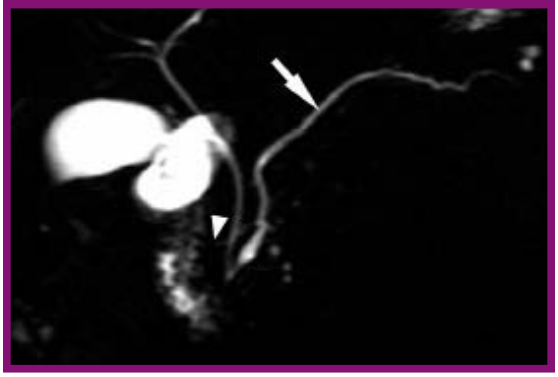
Improve Your MRCP Images with *ChiRho*Stim®

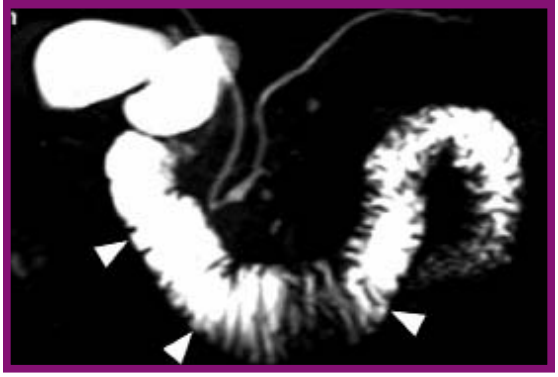
(Human Secretin for Injection)

Turn Static MRCP's into Dynamic Images with Pancreatic Stimulation

Before *ChiRho*Stim®



After *ChiRho*Stim®



Images courtesy of Joseph C. Veniero MD, PhD Cleveland Clinic Foundation

Observed pancreatic function and fluid flow in a fasted patient

*Benefits of ChiRho*Stim®*:*

- Improves visualization of the pancreas by sharpening images[1,2,3,4]
- Reimbursable with code J-2850
- Stable at room temperature for up to 6 months
- Pure synthetic peptide not manufactured by a recombinant process

For additional information on ***S-MRCP***, please visit ***www.smrcp.com*** or call ***1-877-272-4888***

References:

1. Choueiri NE, Balci NC, Alkaade S, Burton FR. *Advanced imaging of chronic pancreatitis.* Curr Gastroenterol Rep. 2010 Apr;12(2): 114-20. Review.
2. Delaney L, Applegate KE, Karmazyn B, Akisik MF, Jennings SG. *MR cholangiopancreatography in children: feasibility, safety, and initial experience.* Pediatric Radiology 2008 Jan;38(1):64-75.
3. Akisik M, Sandrasegaran K, Aisen A, Maglinte D, Sherman S, Lehman GA. *Dynamic secretin-enhanced MR cholangiopancreatography.* Radiographics. 2006 May-Jun;26(3):665-77.
4. Merkel E, Ballie J. *Exocrine pancreatic function: evaluation with MR imaging before and after secretin stimulation.* American Journal of Gastroenterology. 2006 Jan;101(1):137-8.

For highlighted prescribing information using ChiRhoStim® (Human Secretin for Injection) please see reverse side.

HIGHLIGHTS OF PRESCRIBING INFORMATION

The highlights do not include all the information needed to use ChiRhoStim® safely and effectively. See full prescribing information for ChiRhoStim®.

*ChiRho*Stim®
(Human Secretin for Injection)

ChiRhoStim® (Human Secretin) Injection, lyophilized powder for intravenous use, 16 mcg and 40 mcg vials

Initial U.S. Approval: 2004

----------RECENT MAJOR CHANGES----------
Indications and Usage (2.1) 10/2006

----------INDICATIONS AND USAGE----------
ChiRhoStim® injectables are indicated for:
• Stimulation of pancreatic secretions, including bicarbonate, to aid in the diagnosis of exocrine pancreas dysfunction (1.1)
• Stimulation of gastrin secretion to aid in the diagnosis of gastrinoma (1.2)
• Facilitation of identification of the ampulla of Vater and the accessory papilla during endoscopic retrograde cholangiopancreatography (ERCP) (1.3)

----------DOSAGE AND ADMINISTRATION----------
Stimulation of pancreatic secretions, including bicarbonate to aid in the diagnosis of exocrine pancreas dysfunction (2.1)
• 0.2 mcg/kg body weight by intravenous injection over 1 minute.
Stimulation of gastrin secretion to aid in the diagnosis of gastrinoma (2.2)
• 0.4 mcg/kg body weight by intravenous injection over 1 minute.
Facilitation of identification of the ampulla of Vater and the accessory papilla during endoscopic retrograde cholangiopancreatography (ERCP) (2.3)
• 0.2 mcg/kg body weight by intravenous injection over 1 minute.

----------DOSAGE FORMS AND STRENGTHS----------
ChiRhoStim® is available in two strengths:
• As a lyophilized sterile powder in 10 mL vials containing 16 mcg of human secretin. Reconstitute with 8 mL of saline for injection to yield a final concentration of 2 mcg of human secretin /mL (3.1)
• As a lyophilized sterile powder in 10 mL vials containing 40 mcg of human secretin. Reconstitute with 10 mL of saline for injection to yield final concentration of 4 mcg of human secretin /mL (3.2)

----------CONTRAINDICATIONS----------
Patients suffering from acute pancreatitis should not receive ChiRhoStim® until the acute episode has subsided (4).

----------WARNINGS AND PRECAUTIONS----------
• Allergic Reactions (5.1).
• Vagotomy or Inflammatory Bowel Disease (5.2).
• Alcoholic or Other Liver Disease (5.3).

----------ADVERSE REACTIONS----------
Most common adverse reactions (>0.5%) are nausea, flushing, abdominal pain, and vomiting (6).

To report SUSPECTED ADVERSE REACTIONS, contact ChiRhoClin, Inc. at 301-476-8388 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
The concomitant use of anticholinergic agents may make patients hyporesponsive, i.e., may produce a false result (7). Results of secretin testing in these patients should be interpreted with caution.

----------USE IN SPECIFIC POPULATIONS----------
The safety evaluation of ChiRhoStim® in geriatric patients showed no difference from the safety evaluation in the general population (8.5).

See 17 for PATIENT COUNSELING INFORMATION

Revised: 5/2007

CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

1 INDICATIONS AND USAGE
ChiRhoStim® is indicated for:

1.1 Stimulation of pancreatic secretions, including bicarbonate, to aid in the diagnosis of pancreatic exocrine dysfunction,
1.2 Stimulation of gastrin secretion to aid in the diagnosis of gastrinoma, and
1.3 Facilitation of the identification of the ampulla of Vater and accessory papilla during endoscopic retrograde cholangiopancreatography (ERCP).

2 DOSAGE AND ADMINISTRATION

2.1 Stimulation of Pancreatic Secretions, Including Bicarbonate to Aid in the Diagnosis of Exocrine Pancreas Dysfunction:

0.2 mcg/kg body weight by intravenous injection over 1 minute.

Gastroduodenal (Dreiling) Tube Collection Method(1):

A radiopaque, double-lumen tube is passed through the mouth following a 12-15 hour fast. Under fluoroscopic control, the opening of the proximal lumen of the tube is placed in the gastric antrum and the opening of the distal lumen just beyond the papilla of Vater. The positioning of the tube must be confirmed and the tube secured prior to synthetic human secretin testing. Intermittent negative pressure of 25-40 mmHg is applied to both lumens and maintained throughout the test. When duodenal contents have a pH of ? 6, a baseline sample of duodenal fluids is collected for a 10 minute period. A test dose of ChiRhoStim® 0.2 mcg if using the 16 mcg vial (0.1 mL) or 0.4 mcg if using the 40 mcg vial (0.1 mL) is injected intravenously to test for possible allergies. After one minute, if there are no signs of allergic reaction, ChiRhoStim® at a dose of 0.2 mcg/kg of body weight is injected intravenously over 1 minute. Duodenal fluid is collected for 60 minutes thereafter. The aspirate is divided into four collection periods of fifteen minutes each. The duodenal lumen of the tube is cleared with an injection of air after collection of each sample. Wide variation in volume of the aspirate is indicative of incomplete aspiration. Each sample of duodenal fluid is to be chilled and subsequently analyzed for volume and bicarbonate concentration. Exocrine pancreas dysfunction typically associated with chronic pancreatitis is indicated if the peak bicarbonate concentration for any sample < 80 mEq/L.

Endoscopic Collection Method: Endoscopic Pancreatic Function Test (ePFT)(2-4):

After assessment of patients for sedation and analgesia, a test dose of ChiRhoStim® 0.2 mcg if using the 16 mcg vial (0.1 mL) or 0.4 mcg if using the 40 mcg vial (0.1 mL) is injected intravenously to test for possible allergies. After one minute, if there are no signs of allergic reaction, ChiRhoStim® at a dose of 0.2 mcg/kg of body weight is injected intravenously over 1 minute. An upper endoscopy is performed with conscious sedation, after topical anesthetic. All gastric fluid is aspirated through the endoscope and discarded. After small bowel intubation to the junction of the second and third portion of the duodenum, fluid is aspirated for 1 to 3 minutes and collected in 5 separate specimen traps at baseline (0), 15, 30, 45, and 60 minutes after secretin injection. The patients remain intubated with the upper endoscope for one hour in the left lateral decubitus position. Boluses of meperidine and midazolam in a 25:1 mg ratio are administered to maintain analgesia and sedation during the 1-hour procedure. Each sample of duodenal fluid is to be chilled and subsequently analyzed for volume and bicarbonate concentration. Exocrine pancreas dysfunction typically associated with chronic pancreatitis is indicated if the peak bicarbonate concentration for any sample < 80 mEq/L.

2.2 Stimulation of Gastrin Secretion to Aid in Diagnosis of Gastrinoma:

0.4 mcg/kg body weight by intravenous injection over 1 minute.

The patient should fast for at least 12 hours prior to beginning the test. Prior to injection of ChiRhoStim®, two blood samples are drawn for determination of fasting serum gastrin levels (baseline values). Subsequently, a test dose of ChiRhoStim® 0.2 mcg if using the 16 mcg vial (0.1 mL) or 0.4 mcg if using the 40 mcg vial (0.1 mL) is injected intravenously to test for possible allergies. If there are no signs of allergic reaction, ChiRhoStim® at a dose of 0.4 mcg/kg of body weight is injected intravenously over 1 minute; post-injection blood samples are collected after 1, 2, 5, 10, and 30 minutes for determination of serum gastrin concentrations.

Gastrinoma is strongly indicated in patients who show an increase in serum gastrin concentrations of 110 pg/mL over basal level on any of the post injection samples.

2.3 Facilitation of the Identification of the Ampulla of Vater and Accessory Papilla During Endoscopic Retrograde Cholangiopancreatography (ERCP) to aid in cannulation of the pancreatic duct:

0.2 mcg/kg body weight by intravenous injection over 1 minute.

Administration of ChiRhoStim® may be given when difficulty is encountered by the endoscopist in identifying the ampulla of Vater for various reasons including: anatomic deformity secondary to prior surgery, radiation therapy, peptic ulcer disease, tumors, etc. or in identifying the accessory papilla in patients with pancreas divisum. A test dose of ChiRhoStim® 0.2 mcg if using the 16 mcg vial (0.1 mL) or 0.4 mcg if using the 40 mcg vial (0.1 mL) is injected intravenously to test for possible allergies. If there are no signs of allergic reaction, a dose of 0.2 mcg/kg of body weight intravenously over 1 minute may be administered and will result in visible excretion of pancreatic fluid from the orifices of these papillae enabling their identification and facilitating their cannulation.

2.4 ADMINISTRATION

ChiRhoStim® 16 mcg vial:
Dissolve the contents of the ChiRhoStim® 16 mcg vial in 8 mL of Sodium Chloride Injection USP, to yield a concentration of 2 mcg/mL. Shake vigorously to ensure dissolution. Use immediately after reconstitution and discard any unused portion.

ChiRhoStim® 40 mcg vial:
Dissolve the contents of the ChiRhoStim® 40 mcg vial in 10 mL of Sodium Chloride Injection USP, to yield a concentration of 4 mcg/mL. Shake vigorously to ensure dissolution. Use immediately after reconstitution and discard any unused portion.

For both strengths, the reconstituted drug product should be inspected visually prior to administration. If particulate matter or discoloration is seen, the product should be discarded.

3 DOSAGE FORMS AND STRENGTHS

ChiRhoStim® is available in two strengths:

As a lyophilized sterile powder in 10 mL vials containing 16 mcg of human secretin.

As a lyophilized sterile powder in 10 mL vials containing 40 mcg of human secretin.

4 CONTRAINDICATIONS
Patients suffering from acute pancreatitis should not receive ChiRhoStim® until the acute episode has subsided.

5 WARNINGS AND PRECAUTIONS

5.1 Allergic Reactions

Because of a potential allergic reaction to ChiRhoStim® patients should receive an intravenous test dose of 0.1 mL of the respective reconstituted vial. If no signs of allergic reaction are noted after one minute, the recommended dose may be injected slowly over 1 minute. A test dose is especially important in patients with a history of atopic allergy and/or asthma. Appropriate measures for the treatment of acute hypersensitivity reactions should be immediately available. No allergic reactions were observed after the test dose or full dose of synthetic human secretin in 584 patients and volunteers.

5.2 Vagotomy or Inflammatory Bowel Disease

Patients who have undergone vagotomy or who have inflammatory bowel disease may be hyporesponsive to secretin stimulation. This response does not indicate pancreatic disease, and results of secretin stimulation tests in these patients should be interpreted with caution.

5.3 Alcoholic or Liver Disease

A greater than normal volume response to secretin stimulation, which may mask coexisting pancreatic disease, is occasionally encountered in patients with alcoholic or other liver disease. Results of secretin stimulation tests in these patients should thus be interpreted with caution.

6 ADVERSE REACTIONS

Mild to moderate adverse reactions have been noted for synthetic human secretin in clinical studies in 533 patients and 51 healthy volunteers. Two severe adverse reactions, nausea and abdominal pain, occurred in one patient. Table 1 details the type and number of patients with adverse reactions.

TABLE 1
ADVERSE REACTIONS WITH CHIRHOSTIM®

Adverse Reaction	N = 584 Incidence (Patients)
Nausea	11(11)
Flushing	4 (4)
Early removal of Dreiling tube	3 (3)
Abdominal pain	3 (3)
Vomiting	3 (3)
Increased heart rate	2 (2)
Mild Pancreatitis	2 (2)
Upset stomach	2 (2)
Anxiety	1 (1)
Burning in stomach or abdomen	1 (1)
Clammy skin	1 (1)
Decreased O2 saturation	1 (1)
Diarrhea	1 (1)
Faintness	1 (1)
Hypotension	1 (1)
Infiltrated IV	1 (1)
Oral secretions increased	1 (1)
Sedation	1 (1)
Slow heart rate (57 bpm)	1 (1)
Tingling in legs	1 (1)
Unresponsive	1 (1)
Warm sensation in abdomen	1 (1)
Warm sensation in face	1 (1)

Of the 584 patients and healthy volunteers treated with ChiRhoStim®, a total of 29 patients (5%) had at least one adverse reaction.

7 DRUG INTERACTIONS

The concomitant use of anticholinergic agents may make patients hyporesponsive to secretin stimulation and may produce a false result. Any results of secretin stimulation tests in these patients should thus be interpreted with caution.

15 REFERENCES

1. Dreiling DA. Pancreatic secretory testing in 1974. Gut. 1975;16(8):653-7.
2. Stevens T, Conwell DL, Zuccaro G Jr, Van Lente F, Purich E, Khandwala F, Fein S. A randomized crossover study of secretin-stimulated endoscopic and dreiling tube pancreatic function test methods in healthy subjects. Am J Gastroenterol. 2006 Feb;101(2):351-5.
3. Yadav D, Chari ST. The Endoscopic Pancreatic Exocrine Function Test (ePFT): Can it be the New "Gold Standard"? Gastroenterology 2006 Oct;131(4):1349-1350.
4. Conwell DL, Zuccaro G, Purich E, Fein S, Vanlente F, Vargo J, Dumot J, O'laughlin C, Trolli P. The effect of moderate sedation on exocrine pancreas function in normal healthy subjects: a prospective, randomized, cross-over trial using the synthetic porcine secretin stimulated Endoscopic Pancreatic Function Test (ePFT). Am J Gastroenterol. 2005 May;(5):1161-6.
5. Jorpes, E. and Mutt V. On the biological assay of secretin. The reference standard. Acta Physiol Scand. 1966 Mar;66(3):316-25.
6. Chey WY, Chang T-M, Secretin. In: Kasin AJ. Editor. Handbook of Biologically Active Peptides. Elsevier, Amsterdam. 2006;1115-1122.
7. Whitcomb DC. Neurohormonal Control of the Exocrine Pancreas. In:Greeley JR G, editor. Endocrinology of the Gastrointestinal System. Totowa NJ:Humana Press. 1998;239-258.
8. Deveney, C.W., et al. Use of Calcium and Secretin in the Diagnosis of Gastrinoma (Zollinger-Ellison Syndrome). Ann Intern Med. 1977 Dec;87(6):680-6.

16 HOW SUPPLIED/STORAGE AND HANDLING

ChiRhoStim® 16 mcg vial NDC # 67066-005-01
ChiRhoStim® 40 mcg vial NDC # 67066-007-01

16.1 Supplied

ChiRhoStim® is supplied in two strengths:

As a lyophilized sterile powder in vials containing 16 mcg of human secretin.

As a lyophilized sterile powder in vials containing 40 mcg of human secretin.

16.2 Storage

The unreconstituted product should be stored at -20?C (freezer). Expiration date is marked on the label. Protect from light.

17 PATIENT COUNSELING INFORMATION

Since there is no data on pregnant or nursing mothers, physicians should discuss these matters with the patient before using this product.

Manufactured for:
ChiRhoClin, Inc
Burtonsville, MD 20866-6129

Manufactured by:
Bell-More Labs, Inc.
Hampstead, Maryland 21074-0179

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ChiRhoClin, Inc.