For injection: 5 mcg of sincalide as a lyophilized product by Indication:

Intravenous use

KINEVAC (sincalide for injection), for intravenous use

Initial U.S. Approval: 1976

---RECENT MAJOR CHANGES---

Contraindications (4) 03/2018

Warnings and Precautions (5.1) 03/2018

---INDICATIONS AND USAGE---

Kinevac is a cholecystokinin (CCK) analog indicated in adults to:

• stimulate gallbladder contraction, as may be assessed by various methods of diagnostic imaging, or to obtain by duodenal aspiration a sample of concentrated bile for analysis of cholesterol, bile salts, phospholipids, and crystals. (1)

• stimulate pancreatic secretion in combination with secretin prior to obtaining a duodenal aspirate for analysis of enzyme activity, composition, and cytology. (1)

• accelerate the transit of a barium meal through the small bowel, thereby decreasing the time and extent of radiation associated with fluoroscopy and x-ray examination of the intestinal tract. (1)

---DOSEAGE AND ADMINISTRATION---

Recommended Adult Dosage and Administration by Indication: To Stimulate Contraction of the Gallbladder

• 0.02 mcg/kg as a single dose over 30 to 60 seconds via intravenous injection. If satisfactory contraction does not occur in 15 minutes, administer a dose of 0.04 mcg/kg over 30 to 60 seconds (2.1)

• Alternatively consider an intravenous infusion to reduce gastrointestinal adverse reactions: 0.12 mcg/kg diluted in 100 mL of 0.9% Sodium Chloride Injection USP and infused over 50 minutes at a rate of 2 mL per minute. (2.1, 2.2, 5.3)

To Stimulate Pancreatic Secretion in Combination with Secretin

• 30 minutes after initiation of secretin for injection, administer 0.02 mcg/kg diluted in 30 mL of 0.9% Sodium Chloride Injection USP and infused over 50 minutes at a rate of 1 mL per minute. (2.1, 2.2)

To Accelerate Transit of a Barium Meal Through the Small Intestine

• After the barium meal is beyond the proximal jejunum, administer 0.04 mcg/kg over 30 to 60 seconds via intravenous injection. (2.1)

• If satisfactory transit of the barium meal has not occurred in 30 minutes, administer a second dose of 0.04 mcg/kg over 30 to 60 seconds. (2.1)

• Alternatively consider an intravenous infusion to reduce gastrointestinal adverse reactions: 0.12 mcg/kg diluted in 100 mL of 0.9% Sodium Chloride Injection USP and infused over 30 minutes. (2.1, 2.2, 5.3)

---DOSEAGE FORMS AND STRENGTHS---

For injection: 5 mcg of sincalide as a lyophilized powder in a single-dose vial for reconstitution (3)

---CONTRAINDICATIONS---

• History of hypersensitivity to sincalide. (4, 5.1)

• Intestinal obstruction. (4)

---WARNINGS AND PRECAUTIONS---

• Anaphylaxis, Anaphylactic Shock and Other Hypersensitivity Reactions: May occur during or soon after administration. If symptoms occur, discontinue the drug. (4, 5.1)

• Evacuation of Gallstones: Stimulation of gallbladder contraction in patients with small gallbladder stones could lead to the evacuation of the stones from the gallbladder, resulting in their lodging in the cystic duct or in the common bile duct. (5.2)

---ADVERSE REACTIONS---

Most common adverse reactions (≥20%) are:

• abdominal discomfort or pain, and nausea. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Braeace Diagnostics Inc. at 1-800-257-5181 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---DRUG INTERACTIONS---

Drugs that Affect Gallbladder Motility or Contractile Response: May interfere with response to sincalide. Consider discontinuing these drugs prior to administration of Kinevac, when used to stimulate contraction of the gallbladder. (7.1

---FULL PRESCRIBING INFORMATION---

Revised: 12/2018

CONTENTS*

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

6 ADVERSE REACTIONS

7 DRUG INTERACTIONS

8 USE IN SPECIFIC POPULATIONS

9 OBESITY

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

13 NONCLINICAL TOXICOLOGY

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

18 REFERENCES

---GASTROINTESTINAL ADVERSE REACTIONS WITH INTRAVENOUS INJECTION---

Administer Kinevac as an intravenous injection may cause adverse reactions such as nausea, vomiting, abdominal pain or cramping, diziness, and flushing [see Adverse Reactions (6)]. These reactions are generally transient. To reduce the risk of adverse reactions with intravenous injection when used to stimulate contraction of the gallbladder or accelerate transit of a barium meal through the small intestine, administer Kinevac as an intravenous infusion over 50 or 30 minutes, respectively [see Dosage and Administration (2.1, 2.2)].

---PREPARATION INSTRUCTIONS---

For Intravenous Injection

• Reconstitute Kinevac aseptically by adding 5 mL of Sterile Water for Injection USP to the vial.

• Inspect the reconstituted solution visually for particulate matter and discoloration after reconstitution and prior to administration.

• Withdraw the prescribed dose of the reconstituted solution from the vial and administer as an intravenous injection over 30 to 60 seconds, as shown in Table 1. Discard the unused portion.

• Store the reconstituted solution at room temperature. Discard after 8 hours.

For Intravenous Infusion

• Reconstitute Kinevac aseptically by adding 5 mL of Sterile Water for Injection USP to the vial.

---REFERENCES---

Due to the potential for anaphylaxis, appropriate medical support should be readily available when Kinevac is administered. If anaphylaxis or other hypersensitivity reactions occur, immediately discontinue the infusion and initiate appropriate medical treatment. Observe patients closely during and after the infusion. Do not reinitiate Kinevac in patients who have experienced symptoms of hypersensitivity [see Contraindications (4.1)]

5.2 Evacuation of Gallstones

Stimulation of gallbladder contraction in patients with small gallbladder stones could lead to the evacuation of the stones from the gallbladder, resulting in their lodging in the cystic duct or in the common bile duct.

5.3 Gastrointestinal Adverse Reactions with Intravenous Injection

Administration of Kinevac as an intravenous injection may cause adverse reactions such as nausea, vomiting, abdominal pain or cramping, diziness, and flushing [see Adverse Reactions (6)]. These reactions are generally transient. To reduce the risk of adverse reactions with intravenous injection when used to stimulates contraction of the gallbladder or accelerate transit of a barium meal through the small intestine, administer Kinevac as an intravenous infusion over 50 or 30 minutes, respectively [see Dosage and Administration (2.1, 2.2)].

5.4 Preterm Labor or Spontaneous Abortion

Because of Kinevac’s effect on smooth muscle, pregnant patients should be educated that spontaneous abortion or premature induction of labor may occur [see Use in Specific Populations (8.1)]

6 ADVERSE REACTIONS

The following adverse reactions associated with the use of Kinevac were identified in clinical trials or postmarketing reports. Because these reactions were reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency, reliably, or to establish a causal relationship to drug exposure.

The most frequent adverse reactions (20% or greater) are gastrointestinal: abdominal discomfort or pain, and nausea; these may not necessarily indicate an abnormality of the biliary tract unless there is other clinical or radiologic evidence of disease.
8.4 Pediatric Use
The safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use
Clinical studies of Kinevac did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

10 OVERDOSAGE
In the event of an overdose, symptoms related to vagal stimulation, such as gastrointestinal symptoms (abdominal cramps, nausea, vomiting, and diarrhea), hypotension with dizziness or fainting may occur. Overdose symptoms should be treated symptomatically and should be of short duration.

A single bolus intravenous injection of 0.05 mcg/kg (approximately 2 to 3 times the human dose of 0.02 mcg/kg), sincalide caused hypotension and bradycardia in dogs. In addition, higher doses injected intravenously once or repeatedly in dogs caused syncope and ECG changes (approximately 5 times the human dose of 0.02 mcg/kg). These effects were attributed to sincalide-induced vagal stimulation in that all were prevented by pretreatment with atropine or bilateral vagotomy.

11 DESCRIPTION
Kinevac (sincalide for injection) is a cholecystopancreatic-gastrointestinal hormone for parenteral administration. The agent is a synthetically-prepared C-terminal octapeptide of cholecystokinin.

Each single-dose vial of sincalide provides a sterile nonpyrogenic lyophilized white powder consisting of 5 mcg sincalide with 30 mg arginine hydrochloride, 15 mg lysine hydrochloride, 170 mg mannitol, 4 mg methionine, 2 mg pentetic acid, 0.005 mcg polysorbate 20, 9 mg potassium phosphate dibasic, and 0.04 mg sodium metabisulfite. The pH is adjusted to 6.0 to 8.0 with hydrochloric acid and/or sodium hydroxide.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
When injected intravenously, sincalide stimulates gallbladder contraction and reduction in size. The evacuation of bile that results is similar to that which occurs physiologically in response to endogenous cholecystokinin. Sincalide also stimulates pancreatic secretion and intestinal motility causing pyloric contraction and slows gastric emptying. Concurrent administration of sincalide with secretin increases both the volume of pancreatic secretion and the out-put of bicarbonate and enzymes. This combined effect of secretin and sincalide permits the assessment of specific pancreatic function through measurement and analysis of the duodenal aspirate.

12.2 Pharmacodynamics
Following an intravenous (bolus) injection of 0.02 mcg/kg of sincalide, maximal contraction of the gallbladder occurred in 5 to 15 minutes. Sincalide reduced gallbladder radiographic size by at least 40%, which is generally considered satisfactory contraction.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term studies in animals have not been performed to evaluate carcinogenic or mutagenic potential, or possible impairment of fertility in males or females.