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

Initial U.S. Approval: 2004

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Indications and Usage (1) 10/2006

Indications and Usage

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.

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Drug Interactions

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

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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).

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Adverse Reactions

Most common adverse reactions (≥0.5%) are nausea, flushing, abdominal pain, and vomiting (6).

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Contraindications

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

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Warnings and Precautions

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

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See 17 for Patient Counseling Information

Revised 5/2007
A single intravenous dose of synthetic humansecretin at 20 mcg/kg should not be lethal to mice or rabbits.

14 CLINICAL STUDIES
14.1 Stimulation of pancreatic secretions, including bicarbonate to aid in the diagnosis of Chronic Pancreatitis.

ChiRhoStim® administered intravenously stimulates the exocrine pancreas to secrete pancreatic juices, which can assist in the diagnosis of exocrine pancreatic dysfunction. Normal ranges for pancreatic secretory responses to intravenous secretin in patients with defined pancreatic disease have been shown to vary. One source of variation is related to the stage of investigation differences in operative technique. In two parallel studies (CoMA-SRT) and COIWA, a total of 18 patients with a documented history of chronic pancreatitis were given sHS, sPS, bPS, and sPS. The results appear in Figures 1 and 2. In another study, 21 normal volunteers were given sHS. The results appear in Figures 1 and 2.

15 NONCLINICAL TOXICOLOGY

15.1 Nonclinical studies with ChiRhoStim® demonstrated that the potential for the drug to cause harm to the developing fetus and to affect reproductive capacity was demonstrated.

15.2 Nursing Mothers

Synthetic human secretin should be administered to a pregnant woman or can affect reproduction capacity. Synthetic human secretin should be avoided pregnancy only if clearly needed.

15.3 Human Milk

It is not known whether synthetic human secretin is excreted in human milk. Caution should be exercised when synthetic human secretin is administered to a nursing woman.

15.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

15.5 Geriatric Use

Among the 533 patients who have received ChiRhoStim® in clinical trials 18% were 65 years of age or older and 5% were 75 years of age or older. Dosing was the same as for the overall population of patients. No overall difference in safety pharmacology response was observed between elderly and young patients. However, other reported clinical experience has not identified differences between the elderly and the younger groups. This generalisation, but greater sensitivity of some older individuals to ChiRhoStim® cannot be ruled out.

11 DESCRIPTION

Human secretin is a gastrointestinal peptide hormone produced by cells in the duodenum in response to acidification. ChiRhoStim® (human secretin as the acetate) is a purified synthetic peptide with an amino acid sequence identical to the naturally occurring human hormone. Synthetic human secretin is chemically defined as follows:

Molecular Weight: 3308.44
Empirical Formula: C130H220N44O39
C5 H10 O4 N

Structural Formula:

Ser-Asp-Ar-Gly-Pro-Glu-Thr-Ser-Glu-Leu-Ser-Arg-Leu-Glu-Asp-Glu-Asp-Leu-Gln-Leu-Lys-Ala

ChiRhoStim® is available in two strengths:

A: A 10 mcg vial which contains 16 mcg of purified synthetic human secretin, 1.5 mg of L-lysine hydrochloride, 20 mg of mannitol, and 9 mg of sodium chloride. When reconstituted in 10 mL of Sodium Chloride Injection USP each mL of solution contains 2 mcg synthetic secretin for intravenous use. The pH of the reconstituted solution has a range of 3.0 to 5.5.

B: A 10 mcg vial which contains 40 mcg of purified synthetic human secretin, 3.75 mg of L-lysine hydrochloride, 50 mg of mannitol, and 22.5 mg of sodium chloride per mL. When reconstituted in 10 mL of Sodium Chloride Injection USP each mL of solution contains 4 mcg synthetic secretin for intravenous use. The pH of the reconstituted solution has a range of 3.0 to 5.5.

12 CLINICAL PHARMACOLOGY

The primary action of ChiRhoStim® is to increase the volume and bicarbonate content of pancreatic fluid. ChiRhoStim® may also work through vagal-vagal neural mechanisms.

In three crossover studies (CRC 98-1, CRC 98-2, and CRC 99-9) evaluating 21 different patients with a documented history of chronic pancreatitis, synthetic human secretin (sHS) and biologically derived porcine secretin (bPS) were compared to synthetic human secretin (sPS). All of the patients treated with these drugs had peak bicarbonate concentrations of less than 60 mL. Pancreatic secretory response to intravenous synthetic human secretin in 31 normal healthy volunteers has been shown to vary. The total volume over 1 hour of 207 mL. All 35 subjects had bicarbonate concentrations of 78 ± 13 mL.

14.2 Stimulation of gastric secretion to aid in the diagnosis of gastroparesis

ChiRhoStim® administered intravenously stimulates gastric emptying in patients with gastroparesis (Zollinger-Ellison Syndrome), whereas no or only small changes in serum gastrin concentration occurred in normal subjects and in patients with diabetic ulcer disease. Dewey et al. established the high sensitivity and specificity of the secretin stimulation test combined with the accuracy of gastric emptying studies for the diagnosis of gastroparesis and found discordant analysis that an increase from baseline of ≥ 110 pg/mL was the optimal point separating positive and negative tests.

This gastrin response to secretin can be used to support the diagnosis of gastroesophageal reflux disease (GERD) as a provocative test in the evaluation of patients in whom gastroparesis is in a diagnostic consideration.

In a third crossover study, three patients with diabetic ulcer disease were given ChiRhoStim®. All of the patients treated with these drugs had peak bicarbonate concentrations of less than 60 mL. Pancreatic secretory response to intravenous synthetic human secretin in 31 normal healthy volunteers has been shown to vary. The total volume over 1 hour of 207 mL. All 35 subjects had bicarbonate concentrations of 78 ± 13 mL.
Facilitation of identification of the ampulla of Vater and the accessory papilla during endoscopic retrograde cholangiopancreatography (ERCP) to assist in cannulation of the pancreatic ducts

In a randomized, placebo controlled crossover study in 24 patients with pancreas divisum undergoing ERCP, synthetic human secretin administration at a dose of 0.2 mcg/kg resulted in 16 of 24 successful cannulations of the minor duct compared to 2 of 24 for placebo.

15 REFERENCES

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 unconstituted 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.

ChiRhoStim® is a registered trademark of ChiRhoClin, Inc.
Manufactured for:
ChiRhoClin, Inc.
Burtonsville, MD 20866-6129

Manufactured by:
Bell-More Labs, Inc.
Hamptons, Maryland 21074-6179

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