

**PROPOSED REMS FOR SUCRAID ORAL SOLUTION
NDA 20-772 Sucraid (sacrosidase) Oral Solution, 8,500 IU/mL**

Enzyme replacement supplement for Treatment of CSID

QOL Medical LLC
5400 Carillon Point
Kirkland, WA 98033

Contact Information
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PROPOSED RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL(S):

To communicate the manufacturing change for Sucraid (sacrosidase) oral solution and ascertain whether there is any increase in allergy related adverse events for Sucraid (sacrosidase) oral solution following a manufacturing change.

II. REMS ELEMENTS:

A. Medication Guide or PPI

A Medication Guide or PPI was not required as part of this REMS.

B. Communication Plan

QOL Medical will implement a communication plan to healthcare providers to support implementation of this REMS.

A Physician Letter and questionnaire will be sent to existing prescribers within the central pharmacy database, and to future new prescribers informing them of the manufacturing change and requesting that they complete a survey regarding their patients' experience using the new product.

The Physician Letter is appended to the REMS

C. Elements To Assure Safe Use

The elements to assure safe use will mitigate any potential safety risk by alerting both patients and caregivers that the manufacturer of Sucraid has recently changed. Both patients and caregivers are asked to pay attention to and report any reactions to Sucraid that were not

previously experienced. In particular, this would include symptoms associated with allergic reaction: itching, swelling, mucus production, muscle spasms, hives, or rashes. Elements to assure safe use may, to mitigate a specific serious risk listed in the labeling, inform that:

a. Sucraid will be prescribed by healthcare providers who have particular training or experience.

Prescribers in the Sucraid REMS Program will attest to do the following:

- Review the full prescribing information for Sucraid.
- Read the DHCP letter that describes the manufacturing change.
- Carefully evaluate patients receiving the new product, specifically with regard to adverse reactions, including allergic reactions, recurrence of symptoms of CSID (congenital sucrase isomaltase deficiency) with usual diet, and the need for changes in dosing to control symptoms.
- Complete a survey regarding each of my patients' experience using the new product.
- Counsel patients' and/or their caregiver about the need to complete the survey regarding their experience using the new product.

The prescriber survey is appended to the REMS.

b. Sucraid will only be dispensed to each patient with documentation of safe use conditions.

- 1) Sucraid will be shipped directly to each patient or caregiver from a single central Pharmacy.
- 2) QOL Medical will distribute a letter to each patient and/or caregiver who is transferred from Sucraid manufactured with the original sacrosidase (drug substance) manufacturing process to the new manufacturing process for sacrosidase. Patients (or their caregivers) will be requested to complete a questionnaire about their experience using the new product versus their prior experience.

The caregiver/patient letter and questionnaire are appended to the REMS.

D. Implementation System

The Implementation System includes the following:

- QOL will monitor the extent to which prescribers, patients and/or caregivers complete and return the questionnaire
- QOL will monitor the extent to which prescribers are evaluating CSID patients for possible adverse reactions
- Based on monitoring and evaluation of the elements to assure safe use, QOL will take reasonable steps to work to improve implementation of these elements.

E. Timetable for Submission of Assessments

Reports will be submitted to FDA at 18 months, 3 and 7 years following FDA approval of the manufacturing supplement.



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Physician Letter, Revised 6 November 2008

<<DATE>> <<FIRST>> <<LAST>>
<<ADD1>>
<<CITY>>, <<STATE>> <<ZIP>>

Dear <<FIRST>> <<LAST>>:

As you may be aware, Sucraid® (sacrosidase) Oral Solution was approved by the FDA over ten years ago, and for the last five years has been made available by QOL Medical, LLC. The active ingredient (drug substance) in Sucraid is sacrosidase, a yeast-based enzyme that replaces missing or deficient sucrase. Sucrase is an enzyme that helps the body break down and process certain sugars (i.e. sucrose) during digestion. In people who lack the sucrase enzyme, sugar can pass into the intestines where it can interact with bacteria, thereby causing problems such as watery diarrhea, painful gas, bloating, nausea and vomiting.

The supplier of the drug substance has recently changed. QOL Medical needs to make certain that the change in drug substance manufacturing results in a product with the equivalent safety and effectiveness as the prior drug substance. A series of interviews with patients and caregivers familiar with Sucraid is planned.

We request you to note and assess any changes in patient symptoms when you next interview any Sucraid patients and/or family members, then complete and return the enclosed questionnaire. The resulting data from these physician questionnaires will be reported to the FDA. When completing the questionnaire, please be sure to check mark the five items at the top of the page. If you wish to receive a copy of the final data collected, please indicate your interest with any questionnaires you return.

The completed questionnaire may be faxed to 775-640-2736, emailed to info@sucraid.net or mailed in the enclosed, stamped envelope. If you have any questions about this questionnaire or any Sucraid-related matter, please contact us at 866-469-3773, extension 504.

Sincerely,

Trevor G. Blake
Chief Executive Officer
Enclosure



Physician Questionnaire, Revised 6 November 2008

Please check the box for each of the items you have completed with respect to the Sucraid:

- Reviewed the full prescribing information for Sucraid.
- Read the DHCP that describes the manufacturing changes
- Evaluated my Sucraid patients for adverse reactions or allergic responses or recurrent CSID symptoms.
- Have completed the survey for each Sucraid patient.
- Counsel patients and caregivers advising them to complete the survey and provide Sucraid (sacrosidase) Oral Solution

1. Since the new preparation of Sucraid was supplied to the patient, have you noticed any loss of efficacy of the medication? If yes, please describe which symptoms are noted:

- Increased diarrhea
- Increased bloating, gas
- Increased abdominal pain
- Decreased appetite
- Decreased tolerance for sucrose containing foods

2. Since the new preparation of Sucraid was supplied to the patient, have you had to change the dose of Sucraid in order to keep the patient asymptomatic or with a low acceptable level of symptoms while consuming a normal diet?

- No
- Yes – please describe change required:

3. Since the new preparation of Sucraid was supplied to the patient, have you had reports from the patient of any change in the taste, smell, color or any other property of the medicine?

- No
- Yes – please describe any changes noticed:

4. Since the new preparation of Sucraid was supplied to the patient, have you had reports from the patient of any side effects either encountered with the previous Sucraid preparation or new side effects not previously encountered? In particular, has the patient experienced allergic symptoms such as rash, hives, itching or wheezing?

- No
- Yes – please describe adverse reactions:

5. Since taking the new Sucraid, has your patient had any major illness or required hospitalization for any reason?

- No
- Yes – please describe adverse event and possible relation to Sucraid use:

6. Since the new preparation of Sucraid has been made available, have you had any difficulty prescribing or obtaining Sucraid in a timely manner?



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No

Yes – please describe situation:

7. Please list any other observations about the new Sucraid preparation.

Please mail this completed questionnaire to:

QOL Medical, LLC

Sucraid Post-Approval Study

5400 Carillon Point

Kirkland, WA 98033

Alternately, you may send this information by fax at 775-640-2736 or via email at

info@sucraid.net



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Patient/Caregiver Letter,

Dear Patient or Caregiver:

As you may be aware, Sucraid (sacrosidase) Oral Solution was approved by the FDA more than ten years ago. For the last five years Sucraid has been marketed and distributed by QOL Medical, LLC.

The manufacturing site for Sucraid has changed. QOL Medical needs to make sure that the new Sucraid you have received today is just as safe and effective as the old Sucraid. As an important part of this process, we ask you to please take a few minutes to fill out and return the enclosed survey. Please complete the questionnaire after taking the new Sucraid for at least one week.

When done, your survey may be faxed to 775-640-2736, emailed to info@sucraid.net or mailed in the enclosed envelope. If you have any questions about this survey or any Sucraid-related matter, please call 866-469-3773, extension 504.

Sincerely,

Trevor G. Blake
Chief Executive Officer

Enclosure



**Patient Questionnaire
Sucraid (sacrosidase) Oral Solution**

- 1. When did you first start taking Sucraid? **Month:**____ **Year:**____
- 2. Before you started taking Sucraid what were your main symptoms?
 - a) **frequent diarrhea**
 - b) **bloating or gas**
 - c) **cramps**
 - d) **stomach pain**
 - e) **others** _____

- 3. When you started taking Sucraid did all of your symptoms stop?
Circle one: Yes (skip to question 4) **No**

Which of your symptoms did not stop and how many times each day did you have them?

Symptom: _____ **How many times each day** _____

Symptom: _____ **How many times each day** _____

Symptom: _____ **How many times each day** _____

Were these symptoms from specific foods you ate? **Circle one: Yes No**

Which of these symptoms got better or happened less?

- a) **frequent diarrhea**
- b) **bloating or gas**
- c) **cramps**
- d) **stomach pain**
- e) **others** _____

- 4. How much Sucraid do you use everyday? **Scoops:** _____ **Drops:** _____
- 5. Do you take Sucraid every time you eat? **Circle one: Yes No**
- 6. When did you first start taking Sucraid from the new manufacturer **Month:**____ **Year:**____
- 7. What is the *lot number* from the bottle of Sucraid that you are currently taking. The lot number can be found in black type on the bottle label? **Lot** _____
- 8. Since you started taking the newly manufactured Sucraid:

Have you noticed any change in your symptoms?

Circle one: Yes No (skip to question 9)

What symptoms came back and how many times each day do you have these symptoms now?



Symptom: _____ How many times each day _____
 Symptom: _____ How many times each day _____
 Symptom: _____ How many times each day _____

Have you had any allergic symptoms such as rash, hives, itching, or wheezing?
Circle one: Yes No

Do you think these symptoms were from the new Sucraid? **Circle one: Yes No**

Could any other changes in your life be the cause of any return of symptoms (for example, a change in the type or amount of food you eat, a vacation or a move)?
Circle one: Yes No

9. Has your doctor changed your dose of Sucraid? **Circle one: Yes No**
 If yes, explain why _____

10. Have you noticed any change in the new Sucraid? **Circle as many as you want:**
 a) **Yes, change in taste**
 b) **Yes, change in smell**
 c) **Yes, change in color**
 d) **Change in something else (specify) _____**
 e) **No change**

11. What is the patient's age? _____ years old

When you are done answering the questions, please send your survey either by mail, fax, or email:

Using the postage-paid envelope to:
 QOL Medical LLC
 Sucraid Post-Approval Study
 5400 Carillon Point
 Kirkland, W A 98033

Fax to: 775-640-2736
 Email to: info@sucraid.net

If you have any questions about this survey, call 866-469-3773, extension 504.

Thank you for your time and assistance.