCRAID® (sacrosidase) ORAL SOLUTION

## 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®.

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

## A Positive CSID Patient: What Now?

- Frontier Therapies – Optum is the exclusive distributing specialty pharmacy for Sucraid<sup>®</sup> (sacrosidase) Oral Solution
- To prescribe Sucraid<sup>®</sup> 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<sup>®</sup> (sacrosidase) Oral Solution Important Safety Information within this presentation and full Prescribing Information provided with this presentation. Sucraid<sup>®</sup> 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<sup>®</sup> (sacrosidase) ORAL SOLUTION

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

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# QUESTIONS?

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# THANK YOU

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