For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

GRANIZ

(Granisetron Injection)

Compostion :

Each ml contains :

Granisetron Hydrochloride BP

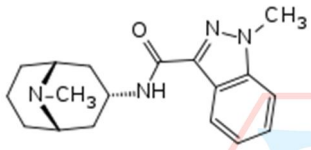
equivalent to Granisetron.....1 mg

Description

Chemical Structure

Chemically Granisetron Hydrochloride is 1-Methyl-N-[(3-endo)-9-

methyl-9-aza bicyclo[3.3.1]non-3-yl]-1H-indazole-3-carboxamide hydrochloride



Clinical Pharmacology

Mechanism of action

Granisetron Injection is an anti nauseant and anti-emetic. It is highly selective antagonist of 5-Hydroxy- tryptamine (5-HT3) receptors.

Radioligand brinding studies have demonstrated that Granisetron injection has negligible affinity for other receptor types including 5-HT and dopamine D, binding sites.

Granisetron injection is effective intravenously, either prophylactically or by intervention, in abolishing the itching and vomiting evoked by administration of cytotoxic drugs or by whole body X-irradation.

Granisetron injection is effective intravenously, in the prevention and treatment of post operative nausea and vomiting.

Pharmacokinetics :

Granisetron is completely absorbed with repaid appearance of metabolities in the plasma, suggestive of presystemic metabolism. Following intravenous dose of 40 ug/kg, the avehrage peak plasma concentration is 30.7 iu/L.

Granisetron is extensively distributed in the body (volume of distribution-200L) and that is about 65% of the drug in the plasma is protein bound.

The pharmacokinetics if Granisetron exhibit considerable interindividual variation and the elimination half life is reported to be around 3 to 4 hours in healthy subjects but about 9 to 12 hours in cancer patients .

Granisetron is rapidly & extrensively metabolised in the liver, In normal volunteers, approximately 12% of the administered dose is eliminated unchanged in the urine whilst that of metabolites amounts to about 49% of dose . The reminder is excreted in faeces as metabolies.

In elderly subjects after single intravenous doses, pharmackinetic parameters were with in the range found for non-elderly subjects in patients with serve renal failure, intravenous dose are generally similar to those in normal subjects.

In patients with hepatic impairment due to neoplastic liver involvement. Despite these changes no dosage adjustment is necessary.

Indications:

Granisetron injection is indicated for the prevention or treatment of nausea and vomiting with the treatment of cancer by radiotherapy and chemotherapy and for the prevention nausea and vomiting.

Dosage and administration :

Cytostatic Therapy

The recommended dosage for Granisetron injection is 40ug/kg administration intravenously within 30 minutes before initiation of chemotherapy. Injection may be administered intravenously either undiluted over 30 seconds or diluted with 5 minutes.

One additional dose of 40ug/kg body weight (up to 3mg) may be administered within a 24-hour period if required. This additional dose should be administered over five minutes.

Administration should be completed prior to the start of cytosatic therapy.

Renally impaired. No special requirements apply.

Hepatically impaired : N special requirements apply.

Post Operative nausea and vomiting

Adults : For prevention in adults, a single dose of 1mg of Granisetron injection should be diluted to 5ml and administered as a slow intravenous injection (over 30 seconds) Administrations should be completed prior induction of anaesthesia.

For treatment of established post-operative nausea and vomiting in adults, a single dose of 1mg of Granisetron injection should be diluted to 5ml and administered by slow intravenous injection (over 30 seconds).

Children : There is no experience in the use of Granisetron injection in the prevention and treatment of post-operative nausea and vomiting in children under 12 years of age. Granisetron injection is not therefore recommended for the treatment of post-operative nausea and vomiting in this age group.

Elderly : As for adults.

Renally impaired : As for adults.

Hepatically impared : As for adults.

Instructions for use & handling :

As a general precaution GRANIZ injection should not be mixed in solution with other drugs.

Prophylactic administration of Granisetron injection should be completed prior to the start of cytostatic therapy or induction of anaesthesia.

Preparation of the infusion :

Children : To prepare the dose of 40ug/kg the appropriate volume is withdrawn and diluted with infusion fluid to a total volume of 10 to 30 ml. Any one of the following solutions may be used: 0.9% w/v Sodium Chloride Injection 0.18% w/v Sodium Chloride Injection and 4% w/v Glucose: Injection; 5% w/v Glucose Injection; Hartman'ns Solution for injection'

Adults : To prepare a dose of 1mg, 1ml should be withdrawn from the vial and diluted to 5ml with 0.9% w/v Sodium Chloride Injection. No other diluents should be used.

Ideally, Intravenous infusion of Granisetron injection should be prepared at the time of administration.

After dilution (see above). or when the container is opened for the first time, the shelf life is 24 hours when stored at ambient temperature in normal indoor illumination, protected from direct sunlight. It must not ne used after 24 hours. If to be stored after preparation.

Granisetron infusions must be prepared under aseptic conditions.

Warnings:

Granisetron injection may reduce lower bowel mobility and therefore patients with sings if subacute intestinal obstruction should be monitored following administration of Granisetron injection. Somnolence has infrequently been reported with Granisetron, and care should be taken when operating hazardous machinery or driving.

An increased incidence of hepatic neoplasms in rodents given very high dose of Granisetron for prolonged periods has been reported, although the relevance of these results to the clinical situation is undermined. Mutagenicity have not been seen in some tests, but an increased incidence DNA syntheses in exposed cells have been reported by some authors.

Precautions :

Pregnancy & Lactation

Whilst animal studies have shown no teratogenic effects. there is no experience of Granisetron injection in human pregnancy. Therefore

Granisetron injection should not be administered to pregnant women unless there are compelling reasons. There is no data on the excretion of Granisetron in breast milk. Breast feeding should therefore be discontinued during therapy.

Side effects :

Granisetron injection has been generally well tolerated in human studies. As reported with other drugs of this class, headache and constipation have been the most frequently noted adverse event but majorities have been mild or moderate in nature, rare cases of hypersensitivity reaction, occasionally severe (eg. anaphylaxis) have been reported.

Other allergic reactions including minor skin rashes have also been reported. In clinical trials. transient increases in hepatic tansaminases (AST, ALT greater than twice the normal limit), has been noted in patients.

Drug Interactions :

n studies in healthy subjects, no evidence of any interaction has been indicated between. Granisetron injection and lorazepam. No evidence of drug interactions has been observed in clinical studies conducted.

The concomitant administration of dexamethasone as an intravenous bolus appears to increase the anti-emetic effect of Granisteron.

No specific interaction studies have been conducted in anaesthetized patients, but Granisetron injection has been safety administered with commonly used anaesthetic and analgesic agents. In addition, in vitro human microsomal studies have shown that the cytochromeP sub family 344 (Involved in the metabolism of some of the main narcotic analgesic agents)

Overdosage :

There is no specific antidote for Granisetron injection, In case of over dosage, symptomatic treatment should be given.

Over dosage of up to 38.5 mg of Granisetron injection has been reported. The patient reported a slight headache but no other sequelae were observed.

Contraindications :

1. Hypersensitivity to Granisetron or releated substances.
2. Subacute intestinal obstruction.

Storage Conditions

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° and 30°C (59° and 86°F).

PRESENTATION :

GRANIZ INJECTION is available in a vial of 1mg /1ml. & 3mg/3ml.

Manufactured in India by:

ZUVIUS LIFESCIENCES PVT. LTD.
A WHO-GMP CERTIFIED COMPANY
B/111, 112, 113, Kanara Business Centre,
Link Road, Ghatkopar (East), Mumbai 400075.
www.zuviuslifesciences.in

Zuvius
LIFESCIENCES