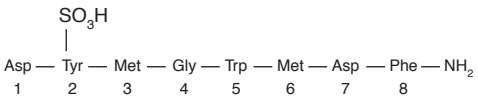
Bracco Diagnostics

875016-H04

KINEVAC®
Sincalide for Injection

DESCRIPTION
Kinevac (Sincalide for Injection) is a cholecystopancreatic-gastrointestinal hormone peptide for parenteral administration. The agent is a synthetically-prepared C-terminal octapeptide of cholecystokinin. Each vial of sincalide provides a sterile nonpyrogenic lyophillized white powder consisting of 5 mcg sincalide with 170 mg mannitol, 30 mg arginine hydrochloride, 15 mg lysine hydrochloride, 9 mg potassium phosphate dibasic, 4 mg methionine, 2 mg pentetic acid, 0.04 mg sodium metabisulfite, and 0.005 mcg polysorbate 20. The pH is adjusted to 6.0 - 8.0 with hydrochloric acid and/or sodium hydroxide prior to lyophilization. Sincalide is designated chemically as L-α-aspartyl-O-sulfo-L-tyrosyl-L-methionylglycyl-L-tryptophyl-L-methionyl-L-α-aspartyl-L-phenylalaninamide. Graphic formula:



$C_{49}H_{62}N_{10}O_{16}S_3$ MW 1143.27 CAS-25126-32-3

CLINICAL PHARMACOLOGY
When injected intravenously, sincalide produces a substantial reduction in gallbladder size by causing this organ to contract. The evacuation of bile that results is similar to that which occurs physiologically in response to endogenous cholecystokinin. The intravenous (bolus) administration of sincalide causes a prompt contraction of the gallbladder that becomes maximal in 5 to 15 minutes, as compared with the stimulus of a fatty meal which causes a progressive contraction that becomes maximal after approximately 40 minutes. Generally, a 40 percent reduction in radiographic area of the gallbladder is considered satisfactory contraction, although some patients will show area reduction of 60 to 70 percent.

Like cholecystokinin, sincalide stimulates pancreatic secretion; concurrent administration with secretin increases both the volume of pancreatic secretion and the output of bicarbonate and protein (enzymes) by the gland. This combined effect of secretin and sincalide permits the assessment of specific pancreatic function through measurement and analysis of the duodenal aspirate. The parameters usually determined are: volume of the secretion; bicarbonate concentration; and amylase content (which parallels the content of trypsin and total protein).

Both cholecystokinin and sincalide stimulate intestinal motility, and may cause pyloric contraction which retards gastric emptying.

INDICATIONS AND USAGE
Kinevac (Sincalide for Injection) may be used: (1) 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; (2) to stimulate pancreatic secretion (especially in conjunction with secretin) prior to obtaining a duodenal aspirate for analysis of enzyme activity, composition, and cytology; (3) to 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.

CONTRAINDICATIONS
The preparation is contraindicated in patients hypersensitive to sincalide and in patients with intestinal obstruction.

WARNINGS
Because of Kinevac's effect on smooth muscle, pregnant patients should be advised that spontaneous abortion or premature induction of labor may occur (see Pregnancy Category B).

PRECAUTIONS
General
The possibility exists that 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. The risk of such an event is considered to be minimal because sincalide, when given as directed, does not ordinarily cause complete contraction of the gallbladder.

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.

Teratogenic Effects
Pregnancy Category B
Reproduction studies in rats in which sincalide was administered subcutaneously at doses up to 12.5 times the maximum recommended human dose revealed no evidence of harm to the fetus due to sincalide. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed (see WARNINGS).

Labor and Delivery
Sincalide should not be administered to pregnant women near term because of its effect on smooth muscle; the possibility of inducing labor prematurely exists. The effects of sincalide on labor, delivery and lactation in animals has not been determined (see WARNINGS).

Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when sincalide is administered to a nursing woman.

Pediatric Use
Safety and effectiveness in children have not been established.

ADVERSE REACTION
Reactions to sincalide are generally mild and of short duration. The most frequent adverse reactions were abdominal discomfort or pain, and nausea; rapid intravenous injection of 0.04 mcg sincalide per kg expectably causes transient abdominal cramping. These phenomena are usually manifestations of the physiologic action of the drug, including delayed gastric emptying and increased intestinal motility. These reactions occurred in approximately 20 percent of patients; they are not to be construed as necessarily indicating an abnormality of the billiary tract unless there is other clinical or radiologic evidence of disease.

The incidence of other adverse reactions, including vomiting, flushing, sweating, rash, hypotension, hypertension, shortness of breath, urge to defecate, headache, diarrhea, sneezing, and numbness was less than 1 percent; dizziness was reported in approximately 2 percent of patients. These manifestations are usually lessened by slower injection rate.

OVERDOSAGE
Although no overdosage reports have been received, gastrointestinal symptoms (abdominal cramps, nausea, vomiting and diarrhea) would be expected. Hypotension with dizziness or fainting might also occur. Overdosage symptoms should be treated symptomatically and should be of short duration. Starting with single bolus i.v. injection comparable to the human dose of 0.4 mg/kg, sincalide caused hypotension and bradycardia in dogs. Higher doses injected once or repeatedly in dogs caused syncope and ECG changes in addition. These effects were attributed to sincalide-induced vagal stimulation in that all were prevented by pretreatment with atropine or bilateral vagotomy.

DOSAGE AND ADMINISTRATION
Reconstitution and Storage
Sincalide for Injection may be stored at room temperature prior to reconstitution.

To reconstitute, aseptically add 5 mL of Sterile Water for Injection USP to the vial. This solution may be kept at room temperature and should be used within 8 hours of reconstitution, after which time any unused portion should be discarded.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

For prompt contraction of the gallbladder, a dose of 0.02 mcg sincalide per kg (1.4 mcg/70 kg) is injected intravenously over a 30- to 60-second interval; if satisfactory contraction of the gallbladder does not occur in 15 minutes, a second dose, 0.04 mcg sincalide per kg, may be administered. To reduce the intestinal side effects (see ADVERSE REACTIONS), an intravenous infusion may be prepared at a dose of 0.12 mcg/kg in 100 mL of Sodium Chloride Injection USP and given at a rate of 2 mL per minute; alternatively, an intramuscular dose of 0.1 mcg/kg may be given. When Kinevac (Sincalide for Injection) is used in cholecystography, roentgenograms are usually taken at five-minute intervals after the injection. For visualization of the cystic duct, it may be necessary to take roentgenograms at one-minute intervals during the first five minutes after the injection.

For the Secretin-Kinevac test of pancreatic function, the patient receives a dose of 0.25 units secretin per kg by intravenous infusion over a 60-minute period. Thirty minutes after the initiation of the secretin infusion, a separate IV infusion of Kinevac at a total dose of 0.02 mcg per kg is administered over a 30-minute interval. For example, the total dose for a 70 kg patient is 1.4 mcg of sincalide; therefore, dilute 1.4 mL of reconstituted Kinevac solution to 30 mL with Sodium Chloride Injection USP and administer at a rate of 1 mL per minute.

To accelerate the transit time of a barium meal through the small bowel, administer Kinevac after the barium meal is beyond the proximal jejunum. (Sincalide, like cholecystokinin, may cause pyloric contraction.) The recommended dose is 0.04 mcg sincalide per kg (2.8 mcg/70 kg) injected intravenously over a 30- to 60- second interval; if satisfactory transit of the barium meal has not occurred in 30 minutes, a second dose of 0.04 mcg sincalide per kg may be administered. For reduction of side effects, a 30-minute IV infusion of sincalide [0.12 mcg per kg (8.4 mcg/70 kg) diluted to approximately 100 mL with Sodium Chloride Injection USP] may be administered.

Sodium Chloride Injection dilutions may be kept at room temperature and should be used within one hour of dilution.

HOW SUPPLIED
Kinevac (Sincalide for Injection) is supplied in packages of 10 single dose vials containing 5 mcg of sincalide per vial (NDC 0270-0556-15).

Storage
Store at 25° C (77° F); excursions permitted to 15-30° C (59-86° F) [See USP Controlled Room Temperature].
U.S. Patent 6,803,046

Rx only

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