

Prescribing Information

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Setron

Granisetron Hydrochloride Injection

Description

Clear glass ampoules, each containing 3 mg granisetron present as the hydrochloride in 3 ml isotonic saline as a clear, colourless or slightly straw-coloured liquid.

The inactive ingredients in the infusion are sodium chloride and Water for Injections.

Clinical Pharmacology

Granisetron is a potent and highly selective 5-hydroxytryptamine (5-HT₃) receptor antagonist with anti-emetic activity.

Pharmacokinetics

Further information

Absorption of Setron is generally not influenced by food and is rapid and complete, though oral bioavailability is reduced to around 60% as a result of first pass metabolism.

Setron is widely distributed with plasma protein binding of approximately 65%. It is rapidly and extensively metabolised mainly by N-demethylation and aromatic ring oxidation followed by conjugation; excretion is both urinary and faecal.

Uses

Setron is indicated for the prevention or treatment of nausea and vomiting induced by ematogenic cancer therapy and cytostatic therapy

Dosage and administration

Setron ampoules are for intravenous administration only.

Adults: 3 mg Setron, which should be administered *either* in 15 ml infusion fluid as an intravenous bolus over not less than 30 seconds *or* diluted in 20 to 50 ml infusion fluid and administered over five minutes.

Prevention: In clinical trials, the majority of patients have required only a single dose of Setron to control nausea and vomiting over 24 hours. Up to two additional doses of 3 mg Setron may be administered within a 24-hour period. There is clinical experience in patients receiving daily administration for up to five consecutive days in one course of therapy. Prophylactic administration of Setron should be completed prior to the start of cytostatic therapy.

Treatment: The same dose of Setron should be used for treatment as prevention. Additional doses should be administered at least 10 minutes apart.

Maximum daily dosage: Up to three doses of 3 mg Setron may be administered within a 24-hour period. The maximum dose of Setron to be administered over 24 hours should not exceed 9 mg.

Concomitant use of dexamethasone: The efficacy of Setron may be enhanced by the addition of dexamethasone.

Elderly: No special requirements apply to elderly patients.

Children: Prevention: A single dose of 40 mcg/kg body weight (up to 3 mg) should be administered as an intravenous infusion, diluted in 10 to 30 ml infusion fluid and administered over five minutes. Administration should be completed prior to the start of cytostatic therapy.

Treatment: The same dose of Setron as above should be used for treatment as prevention.

One additional dose of 40 mcg/kg body weight (up to 3 mg) may be administered within a 24-hour period. This additional dose should be administered at least 10 minutes apart from the initial infusion.

Patients with renal or hepatic impairment: No special requirements apply to those patients with renal or hepatic impairment.

Administration

Adults: To prepare a dose of 3 mg, 3 ml is withdrawn from the ampoule and diluted either to 15 ml with 0.9% w/v Sodium Chloride Injection BP (for bolus administration) or in infusion fluid to a total volume of 20 to 50 ml in any of the following solutions: 0.9% w/v Sodium Chloride Injection BP; 0.18% w/v Sodium Chloride and 4% w/v Glucose Injection BP; 5% w/v Glucose Injection BP; Hartmann's Solution for Injection BP; Sodium Lactate Injection BP; or 10% Mannitol Injection BP (for infusion). No other diluents should be used.

Children: To prepare the dose of 40 mcg/kg the appropriate volume (up to 3 ml) is withdrawn from the ampoule and diluted with infusion fluid (as for adults) to a total volume of 10 to 30 ml.

Contra-indications, warnings, etc

Contra-indication: Hypersensitivity to granisetron or related substances.

Precautions: As Setron may reduce lower bowel motility, patients with signs of subacute intestinal obstruction should be monitored following administration of Setron.

There has been no evidence from human studies that Setron has any adverse effect on alertness. Data from two-year carcinogenicity studies have shown an increase in hepatocellular carcinoma and/or adenoma in rats and mice of both sexes given 50 mg/kg/day (rat dosage reduced to 25 mg/kg/day at week 59). Increases in hepatocellular neoplasia were also detected at 5 mg/kg in male rats. In both species,

drug-induced effects (hepatocellular neoplasia) were not observed in the low-dose group (1 mg/kg).

In several *in vitro* and *in vivo* assays, Setron was shown to be non-genotoxic in mammalian cells.

Drug interactions: In studies in healthy subjects, no evidence of any interaction has been indicated between Setron and cimetidine or lorazepam. No evidence of drug interactions has been observed in clinical studies.

Use in pregnancy and lactation: Pregnancy category B. Whilst animal studies have shown no teratogenic effects, there is no experience of Setron in human pregnancy. Therefore, Setron should not be administered to women who are pregnant unless there are compelling clinical reasons. There are no data on the excretion of Setron in breast milk. Breast feeding should therefore be discontinued during therapy.

Adverse reactions: Setron 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 events, but the majority have been mild to moderate in nature. Rare cases of hypersensitivity reaction, occasionally severe (e.g. anaphylaxis) have been reported. Other allergic reactions including minor skin rashes have also been reported. In clinical trials, transient increases in hepatic transaminases, generally within the normal range, have been seen.

Overdosage: There is no specific antidote for Setron. In the case of overdosage, symptomatic treatment should be given. One patient has received 10 times the recommended intravenous dose of Setron. The patient reported a slight headache but no other sequelae were observed.

Pharmaceutical precautions

Ampoules removed from the pack should be protected from direct sunlight. Do not freeze. Ideally, intravenous infusions of Setron should be prepared at the time of administration. After dilution (see **Dosage and administration**) the shelf-life is 24 hours when stored at ambient temperature in normal indoor illumination protected from direct light. It must not be used after 24 hours. If to be stored after preparation, Setron infusions must be prepared under appropriate aseptic conditions.

As a general precaution, Setron should not be mixed in solution with other drugs.

Package quantities

Ampoules in boxes of 5.

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