GENETIC SUCRASE-ISOMALTASE DEFICIENCY (GSID)

CLINICIAN TRAINING
Genetic Sucrase-Isomaltase Deficiency (GSID) Clinician Training

Introduction

As a clinician you probably encounter patients complaining of bloating, gas, abdominal pain, or bouts of diarrhea on a daily basis, where it may be difficult to arrive at a definitive diagnosis. Sometimes the patients’ symptoms have been going on for years, and they may have seen multiple specialists. The patients may have also tried their own interventions, including taking probiotics, or eliminating gluten and milk from their diet, but are still experiencing frequent symptoms.

For these patients, you might have a routine checklist you go through to narrow down the possible diagnoses. First you rule out symptoms that point to more severe diseases, such as cancer and inflammatory bowel disease. Then you may consider the more common disorders, such as lactose intolerance and irritable bowel syndrome. Genetic Sucrase-Isomaltase Deficiency (GSID) might not be on the list of diagnoses that you consider, or maybe you are not familiar with GSID. The purpose of this booklet is to raise your awareness of the clinical presentation, diagnosis, and management of GSID.

Learning Objectives

After reading this booklet you should be able to

- Identify the clinical symptoms associated with GSID in adults
- Discuss the mechanism of disease in GSID
- Describe the role of sucrose hydrogen breath testing in the diagnosis of GSID
- Interpret results of a sucrose hydrogen breath test
- Describe diet modifications for patients with GSID
- Identify patients that could benefit from sacrosidase treatment

Genetic Sucrase-Isomaltase Deficiency (GSID)

Clinical Presentation

An undiagnosed adult patient with GSID will often have had intermittent symptoms since infancy, when sucrose first gets introduced in their diet. The symptoms in adults range from episodes with diarrhea, or alterations in bowel habits accompanied by abdominal distention and gas, to chronic abdominal pain. The severity and type of clinical symptoms vary, making GSID difficult to diagnose. Often the adult patient is thought to suffer from more common diseases such as irritable bowel syndrome (IBS), and the diagnosis is delayed or missed. The differential diagnosis section later in this module highlights other conditions that have similar symptoms as GSID.
Table 1. Potential Presenting Symptoms of GSID in Adults\textsuperscript{1,3}

- Dyspepsia (indigestion)
- Abdominal distention
- Abdominal pain
- Gas
- Diarrhea

Potential Presenting Symptoms in Infancy and Childhood\textsuperscript{3}

- Watery diarrhea
- Bloating/gas
- Abdominal pain
- Irritability
- Diaper rash
- Failure to thrive
- Nausea/vomiting

Definition

**GSID**

Genetic Sucrase-Isomaltase Deficiency (GSID) is an autosomal recessive disorder caused by mutations in the gene responsible for the production of disaccharidases, specifically sucrase and isomaltase (also referred to as the SI gene). The gene defect results in enzyme deficiency, causing disruptions in the digestion of sucrose and starch. The disorder may present in infancy, childhood, adolescence, or adulthood.\textsuperscript{4,5}

Historically, the term Congenital Sucrase-Isomaltase Deficiency (CSID) was used for a disorder in which all affected individuals were thought to be homozygous for the same mutated allele at the same location of each chromosome in a pair (Figure 1). Newer research has shown that the inheritance pattern of the disease is more complex. The term GSID is now used as a more appropriate umbrella term for all genetically determined sucrase deficiencies. We now know that GSID can present with a compound heterozygous inheritance pattern where affected individuals have two different abnormal alleles (Figure 2). Studies have shown many variants of the SI gene with at least 37 different mutations causing GSID, and variations of the phenotype including symptomatic carriers.\textsuperscript{2,5,6,7,8}

Patients may refer to this condition as sucrose intolerance since there is literature in the social community around this topic. It is important to differentiate that sucrose intolerance may be a broader label than GSID.

Did You Know?

There are at least 37 known disease-causing mutations included in genetic testing for GSID, and more are still being discovered. This should be kept in mind when interpreting results of genetic testing in patients suspected of suffering from GSID, since disease-causing mutations not included in the assays will result in false negative test results.\textsuperscript{8}
Acquired Sucrase-Isomaltase Deficiency (SID)
As the name suggests, acquired sucrase-isomaltase deficiency (SID) is a secondary symptom in the presence of an underlying disease that has resulted in diffuse mucosal damage. There are several known causes for mucosal damage. Usually when the underlying disease is treated, and the mucosal damage is corrected, the symptoms of acquired SID are also corrected.9

Table 2. Potential Etiologies of Sucrase-Isomaltase Deficiency

<table>
<thead>
<tr>
<th>Genetic</th>
<th>Acquired</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal recessive (GSID)</td>
<td>Celiac disease</td>
</tr>
<tr>
<td></td>
<td>Small intestinal bacterial overgrowth</td>
</tr>
<tr>
<td></td>
<td>Inflammatory bowel disease/Crohn’s disease</td>
</tr>
<tr>
<td></td>
<td>Gastroenteritis</td>
</tr>
<tr>
<td></td>
<td>Other causes of mucosal damage</td>
</tr>
<tr>
<td>Homozygote (CSID)</td>
<td></td>
</tr>
<tr>
<td>Compound heterozygote</td>
<td></td>
</tr>
<tr>
<td>Heterozygote symptomatic carrier</td>
<td></td>
</tr>
</tbody>
</table>

Epidemiology
Historically, estimates of GSID in individuals of European descent range from 0.2% to 0.05%. There is a lower prevalence reported in African Americans and Hispanics. The highest prevalences are seen in the Inuit populations of Greenland (5%-10%), Alaska (3%-7%), and Canada (about 3%).2,3

Recent studies have shown that the prevalence might be higher than previously thought. In 750 symptomatic pediatric subjects, S/ polymorphisms were identified10:

- At a similar rate (3.5%) to those reported in previous literature (3%-10%), but population included various ethnicities and races
- More frequently in children with functional diarrhea (4.3%) compared to those with functional abdominal pain (2.7%)
- Primarily in Caucasian and African American subjects
Pathophysiology

Digestion and Absorption of Carbohydrates

Before moving on to discuss the mechanism of disease in GSID, it is important to keep in mind what the normal process is of digesting and absorbing sugars in the intestine. Carbohydrates are classified as either simple or complex. Simple sugars include monosaccharides and disaccharides, whereas complex carbohydrates include oligosaccharides (fibers) and polysaccharides (starch) (Figure 3).

Figure 3. Types of Carbohydrates

In order for carbohydrates to be absorbed in the intestine, they need to be broken down into monosaccharides. This process starts with salivary and pancreatic amylases breaking down starch into oligo- and disaccharides. The digestion continues in the microvilli brush border of the small intestine, where the oligo- and disaccharides are broken down into monosaccharides by the disaccharidases (Figure 4).\(^\text{11}\)
Once the carbohydrates are broken down into monosaccharides, they are absorbed by facilitated diffusion and active transportation across the brush border of the epithelial cells. They then diffuse across the basolateral membranes of the epithelial cells into the bloodstream.\textsuperscript{11}

**GSID Mechanism of Disease**

The sucrase-isomaltase (SI) glycoprotein is part of the disaccharidase enzymes located in the intestinal brush border. SI is responsible for the final step of the digestion of dietary sucrose and starch into the monosaccharides glucose and fructose for absorption (Table 3).\textsuperscript{5}

**Table 3. Disaccharide Substrates of Sucrase-Isomaltase (SI)\textsuperscript{12}**

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Digesting Enzyme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sucrose</td>
<td>Sucrase-Isomaltase 99%</td>
</tr>
<tr>
<td>Maltose</td>
<td>Sucrase-Isomaltase 72%</td>
</tr>
<tr>
<td></td>
<td>Maltase-Glucoamylase 18%</td>
</tr>
<tr>
<td>Isomaltose</td>
<td>Sucrase-Isomaltase 95%</td>
</tr>
</tbody>
</table>
Mutations of the SI gene lead to deficiencies of the SI glycoprotein. As previously mentioned, there are many different mutations leading to GSID, and there is also a large variation in phenotypes. All GSID patients lack fully functional sucrase, while the isomaltase activity can vary from minimal functionality to almost normal activity. The presence of residual isomaltase activity may explain why some patients with GSID are able to better tolerate starch in their diet than others.¹

The enzyme deficiency ultimately leads to malabsorption of dietary disaccharides and starch in the proximal small intestine. The undigested carbohydrates create an osmotic pressure drawing water into the lumen of the intestine, resulting in a large volume of intraluminal fluid. The passage of undigested disaccharides into the large intestine leads to fermentation by the resident colonic bacteria. The sugar molecules are broken down into short-chain fatty acids and gases, including hydrogen (H₂), carbon dioxide (CO₂), and methane (CH₄). When the capacity of colonic bacteria to ferment the undigested carbohydrates and the ability of the colon to reabsorb excess fluid has been exceeded, the result is watery diarrhea, gas, abdominal distension, and pain (Figure 5).¹,¹³

Figure 5. Pathophysiology of GSID

Not all patients with GSID will suffer from the same symptoms. Some experience chronic diarrhea or abdominal pain, while others have both or some other combination of symptoms. The symptoms of patients with GSID are dependent on several factors, including¹

- Residual enzyme activity
- Amount of carbohydrate in the diet
- Rate of gastric emptying
- Small-bowel transit time
• Activity of colonic bacteria
• Absorptive capacity of the colon

Diagnosis
Once you have obtained the patient’s clinical history, and it is indicative of GSID, there are a few test options to consider. The gold standard for diagnosing GSID is performing an esophagogastroduodenoscopy (EGD) to obtain a small intestine biopsy, and send it to a specialized laboratory where measurement of lactase, maltase, sucrase, and isomaltase (palatinase) enzyme activity is performed. Other tests that have been proposed include the Sucraid® (sacrosidase) Oral Solution therapy trial, which has been deemed to be diagnostic in the presence of other symptoms, and two tests that may aid in the diagnosis of GSID: the hydrogen breath test and buccal swab genetic testing.

Tests that Diagnose GSID

Endoscopic Biopsy with Disaccharidase Enzyme Activity Assay
Measuring the enzyme activity of lactase, maltase, sucrase, and isomaltase palatinase in a biopsy from the small intestine is the gold standard of GSID diagnostic tests. In order to diagnose GSID, the endoscopy will show normal small bowel morphology together with the enzyme activities shown in Table 4.

<table>
<thead>
<tr>
<th>Disaccharidase</th>
<th>Enzyme Activity</th>
<th>Normal Range (µmole/min/g protein)</th>
<th>Deficient (µmole/min/g protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sucrase</td>
<td>Absent or markedly reduced</td>
<td>29.0-79.8</td>
<td>&lt;25</td>
</tr>
<tr>
<td>Isomaltase</td>
<td>From absent to slightly reduced</td>
<td>4.6-17.6</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Maltase</td>
<td>Reduced</td>
<td>98.0-223.6</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Lactase</td>
<td>Normal or reduced</td>
<td>16.5-32.5</td>
<td>&lt;15</td>
</tr>
</tbody>
</table>

Sucraid® Therapeutic Trial
Because of the difficulties in diagnosing GSID, it may be warranted to conduct a short therapeutic trial (e.g., one week) of Sucraid® (sacrosidase) Oral Solution to assess response in patients suspected of having GSID. It will be important to determine that the patient has GSID as opposed to acquired SID. Sucraid® is only indicated for GSID. See the full prescribing information in Appendix A.
Tests that Aid in the Diagnosis of GSID

Sucrose Hydrogen Breath Test

Although this test is only to be used to aid in the diagnosis of GSID, it is nevertheless an important test to consider. The sucrose hydrogen breath test measures hydrogen, and some tests also measure methane in breath samples after ingestion of a sucrose load. Healthy individuals do not have a source for hydrogen production in the small intestine, so a rise in breath hydrogen levels would indicate malabsorption of sucrose. Hydrogen will only be produced if unabsorbed carbohydrates reach the bacterial flora in the colon, or if the bacteria migrate into the small intestine, as is the case in small intestinal bacterial overgrowth (SIBO).16 15%-30% of people have bacteria in the gut that convert hydrogen to methane, in which case the breath test could show low or no detectable hydrogen, while the methane levels could be elevated.17,18 When the bacterial fermentation of undigested carbohydrates results in production of hydrogen and methane, the gases pass through the intestinal wall into the blood. Through the blood stream they reach the lungs, where they are exhaled and can be measured with a breath test.17

Administration of the Breath Test

If a patient presents with symptoms that could indicate GSID, you have the option to order a sucrose hydrogen breath test for the patient to administer at home.

The patient ingests sucrose, collects breath samples at timed intervals, and hydrogen and methane levels are determined at the laboratory. Please check with your office on how to order the test for your patient. See a sample order form in Appendix B. The test will be sent directly to the patient’s home where they will perform the test and send the samples directly back to the laboratory for analysis.

The patient will receive instructions on how to administer the test. You should inform the patient of the following restrictions and requirements19:

- 24-hour preparation period prior to the test; 12 hours of dietary restrictions leading up to 12 hours of complete fasting
- Testing takes 3 hours
- Antibiotics must be discontinued 2 weeks prior to the test
- Probiotics must be discontinued 4-5 days prior to the test
- No smoking, sleeping, or exercising for 1 hour prior to and during the test
- Patient may experience symptoms after ingestion of the sucrose load

Dietary Restrictions Prior to Breath Test

The following foods are not allowed for 12 hours before the 12-hour fasting period19:

- Grain products
- Fruits and fruit juice
- Sugar
- Dairy products
- Vegetables
- Nuts and seeds
- Beans
- Beverages containing alcohol

IMPORTANT: Probiotics must be discontinued 4-5 days prior to the test otherwise the test results will be affected
Please see Appendix C for full patient instructions from Commonwealth Laboratories, Inc.

Upon receipt of the completed breath test, results will be available after 24 hours and will be sent to you for interpretation. Please see Appendix D for an example of a full report sheet.

**Interpretation of the Breath Test**

Normal gas levels in the breath samples are hydrogen <20 and methane <12 parts per million (ppm). The test is considered positive if the following peak levels are seen at any time during the test:\(^20,21\):

- Hydrogen concentration ≥20 ppm
- Methane concentration ≥12 ppm
- Combination of hydrogen and methane ≥15 ppm.

If the ingested sucrose is not digested and absorbed in the small intestine, it will reach the colon within 1 to 2 hours, depending on the transit time. The gases released during bacterial fermentation will result in a rise in the levels of hydrogen and methane in the alveolar air reflected in the samples collected at that time (60, 90, and 120 minutes in the examples below).\(^17\)

When utilizing a breath test analyzing both hydrogen and methane in the exhaled air, there are 4 possible outcomes:\(^21\):

- Normal test, sucrose malabsorption is not supported (Figure 6)
- Hydrogen response is elevated above normal, methane response is normal; suggests sucrose malabsorption (Figure 7)
- Methane response elevated above normal, hydrogen response is normal; suggests sucrose malabsorption (Figure 8)
- Combination of hydrogen and methane response suggests sucrose malabsorption (Figure 9, 10)

Following are examples of the 4 testing outcomes for your reference. Please see Appendix D for an example of a full report sheet.

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**Did You Know?**

Although the patient is fasting and only allowed water for the last 12 hours before the test, it is still recommended that they brush their teeth in the morning before the test in order to eliminate hydrogen production by oral bacteria. Toothpaste containing sorbitol or xylitol does not interfere with test results.\(^18,20\)
Figure 6. Normal Test

<table>
<thead>
<tr>
<th>Sample</th>
<th>ppm H₂</th>
<th>ppm CH₄</th>
<th>(f) CO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30 min</td>
<td>2</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>60 min</td>
<td>3</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>90 min</td>
<td>4</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>120 min</td>
<td>5</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>150 min</td>
<td>6</td>
<td>0</td>
<td>7</td>
</tr>
</tbody>
</table>

Summary of 2 Hour Results

Peak increase values for each trace gas are presented below:

- **Peak Hydrogen Production:** 0 ppm  
  Normal <20 ppm
- **Peak Methane Production:** 9 ppm  
  Normal <12 ppm
- **Peak Combined H₂ and CH₄ Production:** N/A ppm  
  Normal <15 ppm

SUCROSE MALABSORPTION IS NOT SUPPORTED BY HYDROGEN ONLY
SUCROSE MALABSORPTION IS NOT SUPPORTED BY METHANE ONLY
COMBINED GAS PRODUCTION NOT APPLICABLE
Figure 7. Hydrogen Response Suggests Sucrose Malabsorption

<table>
<thead>
<tr>
<th>Sample</th>
<th>ppm H₂</th>
<th>ppm CH₄</th>
<th>(f) CO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>30 min</td>
<td>3</td>
<td>0</td>
<td>0.98</td>
</tr>
<tr>
<td>60 min</td>
<td>11</td>
<td>0</td>
<td>0.88</td>
</tr>
<tr>
<td>90 min</td>
<td>80</td>
<td>0</td>
<td>1.06</td>
</tr>
<tr>
<td>120 min</td>
<td>75</td>
<td>0</td>
<td>0.94</td>
</tr>
<tr>
<td>150 min</td>
<td>90</td>
<td>0</td>
<td>0.98</td>
</tr>
</tbody>
</table>

Summary of 2 Hour Results

Peak increase values for each trace gas are presented below:

- **Peak Hydrogen Production:** 88 ppm  Normal <20 ppm
- **Peak Methane Production:** 0 ppm  Normal <12 ppm
- **Peak Combined H₂ and CH₄ Production:** N/A ppm  Normal <15 ppm

**SUCROSE MALABSORPTION IS SUPPORTED BY HYDROGEN ONLY**
**SUCROSE MALABSORPTION IS NOT SUPPORTED BY METHANE ONLY**
**COMBINED GAS PRODUCTION NOT APPLICABLE**
Figure 8. Methane Response Suggests Sucrose Malabsorption

<table>
<thead>
<tr>
<th>Sample</th>
<th>ppm H₂</th>
<th>ppm CH₄</th>
<th>(f) CO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30 min</td>
<td>2</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>60 min</td>
<td>3</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>90 min</td>
<td>4</td>
<td>0</td>
<td>53</td>
</tr>
<tr>
<td>120 min</td>
<td>5</td>
<td>0</td>
<td>43</td>
</tr>
<tr>
<td>150 min</td>
<td>6</td>
<td>0</td>
<td>47</td>
</tr>
</tbody>
</table>

Summary of 2 Hour Results

Peak increase values for each trace gas are presented below:

- Peak Hydrogen Production: 0 ppm, Normal <20 ppm
- Peak Methane Production: 53 ppm, Normal <12 ppm
- Peak Combined H and CH₄ Production: N/A ppm, Normal <15 ppm

SUCROSE MALABSORPTION IS NOT SUPPORTED BY HYDROGEN ONLY
SUCROSE MALABSORPTION IS SUPPORTED BY METHANE ONLY
COMBINED GAS PRODUCTION NOT APPLICABLE
Figure 9. Both Hydrogen and Methane Response Suggests Sucrose Malabsorption

<table>
<thead>
<tr>
<th>Sample</th>
<th>ppm H₂</th>
<th>ppm CH₄</th>
<th>(f) CO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30 min</td>
<td>2</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>60 min</td>
<td>3</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>90 min</td>
<td>4</td>
<td>30</td>
<td>39</td>
</tr>
<tr>
<td>120 min</td>
<td>5</td>
<td>51</td>
<td>45</td>
</tr>
<tr>
<td>150 min</td>
<td>6</td>
<td>71</td>
<td>58</td>
</tr>
</tbody>
</table>

Summary of 2 Hour Results

Peak increase values for each trace gas are presented below:

- Peak Hydrogen Production: 71 ppm, Normal <20 ppm
- Peak Methane Production: 58 ppm, Normal <12 ppm
- Peak Combined H₂ and CH₄ Production: 128 ppm, Normal <15 ppm

SUCROSE MALABSORPTION IS SUPPORTED BY HYDROGEN ONLY
SUCROSE MALABSORPTION IS SUPPORTED BY METHANE ONLY
SUCROSE MALABSORPTION IS SUPPORTED BY COMBINED GASES ONLY
Finally, a test can be deemed invalid if the amount of CO₂ in the sample is low, since this is a sign of poor patient sampling for the following reasons²¹:

- The patient did not cap the tube quickly enough per instructions
- The patient did not capture his/her actual alveolar air (where CO₂ had time to be produced by the lungs)
- The patient did not use the straw
- The patient did not collect his/her breath at all
Usually, the lab will identify these invalid tests and a new test will be provided at no additional cost to the patient by Commonwealth Laboratories. However, if you feel that the test is invalid for whatever reason, please contact Commonwealth Laboratories to send the patient a new test. Figure 11 shows an example of an invalid test.

Figure 11. Invalid Test

<table>
<thead>
<tr>
<th>Sample</th>
<th>ppm H₂</th>
<th>ppm CH₄</th>
<th>(f) CO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>*</td>
<td>*</td>
<td>12.50</td>
</tr>
<tr>
<td>30 min</td>
<td>6</td>
<td>3</td>
<td>0.98</td>
</tr>
<tr>
<td>60 min</td>
<td>0</td>
<td>6</td>
<td>0.88</td>
</tr>
<tr>
<td>90 min</td>
<td>*</td>
<td>*</td>
<td>8.33</td>
</tr>
<tr>
<td>120 min</td>
<td>*</td>
<td>*</td>
<td>25.00</td>
</tr>
<tr>
<td>150 min</td>
<td>*</td>
<td>*</td>
<td>16.67</td>
</tr>
</tbody>
</table>

Summary of 2 Hour Results

Peak increase values for each trace gas are presented below:

- Peak Hydrogen Production: 0 ppm Normal <20 ppm
- Peak Methane Production: 3 ppm Normal <12 ppm
- Peak Combined H₂ and CH₄ Production: N/A ppm Normal <15 ppm

When interpreting the results of the breath test it is important to consider the clinical signs and symptoms of the patient. Keep in mind that a breath test does not provide a definitive diagnosis of GSID, but can be an important diagnostic tool to help evaluate patients with suspected GSID. Some patients will experience severe symptoms when ingesting the sucrose load, and this should be taken into consideration when interpreting the test results.³
It is important to be aware of both false negative and false positive reports. Some of the considerations include\textsuperscript{3,16,22}:

- **False negative reports**
  - Absence of hydrogen-producing bacteria
  - Delayed gastric emptying
  - Antibiotic interference with intestinal bacterial flora

- **False positive reports**
  - SIBO (can cause hydrogen release before normal absorption of sugar would occur)
  - Rapid transit through small intestine
  - Acquired SID (the test can’t distinguish between primary and secondary SID)

If you have any questions, or need help with interpreting the breath test results, you can contact the clinical team at Commonwealth Laboratories by email: interpretations@commlabsinc.com.

**Genetic Testing**

Genetic testing for GSID is also clinically available, but it may not be a useful screening tool due to the variable mutations of the $SI$ gene. There have been over 37 $SI$ mutations identified, and more could be identified in the future. Currently, the assays do not include all variations of pathogenic mutations, therefore false negative results are possible. It may, however, be a useful screening tool in a family with a member who already has confirmed GSID\textsuperscript{8,23}.

**Differential Diagnosis**

As you have already learned, diarrhea and abdominal pain can be two of the main symptoms of GSID, but there are many other diseases that present with diarrhea and other gastrointestinal symptoms. In getting to the right diagnosis, you will have to consider the differential diagnoses. This should be guided by the patient’s age, history, symptoms, and by diagnostic tests. To complicate the process even further, some of these diseases can cause acquired SID, or can occur concurrent with GSID. Overview of differential diagnoses and etiology is seen in Table 5.
Sucraid® (sacrosidase) Oral Solution Important Safety Information

Before we go into treatment options for patients with a diagnosis of GSID, let’s review some important safety information for a pharmaceutical, Sucraid® (sacrosidase) Oral Solution, used to treat the symptoms of GSID.25

**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**

- Although Sucraid® provides replacement therapy for the deficient sucrase, it does not provide specific replacement therapy for the deficient isomaltase.

- Do not use Sucraid® (sacrosidase) Oral Solution with patients known to be hypersensitive to yeast, yeast products, papain, or glycerin (glycerol).

- 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.

- 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 clinician should consider that Sucraid® will enable sucrose hydrolysis and the absorption of those hydrolysis products, glucose and fructose.

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**Table 5. Differential Diagnoses of Diseases Presenting with Similar Symptoms to GSID**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactase deficiency, fructose intolerance, celiac disease</td>
<td>Impaired digestion and absorption</td>
</tr>
<tr>
<td>Infectious disease, giardiasis, SIBO, laxative abuse</td>
<td>Altered secretion</td>
</tr>
<tr>
<td>Celiac disease, inflammatory bowel disease, food allergies</td>
<td>Immune dysregulation</td>
</tr>
<tr>
<td>Cancer, strictures</td>
<td>Altered gut transit</td>
</tr>
<tr>
<td>Irritable bowel syndrome</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
• 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.

Treatment

What can the patient with GSID do to relieve his or her symptoms? There are only a few options, including diet and/or enzyme replacement therapy. Once a GSID diagnosis is made, the clinician and patient will decide on the next steps together. There are 5 different options for the patient to choose from:

• The patient can choose diet only to control their sucrose and/or starch intolerance.
• The patient can choose a trial of Sucraid® (sacrosidase) Oral Solution to treat their sucrase deficiency along with complimentary supportive services from the SucraidASSIST™ program.
• The patient can choose a trial of Sucraid® along with a diet to control starch intake to help relieve symptoms from their starch enzyme deficiency. Again, SucraidASSIST™ can help.
• The patient can decide that they do not want drug or diet, and continue to treat the disease as they have been.
• The patient can consult another clinician regarding their symptoms and the results of their testing.

Please see Appendix G for information on how to order Sucraid® and see Appendix I for more information about the SucraidASSIST™ program.

Diet Modification of Sucrose and Starch

Patients with lactose intolerance can get relief from their symptoms by avoiding or limiting dairy products.
in their diet, so it seems straightforward to instruct patients with GSID to avoid sucrose and starch. However, the sources of sucrose and starch in the diet are much more varied than lactose, so the patient may need a lot of guidance on eliminating sucrose and starch from their diet, preferably with the help of a dietitian.

**Dietary Sources of Carbohydrates**

The typical American consumes about 51% of their calories in the form of carbohydrates, with about 30% of the carbohydrate calories coming from sucrose and about 60% from starch. Sucrose and starch is prevalent in many of the common foods in the American diet and neither nutrient is included on the Nutrition Facts food label. The ingredient label lists the type of sugar and starch. In addition to avoiding the ingredient sucrose, patients are instructed to also avoid cane juice, cane syrup, brown sugar, and powdered sugar, which are just other terms for sucrose. Other polysaccharides or starch ingredients to avoid include maltodextrin, tapioca starch, corn syrup, or glucose polymers. However, ingredients such as dextrose, fructose or high fructose corn syrup would be acceptable on the GSID diet.

**Elimination Phase**

The elimination phase of the modified diet involves elimination of sucrose and starch from the diet for a duration of two weeks. The Adult Diet Guide provides a full listing of low sucrose, low starch foods."See Appendix E. Patients may choose to eat a variety of these foods including dairy foods, protein, non-starchy vegetables, low sucrose fruits, nuts, nut butters, fats, and sucrose free sweeteners. A similar listing of permissible foods can be found at CSIDcares.org: http://csidcares.org/treatment/diet/

There is also a Menu Guide that helps patients plan meals and snacks that are low in sucrose and starch. See Appendix F.

**Sucrose**

- All table sugar is eliminated
- All sucrose containing “sweets”, such as candy, jelly, jams, and syrups are eliminated
- All fruits with a high sucrose content such as apples, bananas, melons, oranges, pineapple, and peaches are eliminated
- All fruit juices and sucrose-containing beverages are eliminated
- Vegetables with a high sucrose content such as carrots are eliminated

**Starch**

- All commonly consumed “complex carbohydrates” such as rice, wheat, grains, quinoa, lentils, and other grains are eliminated
- All baked and processed foods containing starch such as cereals, breads, crackers, pasta, baked goods, and tortillas are eliminated
- Vegetables with a high starch content such as corn, beans, peas, and potatoes are eliminated
- Fruits with a high starch content such as bananas are eliminated
Induction Phase
The induction phase of the modified diet follows the 2 week elimination phase. The elimination diet is very restrictive and it is important that, during the induction phase, patients introduce foods back into the diet to avoid the risk of nutrient deficiencies. One new food is introduced every 3-5 days. Sucrose tolerance levels are established first, then followed by starch tolerance. This process may take many months and successful implementation will require assistance from a dietitian.26

Referral to Dietitian
Once a diagnosis of GSID is confirmed, it's important that a registered dietitian (RD) complete a full evaluation and assess the patient’s diet to ensure that they are meeting their nutritional requirements. The RD will: 4

- Review the patient's diet and symptom history
- Assess nutritional adequacy of the current diet
- Provide an individualized diet plan
- Provide diet education for the patient and family

The SucraidASSIST™ program currently offers free nutritional counseling for patients on Sucraid® (sacrosidase) Oral Solution. Please complete the enrollment form in Appendix G.
Replacement with Sucraid® (sacrosidase) Oral Solution

In addition to modification of the diet, there is enzyme replacement therapy available. Sacrosidase can replace the missing sucrase, but does not provide replacement therapy for any deficiency of the isomaltase enzyme, so it might be necessary to continue restricting starch in the diet even while taking sacrosidase.

Sucraid®

Sucraid® (sacrosidase) Oral Solution is indicated as oral replacement therapy of GSID. See Clinical Studies in Appendix H. Sucraid® is contraindicated in patients with a known hypersensitivity to yeast, yeast products, glycerin (glycerol), or papain. 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.

Sucraid® is taken orally with each meal or snack diluted with two to four ounces of water, milk, or infant formula. The beverage or infant formula should be served cold or at room temperature, and should not be warmed or heated before or after addition of Sucraid®. Sucraid® should not be reconstituted or consumed with fruit juice since its acidity may reduce the enzyme activity. 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 weighing less than 15 kg
- 2 mL (17,000 I.U.) (two full measuring scoops or 56 drops) per meal or snack for patients weighing over 15 kg

SucraidASSIST™ Program

SucraidASSIST™ is a comprehensive support program provided by One Patient Services that offers the following services to patients taking Sucraid®:

- Nurse Case Manager
  - Dedicated case management services
  - Primary point of contact
- Insurance Assessment
  - Insurance verification
  - Prior authorization assistance
  - Research coverage options
- Financial Assistance
  - Copay assistance
  - Deductible support
  - Premium assistance
- Pharmacy Services
  - Prescription fulfillment
  - Delivery to patient or clinician

NOTE: the program cannot provide medical advice to patients but can answer basic questions about diet and the safe and effective use of the product.
• Peer Support Coaching
  o Tips on daily living with Sucraid® (sacrosidase) Oral Solution
  o Access to online support communities

• Nutrition Counseling
  o Dietary consultation
  o Resources for diet management

To prescribe Sucraid® and to enroll a patient in the SucraidASSIST™ services, the clinician will need to fill out the Sucraid® enrollment form. The clinician must complete the following three sections of the form:

1) Patient Information
2) Prescription and Prescriber Information
3) Diagnosis and Prescriber Authorization

The prescribing clinician must sign the appropriate sections and can then submit the form and the breath test results by fax or email using the contact information at the top right corner of the form. If it is not possible to have the patient complete his/her sections of the form when the clinician completes the form, the clinician can still submit the form to the SucraidASSIST™ team. If the patient is available to fill out the form, the patient will need to fill out the following 4 sections:

1) Appropriate bottom portion of the Patient Information section
2) Patient Insurance
3) Patient Financial Information
4) HIPAA authorization

As mentioned earlier, the patient can fill out the form at a later date or the SucraidASSIST™ team will follow up with the patient to help the patient fill out the form. Once all sections of the form have been completed and submitted, then the patient will be contacted by the nurse case manager who will be the primary point of contact for the patient and assist them with all of their questions. Please see Appendix G for the enrollment form.

To learn more about SucraidASSIST™, see Appendix I or visit https://www.sucraid.net/patient-assistance/.
Self-Check Questions

1. Which of the following statements best describe GSID? Select all that apply.
   A. GSID can be diagnosed in children and adults.
   B. GSID is an autosomal recessive disorder.
   C. GSID is an infectious disease.
   D. GSID is caused by mutations in the S/ gene.

2. The elimination phase of the modified diet involves elimination of _______ and _______ from the diet for a duration of two weeks.

3. Match each term to its description by writing the letter corresponding to the best description in each blank.
   1. _____ Lumen of small intestine A. Bacterial fermentation of disaccharides
   2. _____ Intestinal brush border B. Starch is converted to disaccharides by pancreatic amylase
   3. _____ Colon C. Disaccharides are converted to monosaccharides by enzymes

4. Check all of the following that are potential presenting symptoms of GSID in adults.
   - Diarrhea
   - Abdominal distension
   - Bloody stools
   - Bloody stools
   - Steatorrhea
   - Weight loss

5. List the four possible outcomes of the sucrose hydrogen breath test.

______________________________________________________________________________
______________________________________________________________________________
______________________________________________________________________________
______________________________________________________________________________
______________________________________________________________________________
6. A male patient aged 42 years presents with many years of chronic diarrhea, bloating, and abdominal pain. He has previously been diagnosed with irritable bowel syndrome, but you decide to refer him to a sucrose hydrogen breath test based on his history of worsening of symptoms when ingesting starchy foods. Below is the result of his breath test. Which of the following best describe the test results?

A. Normal test, sucrose malabsorption is not supported.
B. Hydrogen response is elevated above normal, methane response is normal; suggests sucrose malabsorption.
C. Methane response elevated above normal, hydrogen response is normal; suggests sucrose malabsorption.
D. Combination of hydrogen and methane response suggests sucrose malabsorption.
Answers to Self-Check Questions

1) A, B, & D

2) Sucrose; starch

3) 1B; 2C; 3A

4) Diarrhea; abdominal distension; weight loss

5) Normal test
   - Increased hydrogen, normal methane
   - Increased methane, normal hydrogen
   - Both hydrogen and methane increased

6) B
References


Appendices
Appendix A. Sucraid® (sacrosidase) Oral Solution PI
Sucrose is normally produced in the brush border of the small intestine, primarily the distal duodenum and jejunum, from the water-soluble sucrase/sacrosidase enzyme complex. This enzyme complex hydrolyzes sucrose, the disaccharide formed by the linkage of glucose and fructose, into its component monosaccharides, glucose and fructose, which are then absorbed into the bloodstream for utilization by the body or stored in the liver and muscle as glycogen. In the presence of endogenous human sucrase and other sugars from starch.

Sucrase is naturally produced in the brush border of the small intestine, primarily the distal duodenum and jejunum, from the water-soluble sucrase/sacrosidase enzyme complex. This enzyme complex hydrolyzes sucrose, the disaccharide formed by the linkage of glucose and fructose, into its component monosaccharides, glucose and fructose, which are then absorbed into the bloodstream for utilization by the body or stored in the liver and muscle as glycogen.

SUCRAID (sucrosidase) oral solution

DESCRIPTION
(Sucrosidase) oral solution is an enzyme replacement therapy for the treatment of genetically determined sucrose–isomaltase deficiency, which is part of congenital sucrase–isomaltase deficiency (CSID).

CHEMISTRY
SUCRAID is a pale yellow, clear solution with a pleasant taste. The active ingredient in SUCRAID contains 8.55 International Units (IU) of the enzyme sucrase in a single-monomer, low molecular weight and solution in a concentrated sucrose liquid. The enzyme is derived from baker’s yeast (Saccharomyces cerevisiae).

It has been reported that the primary amino acid structure of this enzyme consists of 513 amino acids with an apparent molecular weight of 100,000 (g) for the glucosylated monomer (flame 68,000, 116,000, 194,000). The enzyme also catalyzes the production of increased amounts of hydrogen, bloating, abdominal cramps, nausea and vomiting may occur from the fermentation of starch. 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:

Tell your doctor if you are allergic to table sugar (sucrose), or if you have ever had a reaction to any of the following ingredients in SUCRAID: papain, sucrose, or any other ingredients in SUCRAID.

Take this medicine only as directed. It is important to take the correct amount of SUCRAID for your age and size. The dose is based on your weight unless your doctor has directed you otherwise.

PATIENT PACKAGE INSERT: INFORMATION FOR PATIENTS

SUCRAID® (sucrosidase) oral solution

Please read this leaflet carefully before you take SUCRAID® (sucrosidase) 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® (sucrosidase) 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–isomaltase deficiency, which is part of congenital sucrase–isomaltase deficiency (CSID). It 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 some sugars resulting from the digestion of starch. 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.

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, 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.

In the absence of endogenous human sucrase, as in CSID, sucrose is not metabolized. Undigested sucrose in the jejunum is then hydrolyzed by the brush border enzyme sacrosidase into its component monosaccharides, glucose and fructose. SUCRAID can help improve the breakdown and absorption of sucrose (table sugar) from the intestine and can help relieve the gastrointestinal symptoms of CSID.

A generally accepted clinical definition of CSID is a condition characterized by the following stool pattern, an increase in breath hydrogen of > 10ppm when challenged with sucrose after fasting and a negative lactose breath test. However, because of the difficulty in establishing the diagnosis, CSID, it may be warranted to conduct a short 24-hour stool collection (or a 24 hour stool) to assess reactivity in patients suspected of having 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.
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.

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.
Appendix B. Sucrose Malabsorption Breath Test Order Form
Patient Order Form

Requested Test(s)
(Please check test(s))

□ SIBO- Lactulose Breath Test Kit
   (Prescribers Only)
□ SIBO- Glucose Breath Test Kit
   (Available to All)
□ Lactose Malabsorption Breath Test Kit
□ H. pylori Urea Breath Test Kit
□ Fructose Malabsorption Breath Test Kit
□ C. Difficile Test Kit
□ Sucrose Malabsorption Breath Test Kit

Patient Information

Patient: __________________________________________
   (Last)                                                        (MI)                                                        (First)
Address: __________________________________________________
   (Cannot ship to PO Box)
City: __________________________________ State: ______ Zip: ______
SSN:_______________________________ Date of Birth: _____________________________ Sex: ______
   (Optional)
Home Phone: ___________________________ Cell Phone: ____________________________
E-mail: __________________________________________________________________________
Insurance Certification/Authorization #: (if any) ________________________________

Physician Information

Physician: __________________________________________ NPI#:________________________
Provider Specialty: __________________________________________________________________
Address: ________________________________ City: __________________ State: _____ Zip: ______
Office Contact Person: __________________________________ Office Phone: ______________
Office Contact E-mail:__________________________ Office Fax: _______________________
ICD-9-CDM Code(s): ___________________________ - ___________________________ -
Physician Signature: __________________________ Date:________________________
Appendix C. Sucrose Malabsorption Breath Test Patient Instructions
SUCROSE INSTRUCTIONS

Patient Assistance
Please call us directly at 781-659-0704 with any questions regarding insurance coverage, test administration, or any other inquiries you may have. We are here to help in any way possible!

Instructional Video
Our website has a step-by-step video describing how to perform this test. Visit hydrogenbreathtesting.com and click the tab labeled “Taking a Test” to find this instructional video.
Sucrose Tolerance/Malabsorption Breath Test

Please take the time to read this instruction manual thoroughly, and in its entirety, before administering the test. Thank you.

Kit Contents:

- One (1) 5.75” wrapped collection straw
- One (1) sugar substrate packet for ingestion
- Six (6) test tube labels
- Six (6) vacuum-sealed collection tubes
- One (1) bubble wrap bag for packaging and mailing of samples
- One (1) prepaid UPS return shipping label

Time Requirements:

- Dietary restrictions are required for 24 hours prior to the test. Please see enclosed information.
- Test takes 3 hours to perform. Please plan accordingly.

Test Restrictions:

- Discontinue the use of any probiotics for 4-5 days prior to taking test.
- Discontinue the use of any antibiotic for 2 weeks prior to taking the test.
- Do not smoke for at least 1 hour prior to the test, or at any time during the 3 hour test.
- Do not sleep or exercise for at least 1 hour prior to the test, or at any time during the 3 hour test.
- Do not ingest anything other than water while fasting or during the test.
- Please consult with your physician if you: 1) have any health concerns, 2) are on a specialty diet, 3) are on a specific medication such as proton pump inhibitors, laxatives, etc.

*It is advised that any question related to a specific health issue be addressed with your physician or nutritionist before consulting with Commonwealth Laboratories. Any questions specific to the test can be directed to Commonwealth Labs.

Patient Preparation Guidelines:

There is a 24-hour preparation period prior to taking the test: The first 12 hours require a specific diet and the last
12 hours require a complete fasting period; however, you may drink water at any time before and during the test, and you may brush your teeth.

1) Patient must follow a specific diet for 12 hours prior to the 12-hour fasting period.

Permitted foods during the specific diet:
- Lean pork
- Baked or broiled seafood, chicken, turkey, lean beef
- Eggs
- Plain white or brown rice
- Plain quinoa
- Plain coffee or tea
- *Minimal* olive oil, salt, pepper

Foods not permitted during the specific diet:
- Grain products
- Fruits (including fruit juices)
- Sugar (in any form)
- All dairy products
- Vegetables
- Nuts and seeds
- Any beverage containing alcohol
- Beans, soy products

2) Following the 12-hour specific diet, patient must fast for 12 hours.

Commonwealth Labs suggests beginning the 24-hour preparation period in the morning so that patient may follow the specific diet during the day, immediately followed by the fasting period during the night (including time spent sleeping). Test is to be performed the following morning (at least 1 hour after waking up).

**Performing the Test:**

1) Dissolve four (4) level tablespoons (~50 grams) of table sugar (granulated sugar) in eight (8) ounces (250mL) of water.

2) **DO NOT DRINK YET; SET DRINK ASIDE.**

3) Collect your first (baseline) breath specimen in a collection tube.

4) Consume drink immediately following the collection of the first (baseline) breath specimen.

5) Wait 30 minutes after drink consumption and collect specimen number 2.

6) Wait 30 minutes after collection of specimen number 2 and perform collection of specimen number 3.

7) Wait 30 minutes after collection of specimen number 3 and perform collection of specimen number 4.

8) Wait 30 minutes after collection of specimen number 4 and perform collection of specimen number 5.

9) Wait 30 minutes after collection of specimen number 5 and perform collection of specimen number 6.

10) You are finished after collecting specimen number 6.
Please see below for instructions on how to collect your breath samples, as well as how to package and ship the samples back to our laboratory.

**Collection of the Breath Samples:**

1) Unscrew the top of the test tube. Unwrap the collection straw and insert the straw half way into the collection tube.

2) Take a normal breath in (do not inhale deeply), close your mouth around the collection straw, and exhale through the straw into the test tube normally.

3) Exhale normally into the test tube for 2 to 5 seconds until you see the condensation from your breath fill the walls of the test tube.

4) Remove the straw from the test tube and **immediately** screw the tube cap firmly back on top of the test tube.

5) Note: the rubber stopper on the white test tube cap is for laboratory extraction purposes only, and does not have anything to do with the breath specimen collection process.

6) Be sure to complete and apply the included test tube labels to each individual test tube. Make certain to label each sample number correctly.

**HOW TO RETURN YOUR BREATH SPECIMEN TO COMMONWEALTH LABORATORIES:**

*NOTE: Included in each test kit is a prepaid UPS return shipping label for your use. All shipping charges are incurred by Commonwealth Laboratories.*

1) After completing your test, place your collection tubes in the bubble bag provided.

2) Place the bubble bag and the completed lab requisition form in the same box in which the kit was sent to you. **Please note:** If Commonwealth Labs shipped the kit directly to you, then your physician’s signature is on file at the lab and we do not need it on the laboratory requisition form.

3) Seal the box, and then apply the prepaid return shipping label over the box.

4) Upon completion of your test, take the package to any one of the following:
   - Your nearest UPS drop box
   - Your nearest UPS shipping center/store
   - Packages can also be handed to any UPS driver

To find your nearest UPS drop box, shipping location or store, simply call (800) 742-5877 (1-800-PICK-UPS) or visit www.UPS.com and click the “find locations” tab on the left side of the screen.
Please be advised that, barring any medication or health restriction, this kit should be returned to Commonwealth Laboratories within 30 days (1 month) of its receipt or the patient will incur a cost of $40.00 to cover the cost of the test kit. If you cannot adhere to this timeframe because of health or medication restrictions, please notify the lab so we can note this in your record.

**Patient Insurance and Test Payment Guidelines:**

Prior to returning your test kit, please be sure to review the patient insurance and test payment guidelines that are included on the Laboratory Requisition Form.

Please also note that no patient will ever be responsible for an out-of-pocket payment that is greater than $175.

As always, if you have any questions, please contact us:

Commonwealth Laboratories Inc.
www.hydrogenbreathtesting.com

39 Norman Street • Salem, MA 01970
T. 781.659.0704 • 800.292.9019 • F. 781.659.0705
e-mail: customerservice@commlabsinc.com
Appendix D. Sucrose Malabsorption Report Sheet - Sample
Patient Name: Simpon, Bart  
Patient Number: 567385  
Date of Birth: 5/8/1975  
Physician: Dr. Jones  
Address: Lynn, MA  
Date Samples Collected: 12/1/2011  
Date of Assay: 12/10/2011

<table>
<thead>
<tr>
<th>Sample</th>
<th>ppm H₂</th>
<th>ppm CH₄</th>
<th>f(CO₂)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>20 min</td>
<td>2</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>40 min</td>
<td>3</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>60 min</td>
<td>4</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>120 min</td>
<td>5</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>180 min</td>
<td>6</td>
<td>29</td>
<td>0</td>
</tr>
</tbody>
</table>

Peak Hydrogen Production: 23 ppm  
Normal <20 ppm  
Peak Methane Production: 0 ppm  
Normal <12 ppm  
Peak Combined H₂ and CH₄ Production: n/a ppm  
Normal <15 ppm

HYDROGEN RESPONSE SUGGESTS SUCROSE MALABSORPTION  
METHANE RESPONSE ONLY DOES NOT SUGGEST SUCROSE MALABSORPTION  
H₂+CH₄ NOT APPLICABLE

*Standards for an abnormal test: an increase of 20 ppm or more of Hydrogen, 12 ppm or more of Methane, or 15 ppm or more of H₂+CH₄.  
*As the physician, you are responsible for being aware of clinical factors that may affect the interpretation of this test for your patient.  
*These standards are guidelines only. For diagnosis, this information must be supplemented with clinical information that is unavailable to the laboratory.

Hydrogen (H₂) and Methane (CH₄) values are corrected for CO₂ content in the samples.  
The f(CO₂) is the correction factor; this value, when close to 1.00, indicates a good alveolar sample.  
A correction factor over 4.00 indicates a poor sample.
Appendix E. Adult Diet Guide
### Choose Foods That Are Low in Sucrose and Starch

#### Dairy
- Cow's milk
- Cream cheese
- Half and half
- Hard cheeses (cheddar, colby, mozzarella, swiss, parmesan, provolone)
- Plain cottage cheese
- Plain yoghurt sweetened with fructose or dextrose
- Ricotta cheese
- Sour cream
- Whipping cream

**NOTE:**
- Full-fat dairy products may be used if more calories are indicated.
- Avoid processed cheeses or cheese products that contain sucrose or starch fillers.
- If lactose intolerant, avoid dairy foods. Substitute lactose-free milk, unsweetened almond milk, or soy milk for cow's milk. A dietitian can provide other dairy alternatives.

#### Protein
- Beef
- Chicken
- Eggs
- Fish
- Lamb
- Pork
- Tofu
- Turkey

**NOTE:**
- All meats above should be plain.
- Avoid breaded meats.
- Avoid processed meats such as bacon, sausage, luncheon meat, paté, and liverwurst that are cured with sucrose or have starch fillers.

#### Vegetables
- Alfalfa sprouts
- Artichoke*
- Asparagus*
- Bamboo shoots
- Bok choy
- Broccoli*
- Brussels sprouts*
- Cabbage*
- Cauliflower*
- Celery
- Cucumber
- Eggplant
- Green beans
- Greens (collards, kale, mustard, turnip, and chard)
- Lettuce (arugula, endive iceberg, romaine)
- Mung bean sprouts
- Mushrooms
- Peppers (red, green, and yellow)
- Radishes
- Rutabaga
- Spaghetti squash
- Spinach
- Tomatoes
- Turnips
- Yellow squash
- Zucchini

**NOTE:**
- *These vegetables may cause gas in all individuals, not just patients with Genetic Sucrase-Isomaltase Deficiency, and should be monitored closely.

#### Fruits
- Avocado
- Blackberries
- Blueberries
- Cherries
- Coconut (fresh or dried, unsweetened)
- Cranberries
- Currents
- Figs
- Grapes
- Kiwi
- Lemons
- Limes
- Loganberries
- Olives
- Papaya
- Pears
- Pomegranate
- Prunes
- Raspberries
- Rhubarb
- Strawberries

**NOTE:**
- All fruits should be fresh; not cooked, canned, or dried.
- Some fresh, frozen fruits may be included.
- All fruits should be “unsweetened”.

#### Sweeteners
- Granulated fructose
- Granulated dextrose

#### Fats
- Any vegetable oils
- Butter

#### Nuts & Seeds
- Almonds
- Almond butter
- Brazil nuts
- Flax seeds
- Hazelnuts
- Macadamia nuts
- Peanuts
- Peanut butter
- Pecans
- Pumpkin seeds
- Sesame butter (tahini)
- Walnuts

**NOTE:**
- Nuts and seeds can be difficult to digest in general.
- Most nuts and seeds contain varying amounts of sucrose and starch.
- When starting the diet, it is best to avoid nuts and seeds the first two weeks.
- It is important to keep the portion size small (in general a serving is less than 1 ounce for nuts).

### AVOID Foods High in Starch
- Baked goods
- Beans, peas, & lentils
- Breads
- Cereals
- Corn
- Crackers
- Gluten-free starches & grains
- Grains (wheat, oats, rice)
- Pasta
- Potatoes

**Note:** These diet recommendations are for general guidance only. Every case of Genetic Sucrase-Isomaltase Deficiency is unique. Diet consultation with a Registered Dietitian (RD) is recommended.

### ADDITIONAL IMPORTANT SAFETY INFORMATION
- 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.
- 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.

Please see additional Important Safety Information on back page and in enclosed Full Prescribing Information. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.FDA.gov/medwatch or call 1-800-FDA-1088.
(Adult Diet Guide)

Guidelines for Adults with Genetic Sucrase-Isomaltase Deficiency (GSID)
See Sucraid Important Safety Information below and on the back page

Starting Sucraid® (sacrosidase) Oral Solution Therapy with a Low-Sucrose, Low-Starch Diet

Key Points:
- Weeks 1 and 2: Follow a low-sucrose, low-starch diet.
- Week 3: Reintroduce sucrose-containing foods and then foods higher in starch.
- Consult with a Registered Dietitian (RD) for diet assessment, education, and follow up.

Note: These diet recommendations are for general guidance only. Every case of Genetic Sucrase-Isomaltase Deficiency is unique. Diet consultation with a Registered Dietitian (RD) is recommended.

WWW.SUCRAID.NET

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
- Although Sucraid® provides replacement therapy for the deficient sucrase, it does not provide specific replacement therapy for the deficient isomaltase.
- Do not use Sucraid® (sacrosidase) Oral Solution with patients known to be hypersensitive to yeast, yeast products, papain, or glycerin (glycerol).

WWW.SUCRAID.NET

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).

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WWW.SUCRAID.NET

Please see additional Important Safety Information on last page and in Full Prescribing Information on adjacent pages.
Prescribing Information

Sucraid® (sacrosidase) Oral Solution:

DESCRIPTION
Sucraid® (sacrosidase) Oral Solution is an enzyme replacement therapy for the treatment of genetically determined sucrose deficiency, which is part of congenital sucrase-isomaltase deficiency (CSID).

CHEMISTRY
Sucraid is a pale yellow to colorless, clear solution with a pleasant sweet taste. Each milliliter (mL) of Sucraid contains 8,500 International Units (I.U.) of the enzyme, the active ingredient. The chemical name of this enzyme is B-D-fructofuranoside fructohydrolase. The enzyme is derived from baker’s yeast (Saccharomyces cerevisiae).

It has been reported that the primary amino acid structure of the 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 octomer ranging from 100,000 g/mole to 800,000 g/mole. It has an isoelectric point (pI) of 4.5.

Sucraid may contain small amounts of papain. Papain is known to cause allergic reactions in some people. Papain 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 contains sacrosidase in a vehicle comprised of glycerol (50%) and water, and citric acid to maintain the pH at 4.0 to 4.7. (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 following a sucrose challenge (a measurement of excess hydrogen and fructose).

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. This may result in loose stools. Undissolved sucrose in the colon is fermented by bacterial flora to produce increased quantities of hydrogen, methane, and water. As a consequence, excessive gas, bloating, abdominal cramps, nausea, and vomiting may occur.

CLINICAL PHARMACOLOGY
Congenital sucrase-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 sucrase 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 duodenum and jejunum. Sucrose hydrolyzes the disaccharide into its component monosaccharides, glucose and fructose. Isomaltase breaks down disaccharides from starch into primarily the distal duodenum and jejunum. Sucrase hydrolyzes the maltose activity, and normal lactase levels.

INDICATIONS AND USAGE
Sucraid® (sacrosidase) Oral Solution is indicated as oral replacement therapy of the genetically determined sucrose deficiency, which is part of congenital sucrase-isomaltase deficiency (CSID).

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

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

Overdose 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 (one full measuring scoop is 1 mL) of Sucraid taken with each meal or snack. The dose may be increased to 4 mL (17,000 I.U.) per meal or snack or with additional carbohydrate load in the diet.

Do not reconstitute or consume with fruit juice, since its acidity may reduce 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.

2 mL (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 (1 mL equals 28 drops from the Sucraid container tip).

HOW SUPPLIED
Sucraid® (sacrosidase) Oral Solution 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). Product is sterile until opened. Discard four weeks after first opening due to the potential for bacterial growth. Protect from heat and light.

RX only.

Distributed by:
QXL Medical, LLC
Vero Beach, FL 33402

To order or for any questions, call 1-866-409-3773

www.sucraid.net

NDC #7837-111-04

www.sucraid.net

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Sucraid® (sacrosidase) Oral Solution 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). Product is sterile until opened. Discard four weeks after first opening due to the potential for bacterial growth. Protect from heat and light.
Patient Package Insert

INFORMATION FOR PATIENTS

Sucraid® (sacrosidase) Oral Solution

Please read this leaflet carefully before you take Sucraid® (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 SU CRAID

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 of 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 sucrase deficiency, which is part of congenital sucrase-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 some sugars resulting from the digestion of starch. 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, papain, 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. Replace 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 make an accurate dose.

Figure 1. Measure dose with measuring scoop.

1.

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 SU CRAID 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.

GOL Medical, LLC
Vero Beach, Fl 32963
www.sucraid.net
For questions call 1-866-469-3773
Rev 11/14
Part No. 0110
Appendix F. Menu Guide
Prescribing Information

Sucraid® (sacrosidase) Oral Solution is indicated as oral replacement therapy for children and adults with congenital sucrase-isomaltase deficiency (CSID). 

DEFINITION

Sucraid® (sacrosidase) Oral Solution is a solution of sacrosidase. Sucrose is known to be a physiological substrate for the intestinal brush border enzyme sucrase-isomaltase (SI) which is the target of congenital sucrase-isomaltase deficiency (CSID). In the absence of endogenous human sucrase, as in CSID, sucrose is not metabolized, and unhydrolyzed sucrose and starch are not absorbed in the small intestine and their presence in the intestinal lumen may lead to osmotic retention of water. This may result in loose stools.

MECHANISM OF ACTION

Sucrose is a disaccharide composed of one glucose and one fructose molecule. In the absence of endogenous human sucrase, as in CSID, sucrose is not metabolized, and unhydrolyzed sucrose and starch are not absorbed in the small intestine and their presence in the intestinal lumen may lead to osmotic retention of water. This may result in loose stools.

CONTRAINDICATIONS

Sucraid® (sacrosidase) Oral Solution is contraindicated in patients who are hypersensitive to yeast, yeast products, papain, or glycerin (glycerol).

WARNINGS

Severe wheezing, 90 minutes after a second dose of sacrosidase, was probably caused by sacrosidase. He had asthma and was being treated with theophylline and beclomethasone. He died 5 days after his second dose. There are no reports of hypersensitivity reactions to yeast, yeast products, papain, or glycerin (glycerol) in the literature.

SEVERE HYPERSENSITIVITY

If the diagnosis is in doubt, it may be necessary 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 necessary to perform a small bowel biopsy or breath hydrogen test to make a definitive diagnosis of CSID.

LACTATION

Sucraid® (sacrosidase) Oral Solution is not recommended for breast feeding.

LABORATORY TESTS

Sucraid® (sacrosidase) Oral Solution is indicated as oral replacement therapy for children and adults with congenital sucrase-isomaltase deficiency (CSID). In the absence of endogenous human sucrase, as in CSID, sucrose is not metabolized, and unhydrolyzed sucrose and starch are not absorbed in the small intestine and their presence in the intestinal lumen may lead to osmotic retention of water. This may result in loose stools.

To get the full benefit of the treatment, it is important to take Sucraid® (sacrosidase) Oral Solution at the beginning of each meal or snack and the remainder of your dosage be taken during the meal or snack.

Sample Menus for a Low-Sucrose, Low-Starch Diet

<table>
<thead>
<tr>
<th>Menu Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast</td>
<td>Oatmeal with banana and honey</td>
</tr>
<tr>
<td>Snack 1</td>
<td>Apple slices with almond butter</td>
</tr>
<tr>
<td>Lunch</td>
<td>Turkey and cheese wrap</td>
</tr>
<tr>
<td>Snack 2</td>
<td>Carrots and hummus</td>
</tr>
<tr>
<td>Dinner</td>
<td>Grilled chicken with steamed vegetables</td>
</tr>
<tr>
<td>Snack 3</td>
<td>Blueberries with greek yogurt</td>
</tr>
</tbody>
</table>

Nutritional Information

- Calories: 200
- Fat: 10g
- Carbohydrates: 25g
- Protein: 25g

These sample menus are only suggestions to use when following a low-sucrose, low-starch diet. Collectively the menu may not meet your current needs and further advice should be added to the diet over time. Always consult your physician or dietitian for modified diet recommendations.

---

Patient Package Insert

**Information for Parents**

Sucraid® (sacrosidase) Oral Solution

Please read the label carefully before you fill your prescription. The information contained on the label may differ from that provided in this Patient Package Insert.

**Dosage and Administration**

**How to take your medicine:**

Measure your dosage carefully, and administer it immediately before the beginning of the meal or snack, and the remainder of your dosage be taken during the meal or snack.

**Storage:**

Store in a refrigerator at 2°-8° C (36°-46°F). Product is sterile until the measuring scoop with water after each time

**Rx only.

**Visit CEGecs.com or for more information about the low-sucrose, low-starch diet.

**Further diet information, visit the Registered Dietitian (RD) at (305) 274-9082.**

**The RD cannot provide medical advice.

**Refer to the Diet Guide for Genetic Sucrase-Isomaltase Deficiency (GSID) for more information on a low-sucrose, low-starch diet.**

**Note:** All the information contained in this leaflet has been reviewed by medical professionals and is based on the information in the Prescribing Information. It does not contain all the information on Sucraid® (sacrosidase) Oral Solution. For further information, ask your doctor or pharmacist.
**Breakfast**
- Scrambled eggs
- Banana strips (no breading)
- Blueberries
- Milk
- Egg mixture with sausage*, cheese, green peppers, tomatoes, and mushrooms
- Steamed broccoli
- Milk
- Cottage cheese
- Blueberries
- Milk
- Skewer ham*
- Cheese stick
- Grapes
- Milk
- Chicken salad (no sugar)
- Grape
- Cheese stick
- Milk
- Plain yogurt (no sugar)
- Mix in blueberries and
- Milk

**Lunch**
- Mint grilled or baked
- Chicken strips (no breading)
- Cheese stick or cubes
- Red, green, or yellow
- Ranch dressing** for dipping
- Ham and/or turkey with
- Smoked broccoli
- Minимум
- Minimump и
- Mustard for a dipping sauce
- Milk
- Tuna salad (no mayo) –
- Mayonnaise**, eggs, mustard,
- Cucumber, onions, and
- Snow peas – steam and
- Tomato soup – made with
- Melt grated cheese
- Cut up cucumbers, peppers,
- Hard-boiled eggs
- Meat roll ups (roll up
- Cheese sticks or cubes
- Meat slit (roll up tucking and cheese with
- Bowl of strawberries,
- Grilled or baked
- Chicken or peppers
- Spread mayonnaise**
- Milk
- Steamed broccoli
- Tossed salad with dressing**
- Mix the meat and
- 1/2 pickles
- No-noodle lasagna –
- Ground turkey or chicken –
- Milk
- Tossed salad with dressing**
- 1/2 pickles
- Ground turkey or chicken –
- Chili powder
- Soy sauce, mustard, 
- Green beans
- Grilled or baked
- Cheese, and roll it up
- Meat/cheese
- or cream cheese on the
- meat/cheese
- and roll it up
- Steamed broccoli
- Minимум
- Minimump and mustard for a dipping sauce
- Milk
- Baked, grilled, or broiled
- fish (no breading)
- Spinach with ham
- Bacon –
- cucumber, +
+ blueberries, and
+ mayonnaise***, eggs, mustard,
+ celery, broccoli, and
+ fish (no breading)
+ Raisin dressing**
+ + blueberries, and
+ mayonnaise***, eggs, mustard,
+ celery, broccoli, and
+ fish (no breading)
+ Raisin dressing**
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+ mayonnaise***, eggs, mustard,
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+ celery, broccoli, and
+ fish (no breading)
+ Raisin dressing**
+ + blueberries, and
+ mayonnaise***, eggs, mustard,
+ celery, broccoli, and
+ fish (no breading)
+ Raisin dressing**
+ + blueberries, and
+ mayonnaise***, eggs, mustard,
**Notes**

*All meals should be fresh, avoid fillers and sugars. Meals cued with dextrose would be acceptable.*

**Choose a monosaccharide that does not contain sucrose or starch.**

*Take Sucraid® (sacrosidase) Oral Solution as prescribed with all meals and snacks.*

*If you do not drink cow’s milk, be sure to substitute with Lactaid® milk or a sugar-free, plain or unsweetened or skimmed milk.*

*Always read food labels. Even if a food is listed here, check the label to make sure it is safe as ingredients are constantly changing.*

*Dextrose can be purchased online from SODM Food (sodmfoods.com) or from local breweries.*

*Dextrose can be used in place of sugar.*

*You can buy fructose at the grocery store on the aisle where other sugars are found. Fructose can also be ordered online from SODM Food. Fructose can be used in place of sugar.*

*Talk to your physician or dietitian about the overall completeness of your diet and vitamin and mineral supplements as recommended.*

**INDICATION:**

Sucraid® (sacrosidase) Oral Solution is an enzyme replacement therapy for the treatment of genetically determined sucrose intolerance, which is a part of congenital sucrase-isomaltase deficiency (CISD).

**IMPORTANT SAFETY INFORMATION FOR SUCRAID® (SACROSIDASE) ORAL SOLUTION**

**Sucraid® may cause a serious allergic reaction.** If you notice any swelling or difficulty breathing get emergency help right away.

**Sucraid® does not break down some sugars that come from the digestion of starch.** You may need to restrict the amount of starch in your diet. Your doctor will tell you if you should restrict starch in your diet.

**Take Sucraid® as prescribed with all meals and snacks.**

**NEVER HEAT SUCRAID OR PUT IT IN WARM OR HOT BEVERAGES OR INFANT FORMULA.** Do not mix Sucraid® with fruit juice or at least 1 hour before or after fruit juice. Take Sucraid® as prescribed by your doctor. Normally half of the dose of Sucraid® is taken before a meal or snack and the other half is taken during the meal or snack.

**Please see full Prescribing Information on back of menu.**

---

**Breakfast**

- Scrambled eggs
- Fruit strips (no breathing)
- Blueberries
- Milk

**Lunch**

- Black forest ham
- Cheese cubes
- Grapes
- Milk

- Chicken salad (no sugar)
- Gruyere
- Milk

- Plain yogurt (no sugar), mix in blueberries and milk

**Dinner**

- Grilled or baked chicken
- Ground turkey or chicken – milk

- Cooked, mashed green beans
- Grilled or baked chicken – milk

- Hard-boiled eggs
- Raw vegetables

**Snacks**

- Unsweeten yogurt, sweetened with dextrose or fructose
- Blueberries or strawberries milk

- Cottage cheese, sweetened with dextrose or fructose
- Blueberries or strawberries milk

- Cheese stick or cubes
- Meat roll ups (roll up meat/cheese or cream cheese on the toothpick)

**Notes**

*You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.FDA.gov/medwatch or call 1-800-FDA-1088.*

*Tell your doctor if you have diabetes as your blood glucose levels may change if you begin taking Sucraid®. Your doctor will tell you if you should restrict starch in your diet.*

*Tell your doctor if you are allergic to, have ever had a reaction to, or have even had difficulty taking yeast products, paper or gluten (gluten).*

*Tell your doctor if you know diabetes or your blood glucose levels may change if you begin taking Sucraid®. Your doctor will tell you if your diet or diabetes medicines need to be changed.*

*Some patients may have worse abdominal pain, vomiting, nausea or diarrhea. Constipation, difficulty sleeping, headache, nervousness and dehydration has also occurred. Check with your doctor if you have difficulty with one or more of these side effects.*

**Please see full Prescribing Information on back of menu.**
**Breakfast**
- Scrambled eggs
- Cheese, ground turkey, or chicken
- Blueberries
- Milk
- Egg domesticated with mayonnaise*, cheese, ground peanuts, tomatoes, and mushrooms
- Broccoli
- Milk
- Cottage cheese
- Blueberries
- Milk
- Skewer barn*
- Cheese cubes
- Grapes
- Milk
- Chicken salad (no sugar)
- Ceiling cubes
- Cheese stick
- Milk
- Plain yogurt (no sugar)
- Mix in blueberries and milk

**Lunch**
- Plain grilled or baked chicken breast (no breading)
- Cheese stick or cubes
- Red, green, or yellow bell peppers
- Cheese stick or cubes
- Ranch dressing** for dipping
- Spread mayonnaise***
- Deli meat and sliced cheese
- Milk
- Deli meat and sliced cheese
- Spread mayonnaise*** or cream cheese on the meat/chop
- Milk and roll up
- Steamed broccoli
- Milk
- Mix mayonnaise*** and mustard for a dipping sauce
- Sliced ham*
- Blueberries
- Cottage cheese
- Milk
- Plain grilled or baked fish (no breading)
- Spinach with ham
- Salad – cucumbers, radishes, broccoli, and/or blueberries
- Gallen with natural sweetener or cream cheese
- Snow peas – steam and milk
- Grapes, cut up
- Melt grated cheese into soup
- Cut up cucumbers, peppers, celery, and broccoli
- Italian dressing for dipping (no sugar)

**Dinner**
- Grilled or baked chicken
- Chicken strips (no breading)
- Canned, mashed cauliflower (like mashed potatoes) with grated cheese
- Milk
- Grilled or baked pork chops
- Breaded mayonnaise*** with cheese
- Snowed trimmings
- Milk
- Baked, grilled, or broiled fish (no breading)
- Spinach with ham
- Bread – cucumbers, radishes, broccoli, and peppers with ranch dressing**
- Pickled peppers
- No-noodle lasagna – add cumin and/or dill pickles
- + All meats should be fresh; avoid fillers and sucrose. Meats cured with sweeteners and/or mayonnaise that does not contain sucrose or starch.

**Snacks**
- Unsweetened yogurt, sweetened with dextrose or fructose
- Blueberries or strawberries rolled in dextrose or fructose
- Peanut butter, sweetened with dextrose or fructose
- Cheese slices
- Mustard for a dipping sauce
- Meat roll ups (roll up meat/cheese or cream cheese on the toothpick)
- Blueberries or milk
- Unflavored yogurt, sweetened with dextrose or fructose
- Blueberries or strawberries rolled in dextrose or fructose
- Cheese cubes
- Cheese stick
- Milk
- Cheese stick
- Milk
- Grapes
- Milk
- Chicken salad (no sugar)
- Ceiling cubes
- Cheese stick
- Milk
- Plain yogurt (no sugar)
- Sweeten with dextrose or fructose
- Mix in blueberries and milk

**Notes**
- All meats should be fresh; avoid fillers and sucrose. Meats cured with dextrose would be acceptable.
- Be sure salad dressings do not contain sucrose or starch.
  - Choose a mayonnaise that does not contain sucrose or starch.
  - If you do not drink cow’s milk, be sure to substitute with Sucraid® milk or a sugar-free, plain or unflavored or skim milk.
  - Always read food labels. Even if a food is listed here, check the label to make sure it is safe or ingredients are constantly changing.
  - Dextrose can be purchased online from NOW Foods (nowfoods.com) or from local breweries.
  - Dextrose can be used in place of sugar.
  - You can be part of the grocery store’s on the side where other sugars are found. Prune puree can also be ordered online from NOW Foods. Prunes can be used in place of sugar.
  - Talk to your physician or dietitian about the overall completeness of your diet and take vitamin and mineral supplements as recommended.

**INDICATION:**

Sucraid® (sacrosidase) Oral Solution is an enzyme replacement therapy for the treatment of genetically determined sucrose intolerance, which is part of congenital sucrase-isomaltase deficiency (CSID).

**IMPORTANT SAFETY INFORMATION FOR SUCRAID® (SACROSIDASE) ORAL SOLUTION**

- SUCAID® may cause a serious allergic reaction. If you notice any swelling or have difficulty breathing get emergency help right away.
- SUCAID® does not break down some sugars that come from the digestion of starch. You may need to reduce the amount of starch in your diet. Your doctor will tell you if you should reduce starch in your diet.
- Tell your doctor if you are allergic to these or have even had a reaction to, or have ever had a history of taking these products, papain or glycerin (glycerol).
- Tell your doctor if you have diabetes as your blood glucose levels may change if you begin taking Sucraid®.
- Tell your doctor if you have diabetes or your blood glucose levels may change if you begin taking Sucraid®. Your doctor will tell you if your diet or diabetes medicines need to be changed.
- Some patients may have worse abdominal pain, vomiting, nausea or diarrhea. Constipation, difficulty sleeping, headache, nervousness and dehydration have also occurred. Check with your doctor if you notice any of the side effects.
- If you do not drink cow’s milk, be sure to substitute with Lactaid™ milk or a sugar-free, plain or unflavored, or skim milk.
- Never heat Sucraid® or put it in warm or hot beverages or infant formula.
- Do not mix Sucraid® with fruit juice or a taste it with fruit juice.
- Take Sucraid® as prescribed by your doctor. Normally half of the dose of Sucraid is taken before a meal or snack and the other half is taken during the meal or snack.
- You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.FDA.gov/medwatch or call 1-800-FDA-1088.

**WWW.SUCRAID.NET**

Please see full Prescribing Information on back of menu.
Sucraid® (Saccharose Isomaltase) Oral Solution

**Prescribing Information**

**PRODUCT DESCRIPTION**
Sucraid® (Saccharose Isomaltase) Oral Solution is an enzyme replacement therapy for the treatment of sucrase-isomaltase deficiency (CSID). CSID is a genetically determined deficiency of the enzyme sucrase, which is necessary for the digestion of starch. Therefore, you may need to restrict the amount of starch in your diet. Your physician or dietitian can provide information on a low-sucrose, low-starch diet that is appropriate for you.

**INDICATIONS AND USAGE**
Sucraid® is indicated for use in the treatment of CSID. It is an enzyme replacement therapy for the treatment of CSID in children and adults. It is not intended for use in the treatment of other diseases or conditions.

**DOSAGE AND ADMINISTRATION**

1. ** Initiate symptomatic and supportive therapy.

2. ** Measure an accurate dose.

3. ** Administer Sucraid with meals and snacks.

4. ** Store in a refrigerator at 2°C - 8°C (36°F - 46°F) until it has been reconstituted.

**CONTRAINDICATIONS**

Sucraid® is contraindicated in patients with known hypersensitivity to sucrose, lactose, yeast, yeast products, or glycerin.

**WARNINGS**

**Skin testing**
Sucraid has been reported to be a source of uncommon allergic reactions. If you notice any swelling or have difficulty breathing, get emergency help right away. Before using Sucraid, make sure you have read the Patient Package Insert (PPI), which contains important information about the drug, including how to take it, how to store it, and what to do if you miss a dose.

**SIDE EFFECTS**

Sucraid® may cause a variety of abnormalities, and some may be serious. Be sure to read the PPI before you begin taking the drug. Only your doctor can determine whether the benefits of taking the drug outweigh the risks.

**PRECAUTIONS**

Sucraid® is intended for use by persons with known sucrase-isomaltase deficiency. Do not forget to take it regularly as directed by your doctor. If you do not take it regularly, it will not work as it should. If you have any questions or concerns, please talk to your doctor or pharmacist.

**OVERDOSAGE**

If you think you might have taken too much Sucraid®, call your doctor or local poison control center right away.

**PREGNANCY**

Sucraid® is not expected to cause harm when administered to a pregnant woman or to cause fetal harm when taken by a pregnant woman. However, it is recommended that you consult your doctor before taking Sucraid® if you are pregnant.

**NURSING MOTHERS**

It is not known whether Sucraid® is excreted in breast milk. Consult your doctor before using Sucraid® if you are a nursing mother.

**EFFECTS ON ABILITY TO DRIVE OR OPERATE MACHINERY**

If you have any questions or concerns, please talk to your doctor or pharmacist.

**ADVERSE REACTIONS**

Sucraid® may cause a variety of abnormalities, and some may be serious. Be sure to read the PPI before you begin taking the drug. Only your doctor can determine whether the benefits of taking the drug outweigh the risks.

**FOR PATIENTS**

Sucraid® (Saccharose Isomaltase) Oral Solution is an enzyme replacement therapy for the treatment of sucrase-isomaltase deficiency (CSID). CSID is a genetically determined deficiency of the enzyme sucrase, which is necessary for the digestion of starch. Therefore, you may need to restrict the amount of starch in your diet. Your physician or dietitian can provide information on a low-sucrose, low-starch diet that is appropriate for you.

**DOSAGE AND ADMINISTRATION**

1. ** Initiate symptomatic and supportive therapy.

2. ** Measure an accurate dose.

3. ** Administer Sucraid with meals and snacks.

4. ** Store in a refrigerator at 2°C - 8°C (36°F - 46°F) until it has been reconstituted.

**CONTRAINDICATIONS**

Sucraid® is contraindicated in patients with known hypersensitivity to sucrose, lactose, yeast, yeast products, or glycerin.

**WARNINGS**

**Skin testing**
Sucraid has been reported to be a source of uncommon allergic reactions. If you notice any swelling or have difficulty breathing, get emergency help right away. Before using Sucraid, make sure you have read the Patient Package Insert (PPI), which contains important information about the drug, including how to take it, how to store it, and what to do if you miss a dose.

**SIDE EFFECTS**

Sucraid® may cause a variety of abnormalities, and some may be serious. Be sure to read the PPI before you begin taking the drug. Only your doctor can determine whether the benefits of taking the drug outweigh the risks.

**PRECAUTIONS**

Sucraid® is intended for use by persons with known sucrase-isomaltase deficiency. Do not forget to take it regularly as directed by your doctor. If you do not take it regularly, it will not work as it should. If you have any questions or concerns, please talk to your doctor or pharmacist.

**OVERDOSAGE**

If you think you might have taken too much Sucraid®, call your doctor or local poison control center right away.

**PREGNANCY**

Sucraid® is not expected to cause harm when administered to a pregnant woman or to cause fetal harm when taken by a pregnant woman. However, it is recommended that you consult your doctor before taking Sucraid® if you are pregnant.

**NURSING MOTHERS**

It is not known whether Sucraid® is excreted in breast milk. Consult your doctor before using Sucraid® if you are a nursing mother.

**EFFECTS ON ABILITY TO DRIVE OR OPERATE MACHINERY**

If you have any questions or concerns, please talk to your doctor or pharmacist.

**ADVERSE REACTIONS**

Sucraid® may cause a variety of abnormalities, and some may be serious. Be sure to read the PPI before you begin taking the drug. Only your doctor can determine whether the benefits of taking the drug outweigh the risks.
Each milliliter (mL) of Sucraid contains 8,500 International Units of β-D-fructofuranoside fructohydrolase. The name of this enzyme is β,D-fructofuranoside fructohydrolase. The recommended dosage is 1 or 2 mL (8,500 to 17,000 I.U.) or 1 or 2 full measuring scoops (28 drops from the bottle tip) of Sucraid per meal. The dose did not vary with age or sucrose intake. A full measuring scoop is 1 mL. Patients should be instructed to discard any remaining sucrose from the bottle after each use.

**Prescribing Information**

**INDICATIONS AND USAGE**

Sucrase-isomaltase deficiency (CSID) is a chronic, lifelong, inherited disorder, characterized by the complete or almost complete lack of endogenous sucrase activity, a deficiency accounting for 5% to 10% of the world’s population. In the absence of endogenous human sucrase, as in CSID, sucrose is not hydrolyzed to its constituent simple sugars, glucose and fructose, but instead is metabolized via alternative mechanisms. These include intestinal bacterial fermentation and the extraintestinal absorption of sucrose as an intact molecule. As a result, patients with CSID may have increased intestinal bacterial growth, which may lead to the production of gas, as well as sudden, severe, abdominal pain, bloating, flatulence, diarrhea, and occasionally, constipation. The incidence of flatulence and loose stools may increase when dietary intake of sucrose is substantially altered, which may require a small bowel biopsy or breath hydrogen test to make a diagnosis.

**SUGGESTED THERAPY**

For patients with CSID, Sucraid is indicated for the treatment of genetically determined sucrase deficiency, which is part of the management of CSID, a result of decreased or absent sucrase activity. CSID is usually characterized by a significantly greater number of hard and formed stools as well as with increased symptoms, such as flatulence, abdominal pain, bloating, and constipation when dietary intake of sucrose is substantially altered, which may require a small bowel biopsy or breath hydrogen test to make a diagnosis.

**HOW SUPPLIED**

Sucralid is a pale yellow to colorless, clear solution with a pleasant sweet taste. Each milliliter (mL) of Sucraid contains 8,500 International Units of β-D-fructofuranoside fructohydrolase. The name of this enzyme is β,D-fructofuranoside fructohydrolase. The recommended dosage is 1 or 2 mL (8,500 to 17,000 I.U.) or 1 or 2 full measuring scoops (28 drops from the bottle tip) of Sucraid per meal. The dose did not vary with age or sucrose intake. A full measuring scoop is 1 mL. Patients should be instructed to discard any remaining sucrose from the bottle after each use.

**SUGGESTED THERAPY**

For patients with CSID, Sucraid is indicated for the treatment of genetically determined sucrase deficiency, which is part of the management of CSID, a result of decreased or absent sucrase activity. CSID is usually characterized by a significantly greater number of hard and formed stools as well as with increased symptoms, such as flatulence, abdominal pain, bloating, and constipation when dietary intake of sucrose is substantially altered, which may require a small bowel biopsy or breath hydrogen test to make a diagnosis.
Appendix G. SucraidASS/ST™ Enrollment Form
Patient Information

Patient Name ___________________________________________  DOB __/__/____  Today’s Date __/__/____
Parent/Guardian Name ___________________________________________  Relationship to Patient _________________________________
Home Address ___________________________________________  City __________________________
State _________  Zip ______________________      Preferred Contact # ___________________________ Alternate # ________________________
Preferred Language ___________________________________     Email _________________________________________________________________
Shipping address (if different from above) ________________________________________________________________________________________
Best Time to Contact __________________________________  Allergies ________________________________________________________________

I authorize SucraidASSIST™ to leave a message, including the prescription name Sucraid® (sacrosidase) Oral Solution, if I am unavailable when they call. □ Yes  □ No

SucraidASSIST™ is a personalized program for Sucraid® patients and their prescribers. This support program provides insurance benefit verification, insurance appeals assistance, copay assistance, financial assistance, peer support coaching, nutrition counseling and educational resources related to your disease. In addition, as part of the support program, we offer nurse call support services to provide information and respond to your questions regarding your disease and Sucraid®.

I would like to participate in these services: □ Yes  □ No  Patient/Parent Signature (required) ______________________________________

Please review and sign the HIPAA statement on page 2.

Prescription and Prescriber Information

☐ Sucraid® Rx 8500 IU/mL Prescription

Take_______mLs by mouth with snacks and meals.
See package insert for full dispensing instructions (typically 1mL for pts < 15kg and 2mLs for pts >15kg)

_____ # of meals per day + _____ # of snacks per day = _____ total meals & snacks per day

☐ 30-day supply ☐ 60-day supply ☐ 90-day supply (as allowed by insurance)

I authorize One Patient Services, LLC to act as an agent of prescriber on my behalf for the limited purposes of transmitting this prescription to the appropriate pharmacy.

Signature Required (no stamps allowed):
Dispense as written_________________________ Date___________________or
Substitution allowed_________________________ Date___________________

Prescriber must review and sign the Diagnosis section on page 2.

Please fax a copy of the front and back of the patient’s insurance card or complete the information below

PRIMARY INSURANCE:
Name of Insured_________________________  Policy # __________________________  Group # __________________________
Phone # __________________________  Rx Drug Card # __________________________

SECONDARY INSURANCE:
Name of Insured_________________________  Policy # __________________________  Group # __________________________
Phone # __________________________  Rx Drug Card # __________________________

Patient Financial Information (Only required if financial assistance is needed)
Current Annual Household Income: $_________________________  Number of People in Household: 1 2 3 4 5 6  Other: _________
Diagnosis and Prescriber Authorization

Diagnosis (Please include ICD-10 code): ____________________

Description: __________________________________________

I certify that I have received the appropriate permission and written authorization from the patient to release the medical and/or patient information referenced on this form relating to the above referenced patient to One Patient Services, LLC, QOL Medical, LLC, and its affiliated companies, agents and representatives, and contracted third parties for the purposes of seeking reimbursement support, verifying insurance coverage and/or the evaluation of the patient’s eligibility for alternate sources of funding, contacting the patient for the purpose of enrollment in the SucraidASSIST™ support program, and to facilitate product fulfillment via the dispensing specialty pharmacy.

Prescriber Name (Please print) ___________________________________________________________________________________________

Prescriber Signature (Required) ___________________________________________________________________________________________

Authorization to Use and Disclose Protected Health Information (“Authorization”): I authorize my pharmacy, Accredo Health Group, Inc. (Accredo), QOL Medical, LLC, the maker of Sucraid®, One Patient Services, LLC, Sucraid® support service provider, dietary consultants, my physicians, and other healthcare providers, pharmacists, insurers, and any agent or representative of any of these parties (collectively, “Authorized Parties”) to obtain individually identifiable health information (“IIHI”) regarding me and my medical condition, symptoms, treatments, family medical history, insurance coverage and payment history, and diet, and to collect, use, and disclose my IIHI among each other to/from third parties (which may include insurers, public funding programs, social workers, advocacy organizations, assistance organizations, healthcare providers, dietary consultants, and other persons or entities as any of the Authorized Parties may deem appropriate) to: (1) coordinate my treatment; (2) facilitate reimbursement support and obtain payment for my treatment; (3) provide me and my healthcare providers with free educational materials, dietary support, and/or peer consultation (4) conduct healthcare marketing activities, including those for which Accredo or One Patient Services, LLC receives compensation (5) conduct clinical assessments regarding therapeutic response to Sucraid® and (6) carry out any other purpose required or permitted by law. I understand that any of the Authorized Parties may need to contact me for additional information. For purposes of this authorization, I understand that my IIHI includes any individually identifiable information about me such as my social security number, contact information, medical condition or other health information, and treatment and payment history relating to my past, present, and future use of Sucraid® and other healthcare items or services. I understand that once my information is disclosed under this authorization, it may be further disclosed and no longer protected by federal confidentiality laws. I understand that treatment by my physician and payment, enrollment, or eligibility to receive Sucraid® is not conditioned upon the signing of this authorization. However, if I refuse to sign this authorization, my ability to receive support services related to my use of Sucraid® may be limited. I understand that this authorization will remain in effect until the later of ten (10) years from the date of my signature or five (5) years following my discontinuance of purchase of Sucraid® unless I revoke it by sending written notice to the One Patient Services Manager at One Patient Services, 7003 Presidents Drive, Suite 800, Orlando, FL 32809. If I revoke this authorization, One Patient Services, LLC will communicate my revocation to the Authorized Parties and will stop using and disclosing my information as soon as possible. However, my revocation will not affect any prior use or disclosure of IIHI made in reliance on this authorization and my revocation will not affect my treatment by my physician. If I have questions about disclosures of my IIHI, I may contact the Privacy Officer at One Patient Services at sucraid@onepatientservices.com. I understand that I have the right to receive a copy of this authorization. I further understand that I have the right at any time to refuse nursing support, dietary support or peer consultation.

Patient Name (please print) __________________________________________ Date ______________________

Patient Signature (or representative) ___________________________ Relationship to Patient (if applicable) ___________________________
Appendix H. Clinical Studies on Sucraid®

Clinical Studies of Sucraid® (sacrosidase) Oral Solution

The following four studies were conducted to examine the efficacy and clinical evidence of Sucraid® (sacrosidase) Oral Solution.25

Study #1


Study Design

In this study, Robayo-Torres and colleagues examined both the ability of a ¹³C-labeled breath test to detect GSID/CSID without the need for a duodenal biopsy and the effect of sacrosidase supplementation on breath test results. A total of 10 GSID patients (diagnosed by low biopsy sucrase activity) and 10 control patients who had undergone endoscopy and biopsy because of dyspepsia or chronic diarrhea, but with normal mucosal enzyme activity, were tested. Patients were separately administered uniformly labeled oral ¹³C-glucose and ¹³C-sucrose loads. After each administration, ¹³C-CO₂ breath enrichment was assayed using an infrared spectrophotometer. Tests were repeated after adding Sucraid®. Results were measured by calculating the mean percentage coefficient of glucose oxidation (%CGO).

Results

In the control group, there was an average of 146% ± 45.5% mean percentage coefficient of glucose oxidation (%CGO); in contrast, the %CGO in the CSID group was 25% ± 21% (P<0.001), demonstrating that ¹³C-breath testing clearly distinguished among patients with and without GSID.

The test had 100% sensitivity and 100% specificity (confidence interval = 74-100%) for detection of low duodenal sucrase activity. All patients with GSID showed a correction of sucrase deficiency with oral Sucraid® supplementation.

Conclusion

The ¹³C-sucrose breath test was accurate and specific as a noninvasive confirmatory test of CSID. All patients with GSID showed correction of sucrase deficiency with oral Sucraid® supplementation.

Study #2


In a study published in 1999 by Treem and colleagues, the efficacy and safety of sacrosidase oral solution was examined in children with confirmed GSID consuming a normal sucrose- and carbohydrate-containing diet.
Patients

Patients with GSID/CSID were recruited from the practices of members of the North American Society for Pediatric Gastroenterology. Criteria for inclusion were:

- History of chronic, watery diarrhea with an acid pH <6.0
- Small intestinal biopsy specimens with measurement of tissue disaccharidase levels
- Sucrase activity <10% of control specimens
- Normal or decreased maltase activity
- Normal lactase levels and a normal result in a lactose breath hydrogen test
- Normal villous architecture of the small intestine

A total of 28 patients with GSID were enrolled in this randomized, multicenter, double-blind, controlled trial. All patients were infants or children (12 boys) between the ages of five months and 11.5 years (mean age, four years; median, two-and-a-half years). At baseline, the mean body weight of subjects was 16.5 kg.

Study Design and Treatments

The trial consisted of two phases. The breath hydrogen phase consisted of three single-dose treatments (placebo, sacrosidase, and sacrosidase with milk). Patients were subsequently randomized to one of four doses of sacrosidase for a 10-day treatment period, and crossed over to other dosages in random order until a 40-day treatment period was completed. Dosing of sacrosidase was weight-dependent: 1 mL/meal if weight was ≤15 kg; 2 mL/meal if >15 kg.

Assessments and End Points

Stool frequency and consistency measures, symptoms, and dietary data were recorded daily and compared with a baseline period in which patients had consumed a sucrose-free diet without sacrosidase. Dietary assessment of sucrose and carbohydrate consumption was summarized for each treatment period during the dose-response phase to verify whether patients were compliant with a "normal" diet (2 g/kg/d sucrose and 5 g/kg/d carbohydrate).

The primary efficacy variables included total stools and total symptoms scores collected during the dose-response phase. All other measurements were secondary. During the dose-response phase, the number of stools and severity of symptoms (gas, bloating, nausea, vomiting, and abdominal cramps) were recorded daily by each patient and assigned values ranging from zero (none) to three (severe). A post hoc responder assessment (asymptomatic yes/no) was also determined.

Results

Of the 28 patients in this trial who received ≥1 dose of sacrosidase, 26 (93%) completed the trial.

In the placebo phase, 28 patients in the trial who consumed a sucrose-free diet, the percentage reporting severe or moderate gastrointestinal symptoms was as follows: 75% diarrhea, 67% gas, 60% stomach pain, and 20% nausea.
In the dose response phases, significant differences were observed between the two higher concentrations (undiluted and 1:10 dilution) and the two lower concentrations (1:100 and 1:1,000 dilution) for both of the primary outcome variables—total stools and total symptoms score.

Overall, 81% of patients were asymptomatic while receiving full-strength sacrosidase. 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 aged ≥3 years, 77% became asymptomatic, suggesting that therapeutic response does not differ significantly according to age.

Only 4 patients in the trial experienced adverse events, including wheezing, vomiting, pallor, and dehydration. Three completed the trial and continued in an open-label trial with sacrosidase. The remaining patient, who was hospitalized for wheezing and withdrew from the trial, had pre-existing asthma. Most of the adverse events were attributed to concurrent illnesses common in childhood and were probably unrelated to sacrosidase.

Conclusions

The results of this trial indicate that sacrosidase is an effective treatment for GSID. By taking sacrosidase with each meal, patients were able to eat a more normal carbohydrate- and sucrose-containing diet without developing major gastrointestinal symptoms. This study indicates that use of sacrosidase may reduce the high incidence of GI complaints in this patient population.

Study #3


In this study, published by Treem and colleagues in 1993, the ability of sacrosidase to reduce the breath hydrogen response to an oral sucrose test was examined. Additionally, the ability of sacrosidase to reduce symptoms of sucrose malabsorption was assessed.

Study Design

A variety of methods were used to examine the enzymatic quality and stability of sacrosidase. The clinical activity of sacrosidase was evaluated in patients with a positive diagnosis of GSID who underwent double-blind, placebo-controlled breath hydrogen tests, followed by an eight-week dose-response study conducted while consuming a diet containing a moderate amount of sucrose. During this period, patients were treated with four different concentrations of sacrosidase for 14 days each.

Results

Sacrosidase was found to be stable at 4°C and retained full activity between pH 1.0 and 6.2. Pepsin digestion of the enzyme in vitro was completely eliminated by bovine serum albumin.

A total of 14 patients with GSID (five male; mean age 7.6 years) were enrolled in the study. All patients had normal lactose breath H₂ test results and abnormal sucrose breath H₂ tests. Overall, there was a significant reduction in cumulative breath H₂ ($P<0.001$) and peak breath H₂ ($P<0.002$) when sucrose
was ingested with sacrosidase compared with placebo. Twelve patients completed an eight-week field trial of four different concentrations of sacrosidase, ranging from a 1:100 dilution to a 1:100,000 dilution. Of note, there was a strong dose-response relationship, with patients who received the lowest dilution experiencing the fewest symptoms. Most patients tolerated a sucrose-containing diet with minimal symptoms while ingesting 1 ml of the 1:100-diluted yeast solution with each meal. With increasingly dilute yeast solution, symptoms of diarrhea, abdominal pain, and excessive gas were increasingly prevalent.

Conclusions

In this preliminary study, sacrosidase was shown to be effective in reducing symptoms of CSID. The results indicated that early intervention in patients with CSID might prevent chronic watery diarrhea and poor weight gain during infancy. There was a clear dose-response relationship in the higher concentrations of sacrosidase, which provided greater efficacy. Sacrosidase was stable at temperatures achievable in domestic refrigerators.

Study #4


Study Design

This uncontrolled open-label, long-term trial evaluated the safety, patient acceptability, and effectiveness of Sucraid® (sacrosidase) Oral Solution in treating patients with GSID/CSID consuming a sucrose-containing diet. Upon completion of the previous controlled trials involving Sucraid®, 34 GSID patients from six months to 28 years of age (median age about three years) were allowed to continue treatment with Sucraid® for two to 54 months (a total of over 900 months of Sucraid® therapy). Patient dosing varied from currently approved patient dosing.

Results

The 34 patients treated in the trial represent a total of over 900 patient-months of Sucraid® therapy. A total of 31 adverse events were recorded in fourteen patients (41%). Some adverse events were considered as possibly related to treatment, while others were deemed unrelated.

No patients discontinued due to adverse events. Three patients experienced serious adverse events, and all three continued treatment with Sucraid®.

Conclusions

The results of this long-term trial indicate that Sucraid® was well-tolerated and an effective treatment for the gastrointestinal symptoms of GSID as used in this trial. Sucraid® allowed GSID patients enrolled in this study to consume a sucrose-containing diet over the long term by attenuating the characteristic gastrointestinal symptoms of GSID.
Appendix I. SucraidASSIST™ Program Information
(One Call)

SucraidASSIST™ Access & Support Services In Sucraid® Therapy

Comprehensive Patient Support Program

Nurse Case Manager
- Dedicated case management services
- Primary point of contact

Insurance Assessment
- Insurance verification
- Prior authorization assistance
- Research coverage options

Financial Assistance
- Copay assistance
- Deductible support
- Premium assistance

Pharmacy Services
- Prescription fulfillment
- Delivery to patient or physician

Peer Support Coaching
- Tips on daily living with Sucraid®
- Access to online support communities

Financial Assistance

Pharmacy Services

Nutrition Counseling
- Dietary consultation
- Resources for diet management

NOTE: We cannot provide medical advice to you but can answer basic questions about diet and the safe and effective use of the product.

SucraidASSIST™ is provided by One Patient Services.

WWW.SUCRAID.NET | SUCRAID@ONEPATIENTSERVICES.COM

TO ORDER
Sucraid® (sacrosidase) Oral Solution,
call: 1-800-705-1962
fax: 1-800-632-1944

How to Order

1 CALL SucraidASSIST™
   1-800-705-1962
to speak to a Sucraid® Nurse Case Manager about a free trial or a prescription for Sucraid®.

2 FAX Sucraid® Enrollment Form
   1-800-632-1944
to download form, visit www.sucraid.net.

3 SucraidASSIST™ will review insurance benefits and offer financial assistance as needed.
   SucraidASSIST™ will ensure that each patient has affordable access to Sucraid® therapy.

4 SucraidASSIST™ will call the patient or physician to schedule delivery of Sucraid®.

SucraidASSIST™ is provided by One Patient Services.

WWW.SUCRAID.NET | SU CRAID@ONEPATIENTSERVICES.COM