



SCHEDULING STATUS: S4

PROPRIETARY NAME (AND DOSAGE FORM):

GRANICIP 1 mg (Tablets)

GRANICIP 2 mg (Tablets)

COMPOSITION:

GRANICIP 1 mg: Each film-coated tablet contains granisetron hydrochloride equivalent to 1 mg granisetron.

GRANICIP 2 mg: Each film-coated tablet contains granisetron hydrochloride equivalent to 2 mg granisetron.

PHARMACOLOGICAL CLASSIFICATION:

A 5.7.2 Anti-emetics and anti-vertigo preparations.

PHARMACOLOGICAL ACTION:

Pharmacodynamics:

Granisetron is a selective antagonist of 5-hydroxytryptamine (5-HT)₂-receptors with anti-emetic properties. Results from radioligand binding studies have shown that granisetron has negligible affinity for other receptor types, including 5-HT and dopamine D₂-binding sites.

Pharmacokinetics:

Granisetron is absorbed after oral administration, with peak plasma concentrations occurring 2 hours after dosing. Due to first-pass metabolism, the oral bioavailability of granisetron is about 60%. Granisetron has an apparent volume of distribution of about 3 L/kg. Plasma protein binding is approximately 65%. The pharmacokinetics of granisetron exhibit considerable inter-individual variation. The elimination half-life is reported to be approximately 3 – 4 hours in healthy individuals and about 9 – 12 hours in cancer patients. Granisetron is metabolised primarily by 7-hydroxylation, with less than 20% of a dose recovered unchanged in urine, and the remainder being excreted in faeces and urine as metabolites.

Granisetron clearance is not affected by renal impairment, but is lower in the elderly and in patients with hepatic impairment.

INDICATIONS:

GRANICIP tablets are indicated for the prevention of nausea and vomiting associated with chemotherapy and radiotherapy.

CONTRA-INDICATIONS:

GRANICIP is contra-indicated in:

- Patients with hypersensitivity to any of the ingredients contained in **GRANICIP**.
- Children under the age of 2 years.

WARNINGS:

Since treatment with **GRANICIP** may reduce motility of the lower bowel, patients with signs of subacute intestinal obstruction require monitoring after **GRANICIP** administration.

A patient should not receive more than 9 mg (120 µg/kg) **GRANICIP** over a 24-hour period.

INTERACTIONS:

Following hepatic enzyme induction with phenobarbital, total plasma clearance of intravenous granisetron increases with approximately one-quarter.

GRANICIP may be co-administered with benzodiazepines, neuroleptics and anti-ulcer medicines that are commonly co-prescribed with anti-emetic agents. Furthermore, there was no apparent interaction between **GRANICIP** and emetogenic cancer chemotherapies.

Although no specific interaction studies have been performed in anaesthetised patients, **GRANICIP** has been safely administered with agents commonly used during anaesthesia and for analgesia. Furthermore, **GRANICIP** does not modify the cytochrome P450 subfamily 3A4 (involved in the metabolism of some of the main narcotic analgesic agents) as evidenced by *in vitro* human microsomal studies.

PREGNANCY AND LACTATION:

The safety and efficacy of **GRANICIP** have not been established during pregnancy and lactation. There are no studies in pregnant women. It is also not known whether granisetron is excreted in human milk. **GRANICIP** should therefore only be used during pregnancy or lactation in situations where the potential benefit of **GRANICIP** to the mother justifies the potential risk to the foetus or the nursing infant.

DOSAGE AND DIRECTIONS FOR USE:

Nausea and vomiting induced by chemotherapy:

Adults:

The dose of **GRANICIP** is 1 mg twice daily or 2 mg once daily. **GRANICIP** can be administered for up to one week following cancer therapy. The initial **GRANICIP** dose should be administered within one hour prior to the start of cytostatic therapy.

There is limited experience with the administration of **GRANICIP** beyond 7 cycles of chemotherapy.

Nausea and vomiting induced by radiotherapy:

Adults:

GRANICIP 2 mg once daily. The initial dose should be given within 1 hour prior to the start of radiotherapy. **GRANICIP** can be administered for up to one week after radiotherapy.

Special groups:

Present experience indicates that no dosage adjustment is required in elderly patients or in patients with impaired renal or hepatic function; however, **GRANICIP** should be administered with caution to these patients.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Side-Effects:

The following side-effects may occur with use of **GRANICIP**:

Haematological/Lymphatic system disorders:

Less frequent: Anaemia, leucopenia and thrombocytopenia have been reported.

Neuropsychiatric system disorders:

Frequent: Headache.
Less frequent: Fainting, agitation, dizziness, drowsiness and insomnia.

Cardiovascular system disorders:

Less frequent: Dysrhythmias and chest pain.

Gastrointestinal system disorders:

Frequent: Constipation, abdominal pain and diarrhoea.
Less frequent: Dyspepsia and unusual taste in mouth. Anorexia has also been reported.

Hepatobiliary system disorders:

The following side-effects have been reported and frequencies are unknown: A rise in hepatic transaminases may occur.

Skin and appendages disorders:

Less frequent: Alopecia has been reported.

General disorders:

Frequent: Unusual tiredness or weakness.

Less frequent: There have been reports of allergic reactions, including anaphylaxis. Less frequently, there have been reports of other allergic reactions, including minor skin rashes. Fever may occur.

Special Precautions:

Effects on the ability to drive and use machinery: **GRANICIP** may cause somnolence and this should be taken into account.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Headache may occur following overdose with **GRANICIP**. There is no specific antidote. In the event of overdose, treatment should be symptomatic and supportive.

IDENTIFICATION:

GRANICIP 1 mg: White to off-white, barrel-shaped, film-coated, biconvex tablets with 'G1' debossed on one side and plain on the other.
GRANICIP 2 mg: White to off-white, barrel-shaped, film-coated, biconvex tablets with 'G2' debossed on one side and plain on the other.

PRESENTATION:

GRANICIP 1 mg: Tablets in aluminium foil blister strips in packs of 5 or 10 tablets.
GRANICIP 2 mg: Tablets in aluminium foil blister strips in packs of 5 or 10 tablets.

STORAGE INSTRUCTIONS:

Store below 25°C. Protect from light. Keep the blisters in the outer carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS:

GRANICIP 1 mg: 41/5.7.2/0397

GRANICIP 2 mg: 41/5.7.2/0398

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATES OF REGISTRATION:

CIPLA MEDPRO (PTY) LTD
Rosen Heights, Pasita Street,
Rosen Park, Bellville 7530

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

February 2009

© CIPLA MEDPRO (PTY) LTD

GF07 A

