Sucrada® (sacrosidase) Oral Solution:

DESCRIPTION

Sucrada® (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

Sucrada® is a pale yellow to colorless, clear solution with a glucose content of 90% (w/w) of the sucrose content of the original Saccharomyces cerevisiae. The enzyme is derived from baker’s yeast (Saccharomyces cerevisiae).

It has been reported that the primary enzyme and the structure of this enzyme consists of 512 amino acids with an apparent molecular weight of 100,000 for the glycosylated protein (range 96,000-110,000). Proteins also suggest that the protein exists in solution as a monomer, dimer, tetramer, and octamer ranging from 100,000 g/mol to 800,000 g/mol. It has an isoelectric point (pI) of 4.6.

Sucrada may contain small amounts of asparagine. Patients known to cause allergic reactions in many people. Patients may be more sensitive to the reactions during the manufacturing process to digest the stool of the yeast and may not be completely removed during subsequent processing steps.

Sucrada contains sacrosidase in a vehicle comprised of glucose (50% v/v), water, and citric acid to maintain the pH at 4.0 to 4.7. Glucose (sucrose) is the only sugar contained in the recommended doses of Sucrada that has no reported toxicity.

This enzyme preparation is fully soluble with water, milk, and infant formula. Do NOT HEAT SOLUTIONS CONTAINING SUCRADA. Do not put Sucrada in warm or hot liquids.

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 partial lack of sucrase activity and a very marked reduction in isomaltase activity; a moderate decrease in maltase activity, and normal lactase levels.

Sucrada is produced in the brush border of the small intestine, primarily the duodenum and jejunum, physiologically to break down disaccharides sucrose and isomaltose. Fructose breakdown takes place downstream from those two simple sugars. Sucrada does not contain isomaltase.

In the absence of endogenous human sucrase, as in CSID, the inability to produce sufficient amounts of hydrolytic enzymes will result in severe lack of the ability to absorb and digest the disaccharides sucrose and isomaltose. If left untreated, ceroidosis occurs. It may result in stool weight.

Unabsorbed sucrose in the colon is fermented by bacterial flora to produce increased amounts of hydrogen, methane, and water. As a consequence, excessive gas, bloating, abdominal cramps, nausea, and vomiting may occur.

Chronic malabsorption of disaccharides may result in malnutrition. Undiagnosed/unidentified CSID patients often fail to thrive and fail behind in their expected growth and development curves. Previously, the treatment of CSID has required the continual use of a strict sucrose-free diet.

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

A generally accepted clinical definition of CSID is a condition characterized by the following: 1) deficient intestinal hydrolysis of sucrose to glucose and fructose, 2) an increase in breath hydrogen at 70-90 mm Hg when challenged with a sucrose load after fasting for a 2-4 hour period without breath hydrogen below 10.5 mm Hg, and 3) the presence of symptoms characteristic of CSID in patients suspected of having CSID.

CLINICAL STUDIES

Two-phase clinical response preceded by a breath hydrogen phase double-blind, multi-center, crossover that was conducted in 25 patients aged 4 months to 18 years of age. The patients were challenged with an oral sucrose loading containing diet while measuring one of four doses of sacrosidase: full strength (900 I.U./mL) and three dilutions: 1:100 (90 I.U./mL), 1:1000 (9 I.U./mL) and 1:10,000 (0.9 I.U./mL) in random order for a period of 20 days. Patients who weighed more than 15 kg received 1 mL per meal, those weighing more than 15 kg received 2 mL per meal. The dose did not vary with age or sucrose intake. A dose-response relationship was shown between the two higher and the two lower doses. The two higher doses of sacrosidase were associated with significantly lower total starch and higher proportions of patients having lower total symptom scores, the primary efficacy end-points. In addition, higher doses of sacrosidase were associated with a significantly greater number of stool formation and consistency below 15 g. A significant trend was also noted for a higher proportion of normal stools and higher proportions of patients having lower total symptom scores, the secondary efficacy end-points.

Analysis of the overall symptomatic response as a function of age indicated that in CSID patients aged 3 to 5 years of age, 90% became asymptomatic. In patients over 3 years of age, 77% became asymptomatic. Thus, the age-response relationship was not differ significantly according to age.

A second study of similar design and execution on the first used 4 different dilutions of sacrosidase: 1:100 (90 I.U./mL), 1:1000 (9 I.U./mL), 1:10,000 (0.9 I.U./mL), and 1:100,000 (0.09 I.U./mL). There were inconsistent results with regards to the primary efficacy parameters. In both trials, however, patients showed a marked decrease in breath hydrogen output when they received sacrosidase in comparison to placebo.

INDICATIONS AND USAGE

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

CONTRAINDICATIONS

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

WARNINGS

Sore throat, 90 minutes after a second dose of sacrosidase, associated with elevated white blood cell count above 5.0 x 10^9/L.

No other side effects during treatment with Sucrada were observed. Other side effects may also occur. You should notify your doctor if you notice any of these or any other side effects during treatment with Sucrada, check with your doctor.

Precautions

Stop taking Sucrada 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 Sucrada is supplied with a plastic screw cap which covers a dispenser tip. Remove the outer cap and measure out the required dose. Reseal the bottle after use by replacing and twisting the cap until tight.
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 mixed with the measuring device since it will not measure an accurate dose. Measure your dose with the measuring scoop provided (see Figure 1). Do not use a kitchen teaspoon or other measuring device since it will not measure an accurate dose.

Figure 2. Mix dose in beverage or infant formula.

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

Storing your medicine: Sucraid is available in 4 fluid ounce (118 mL) see-through plastic bottles, packaged two bottles per box. A 1 mL measuring scoop is provided with each bottle. Always store Sucraid in a refrigerator at 36°F - 46°F (2°C - 8°C). Protect Sucraid from heat and light.

If your bottle of Sucraid has expired (the expiration date is printed on the bottle label), throw it away.

Keep this medicine in a safe place in your refrigerator where children cannot reach it.

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For questions call 1-866-469-3773
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Part No. 0110

The effects of Sucraid have not been evaluated in patients with secondary (acquired) disaccharidase deficiencies.

INFORMATION FOR PATIENTS

See Patient Package Insert. Patients should be instructed to discard bottles of Sucraid 4 weeks after opening due to the potential for bacterial growth. For the same reason, patients should be advised to re-measure the dosing cap with water after each use.

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

USE IN DIABETICS

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

LABORATORY TESTS

The oral fructose test for diagnosis of CSID is the measurement of intestinal disaccharidases following small intestinal biopsy.

Other tests used alone may be inaccurate; for example, the breath hydrogen test (high-resistance of false negatives) or oral sucrose tolerance test (high incidence of false positives). Differential urinary disaccharide test (low incidence of false negatives) or oral sucrose tolerance test (high incidence of false negatives) or oral sucrose breath hydrogen test to make a definitive diagnosis of CSID. The event resulted in withdrawal of the patient from the trial but resolved with no sequelae.

OVERDOSE

Overdose with Sucraid has not been reported.

RECOMMENDATIONS

The recommended dosage is 1 to 2 mL (8,500 to 17,000 I.U.) or 1 to 2 full measuring scoops (each full measuring scoop equals 1 mL; 28 drops from the measuring scoop or 28 mL of water, milk, or infant formula). The dosage should be adjusted according to the patient's body weight.

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DOSEAGE AND ADMINISTRATION

The recommended dosage is 1 to 2 mL (8,500 to 17,000 I.U.) or 1 to 2 full measuring scoops (each full measuring scoop equals 1 mL; 28 drops from the Sucraid container or 1 mL taken orally with each meal or snack divided by 1 mL equals 8,500 to 17,000 I.U. of water, milk, or infant formula). The dosage should be adjusted according to the patient's body weight.

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