CRALFATE

क्रालफेट

Sucralfate

CRALFATE

Brand Name and Generic Name

Cralfate 180ml

Each 5 ml of suspension contains sucralfate USP 500mg

Strength of Active Ingredient(s)

Cralfate 180ml

Each 5 ml of suspension contains sucralfate USP 500mg

Product Description

Sucralfate is a medication used to treat duodenal ulcers, epithelial wounds, chemotherapy-induced mucositis, radiation proctitis, ulcers in Behcet disease, and burn wounds. Sucralfate exhibits its action by forming a protective layer, increasing bicarbonate production, exhibiting anti-peptic effects, promoting tissue growth, regeneration, and repair. The medication has a relatively safe profile as there is negligible absorption from the enteral system. This activity outlines the indications, mechanism of action, methods of administration, significant adverse effects, contraindications, toxicity, and monitoring, of sucralfate, so providers can direct patient therapy in conditions where it has therapeutic benefit as part of the interprofessional team.

Pharmacodynamics & Pharmacokinetics

Pharmacodynamics:

Sulfated polysaccharide has been known for a long time to possess an inhibitory action on proteolytic activity of pepsin and a preventive action on experimental peptic ulcerations. Sucralfate, a disaccharide sulfate, has been shown to have a strong antipepsin and antiulcer action. Contrary to the more polymerized saccharides, sucralfate is devoid of any anti-coagulant activity. Moreover, it has been found that enhanced antiulcerogenic activity was more pronounced with the aluminum salt of the disaccharide sucralfate.

Sucralfate produces distinct morphologic and functional changes in the normal gastric mucosa: mucus release, changes in ion transport and increased release of luminal prostaglandins. Several studies have shown that it can increase the synthesis and release of prostaglandin E2 from the mucosa. This mechanism may in part explain its effective cytoprotective properties. Results of in vivo and in vitro studies show that sucralfate produced an adherent and cytoprotective barrier at the ulcer site which resisted degradation by acid and pepsin. Laboratory and clinical studies indicate that sucralfate promotes the healing of gastric and duodenal ulcers by a three-way action:

1) Formation of a chemical complex that binds to the ulcer site to establish a protective barrier.
2) Direct inhibition of the action of pepsin and bile.
3) Blockage of the back diffusion of gastric acid across the barrier.

The binding of sucralfate was demonstrated in rats with experimentally-induced ulcers. After a single dose of sucralfate, the ulcerated organs were excised and washed with a fluorescent compound that was taken up by sucralfate. Under ultraviolet light, the sucralfate showed affinity for the areas of ulceration, substantiating the binding action. The affinity of sucralfate for the ulcer site was further substantiated in a study where patients were scheduled for gastric resection. Each patient received the same daily dose of sucralfate, with the interval from the last dose to operation time varying from 2 to 16 hours. At all of these intervals, the concentrations of sucralfate in ulcer craters were 4 to 30 times higher than the concentrations in tissue specimens from the normal mucosa in the same patients. The antipepsin activity of sucralfate has been demonstrated in several in vivo and in vitro studies. The principal action of sucralfate is unknown. The following actions of sucralfate have been the object of study in vitro, but the in vivo actions remain unknown: Antipeptic effects - It prevents hydrolysis by preventing the formation of the enzyme-substrate complex. It adsorbs pepsin and decreases its concentration. Site-protective effects - By forming a polyanion gel, it acts as a physical barrier between luminal contents and mucosa. Effects on mucus - Increases mucous hydrophobicity, viscosity, sulfation, and aluminum and carbohydrate content, which leads to improved mucosal protection from acid. It also increases the production of mucus by increasing prostaglandin production. Sucralfate prevents the breakdown of mucus by pepsin A, reducing ulcerogenesis. Effect on bicarbonate output - It increases prostaglandin-dependent and independent bicarbonate production by stomach and duodenum. Effects on tissue growth, regeneration, and repair - It binds epidermal growth and tissue growth factors to tissues and facilitates repair.

Pharmacology:

The time of onset is 1 to 2 hours. Only 5% of the dose is absorbed when taken orally; sucralfate is considered a non-systemic medication.

The drug's duration of action is up to 6 hours.

Sucralfate is not systemically metabolized and is primarily excreted unchanged in the feces.

Absorption: Sucralfate is only minimally absorbed from the gastro-intestinal tract. The small amounts that are absorbed are excreted primarily in the urine. Absorption of aluminium from sucralfate may be increased in patients on dialysis or with renal dysfunction.

INDICATIONS:

Sucralfate is a unique anti-ulcer drug. It is a basic aluminum salt of sucrose octasulfate. The labeled use of sucralfate is as below:

Treatment of duodenal ulcer: Sucralfate is FDA approved for the treatment of duodenal ulcers up to 8 weeks (short term). Duodenal ulcers are treated with 1g four times daily for eight weeks, followed by 1 g twice daily for maintenance therapy. The efficacy of sucralfate in the treatment of duodenal ulcers is shown to be comparable to that of cimetidine and intensive antacid therapy.Sucralfate forms a protective coat and protects the gastric mucosa from pepsin, pectic acid, and bile salts. It binds to positively charged proteins in exudates, locally

forming a thick viscous substance. As outlined below, sucralfate has also been used to treat various off-label (non-FDA approved) conditions.

Dyspepsia: It is shown to reduce the frequency and intensity of dyspeptic symptoms and gastric erosion during NSAID therapy, and the efficacy is similar to that of an H-2 receptor blocker. Treatment of epithelial wounds: Sucralfate has also been used as a topical drug in treating various epithelial wounds such as ulcers, inflammatory dermatitis, mucositis, and burns wounds. Several studies have been conducted to study the efficacy of sucralfate in the treatment of epithelial wounds. A study done by Tsakayannis et al. showed that the venous ulcer that failed conventional therapy responded to treatment with topical sucralfate.Sucralfate increases the bio-availability of growth factors, especially fibroblast growth factor (FGF), which has a pivotal role in angiogenesis and, in turn, promotes epithelial wound healing. Treatment of chemotherapy-induced mucositis: A study done by McCullough showed that high potency sucralfate accelerates the activation of growth factor and is useful in treating chemotherapy-induced mucositis of the oropharynx and alimentary tract. This resulted from administering 1.5 g of sucralfate three times daily at the onset of mucositis for two days, followed by 1.5 g two times daily throughout the course of cancer therapy and two weeks after the completion of treatment. Treatment of radiation proctitis: Sucralfate paste enema has shown clinical improvement in hemorrhagic radiation proctitis treatment. This therapy uses a low volume paste in an enema applicator, and pre and post-treatment improvements were assessed using clinical proctitis scores with a positive outcome. A study done by Kocchar et al. has shown that sucralfate enema is better than oral sulfasalazine in the short-term treatment of radiation proctitis.Prevention of ulceration of diversion colitis: The use of enemas containing sucralfate is shown to preserve the mucus layer covering the epithelium, thereby reducing inflammation in diversion colitis. The concentration of sucralfate used in the enema is 2 g/kg/day.Stress ulcer prophylaxis in ventilated patients: Research has shown that sucralfate is better for stress ulcer prophylaxis when compared to H-2 blockers or antacids in patients receiving ventilation therapy as the latter increases the pH of gastric contents causing stagnation of gram-negative bacilli and subsequently increasing the risk of nosocomial pneumonia.

Behcet Disease: Topical sucralfate 1 g/5mL four times daily alone or in combination with topical corticosteroids reduces pain and promotes the healing of oral ulcers in Behcet disease. Sucralfate suspension is the dosage form for treating oral ulcers in Behcet disease.

DOSAGE & INDICATIONS: For the treatment of duodenal ulcer not related to NSAID use.

For active disease.Oral dosage

Adults: 1 g PO four times per day, given 1 hour before meals and at bedtime for 4—8 weeks or less if healing has been effectively demonstrated.

For maintenance therapy of duodenal ulcer.Oral dosage (tablets only)

Adults: 1 g PO two times per day on an empty stomach.

For the treatment of gastric ulcer not related to NSAID use or for treatment of esophagitis associated with gastroesophageal reflux disease (GERD).Oral dosage

Adults: 1 g PO four times per day given one hour before meals and at bedtime. For NSAID-induced ulcer prophylaxis†.Oral dosage

Adults: Several studies have evaluated sucralfate as an agent to prevent NSAID-induced ulcers. In a small study of healthy males, sucralfate 1 g PO four times per day was superior to placebo in preventing gastric injury due to aspirin. Endoscopy was not used in this study. However, some clinicians feel that sucralfate has no place in the prevention or therapy of NSAID-induced gastric ulcer and does not appear to prevent NSAID-associated duodenal ulcer. In a comparison with misoprostol to prevent the development of NSAID-induced gastric ulcer in patients during 3 months of continuous NSAID administration, the incidence of gastric ulcer was 1.6% in the misoprostol group and 16% in the sucralfate group. The sucralfate dose in this study was 1 g PO four times per day given one hour before meals and at bedtime. For stress gastritis prophylaxis† in critically ill patients.

Oral dosage:

Adults: 1 g PO 4 times daily.

For the palliative treatment of aphthous ulcer, or for the palliative treatment of stomatitis due to chemotherapy or radiation therapy.

Oral rinse dosage (sucralfate suspension)

Adults: 5-10 ml (500 mg to 1 g) PO swished in the mouth for several minutes and spit or swallowed, four times per day. Retain in the mouth for several minutes while swishing to insure contact time with affected oral mucosal surfaces.

For the alternative treatment of proctitis due to ulcerative colitis or radiation injury.Rectal dosage (rectal suspension retention enema, commercial dosage form not available in U.S) Adults: Doses range from 2-4 g per 15-20 ml (3 g/15 ml is a common dosage for radiation proctitis) PR once or twice daily or as 20 g/100 ml PR once or twice daily (for ulcerative proctosigmoiditis) in literature reports. Prophylactic use (rectally or orally) to prevent radiation injury does not appear to be effective. Extemporaneous compounds vary and have not been adequately characterized for stability or other attributes (see Administration). One case report described using the commercially available oral suspension to deliver a 2 g/20 ml dosage PR twice daily ; however, the effect of formulation excipients on the rectal mucosal or in regard to safety, efficacy, or tolerability are not known.

Indicates off-label use

MAXIMUM DOSAGE

Adults: 4 g/day PO.

Elderly: 4 g/day PO.

Adolescents: 4 g/day PO.

Children: Maximum dosage not established. 80 mg/kg/day PO or alternatively, up to 2000 mg/day PO has been suggested for most indications.

ADMINISTRATION

Oral Administration

Take on an empty stomach at least 1 hour prior to a meal and at bedtime. Antacids may be prescribed as needed for relief of pain but should not be taken within one-half hour before or after a sucralfate dose.

Shake well prior to each administration; measure the dosage with a calibrated oral measuring device.For enteral tube administration, flush the tube with 30 mL of water (adults) before and after administering the drug.

DOSAGE AND ADMINISTRATION

Tablets

The recommended adult oral dosage of Sucralfate for duodenal and gastric ulcer is one tablet of 1 g four times a day, one hour before meals and at bedtime, on an empty stomach. For duodenal ulcer, Sucralfatemay also be administered as two 1 g tablets twice daily, on waking and at bedtime on an empty stomach. In duodenal ulcers, while healing with Sucralfateoften occurs within two to four weeks, treatment should be continued for a maximum of 8 to 12 weeks unless healing has been demonstrated by X-Ray and/or endoscopic examination. In the case of gastric ulcers, an alternative treatment should be considered if no objective improvement is observed following 6 weeks of Sucralfatetherapy. However, patients with a large gastric ulcer that has demonstrated a progressive healing tendency may require an additional 6 weeks of treatment. For the prophylaxis of duodenal ulcer recurrence, the recommended dosage is one tablet of 1 g twice daily, on an empty stomach. Treatment may be continued for up to one year. For relief of pain, antacids may be added to the treatment. However, antacids should not be taken within ½ hour before or after Sucralfateintake.

Suspension

SUCRALFATE SUSPENSION

Sucralfatemust not be administered intravenously.

The recommended adult dose of SUCRALFATE SUSPENSION for the treatment of (acute) duodenal ulcer is 2 g twice a day on waking and at bedtime on an empty stomach. For the prophylaxis of gastrointestinal hemorrhage due to stress ulceration, administer 1 g orally or via nasogastric tube four to six times a day. To prevent clogging of the nasogastric tube flush with 10 mL of water following each administration. The duration of treatment for prophylaxis of stress ulceration must be individually determined. Treatment should be continued for as long as one or more of the risk factors for stress ulceration is present but normally not for more than 14 days.

Duration of continuous treatment in patients with chronic renal failure receiving dialysis should be evaluated by periodic monitoring of serum aluminum levels, due to the possibility of aluminum accumulation in these patients. According to information widely available in the literature, patients with serum aluminum concentrations that approach 100 g/L should be carefully monitored for symptoms of aluminum toxicity and treatment should be discontinued if such symptoms appear.

There is no evidence to indicate that patients with chronic renal failure, who do not require dialysis, are at risk of developing aluminum toxicity while receiving the recommended doses of sucralfate. Physician discretion should be exercised when considering the duration of treatment.

ADVERSE REACTIONS

Severe: Bezoar (Delayed / Incidence not known), angioedema (Rapid / Incidence not known), anaphylactoid reactions (Rapid / Incidence not known), aluminum toxicity (Delayed / Incidence not known)

Moderate: Constipation, edema, dyspnea, hypophosphatemia, hyperglycemia

Mild: Dizziness, headache, nausea, rash, flatulence, vomiting, back pain, drowsiness, xerostomia, pruritus, vertigo, urticaria Cases of hypersensitivity have been reported with the use of sucralfate, including anaphylactic reactions, bronchospasm, dyspnoea, laryngeal oedema, lip swelling, oedema mouth, pharyngeal oedema, pruritus, rash, respiratory tract oedema, swelling face and urticaria.

Use in Pregnancy

Teratogenicity studies have been performed in mice, rats, and rabbits at doses up to 50 times the human dose and have revealed no evidence of harm to the fetus due to sucralfate. 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.

Pediatric Use

Clinical experience in children is limited. Therefore, sucralfate therapy cannot be recommended for children under 14 unless, in the judgment of the physician, anticipated benefits outweigh the potential risk.

Lactation

It is not known whether the drug is excreted in human milk. Caution should be exercised when Sucralfate is administered to breast feeding women.

CONTRAINDICATIONS

Patients with known hypersensitivity to the active substance or to any of the excipients.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Overdosage has never been observed with Sucralfate and appears to be unlikely since, using maximal doses of up to 12 g/kg/body weight in a variety of animal species, a lethal dose could not be established. Overdosage is likely to be associated with symptoms similar to those described in the ADVERSE REACTION section, such as constipation. These should be treated symptomatically. In a clinical trial on healthy men of overdose with sucralfate, most cases remained asymptomatic, but symptoms of abdominal pain, nausea, and vomiting were reported in a few cases. Acute oral toxicity studies in animals, using doses up to 12 g/kg body weight, could not find a lethal dose. Risks associated with overdose, should, therefore, be minimal.

DOSING CONSIDERATIONS

Hepatic Impairment: Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed. Renal Impairment: CrCl > 30 ml/min: Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed. CrCl <= 30 ml/min: Sucralfate contains aluminum; systemically absorbed in small amounts. Patients with renal failure can develop aluminum accumulation due to impaired aluminum excretion. Use with caution in patients with renal failure.

Intermittent hemodialysis: Sucralfate contains aluminum, which may be systemically absorbed in small amounts. Aluminum does not cross dialysis membranes because of high plasma protein binding, and may accumulate in patients on dialysis.

Storage

How Supplied

CRALFATE Suspension : Each 5 mL of suspension contains 500mg of sucralfate. Supplied in bottles of 180 mL. Shake well before using.

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Manufactured by:
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