1.3.1.1.1 PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

1 NAME OF THE MEDICINE

ADCO GRANISETRON 1 mg/1 ml injection

ADCO GRANISETRON 3 mg/3 ml injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

ADCO GRANISETRON 1 mg/1 ml: Each ampoule contains 1 mg granisetron (as hydrochloride) per 1 mL.

ADCO GRANISETRON 3 mg/3 ml: Each ampoule contains 3 mg granisetron (as hydrochloride) per 3 mL.

Sugar free

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Injection

A clear, colourless aqueous solution free from visible particulate matter.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

R.Naidoo

ADCO GRANISETRON ampoules are indicated for the prevention or treatment of nausea and vomiting induced by cytostatic therapy and for the prevention and treatment of postoperative nausea and vomiting.

4.2 Posology and method of administration

Posology

Cytostatic therapy:

Adults:

Intravenous:

The dose of ADCO GRANISETRON is 3 mg (corresponding to a dose of approximately 40 µg/kg) which should be administered either as a slow intravenous injection (over 30 seconds) or diluted as directed in 20 to 50 ml infusion fluid and administered over 5 minutes by slow infusion.

Maximum daily dose:

Up to two additional doses of 3 mg ADCO GRANISETRON may be administered either as intravenous injection (over 30 seconds) or as a 5 minute infusion. Additional administration should be administered at least 10 minutes apart. The maximum dose of ADCO GRANISETRON infusion to be administered over 24 hours should not exceed 9 mg (120 µg/kg). The experience of the use of granisetron beyond 7 cycles of chemotherapy is limited.

Special populations:

Although present experience indicates that no dosage adjustment is required, care should be exercised when administering ADCO GRANISETRON to elderly patients and patients with renal or hepatic impairment.

Paediatric population:

Children:

Intravenous

R.Naidoo

Prevention: A single dose of 10 to 40 µg/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 5 minutes. Administration should be completed prior to the start of cytostatic therapy.

Treatment: The same as for prevention. One additional dose of 10 to 40 µg/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.

Postoperative nausea and vomiting:

Adults:

Intravenous:

For prevention in adults prior to induction of anaesthesia, a single dose of 1 mg of ADCO GRANISETRON should be administered as a slow intravenous injection (over 30 seconds).

For the treatment of established postoperative nausea and vomiting in adults, a single dose of 1 mg ADCO GRANISETRON should be administered by slow intravenous injection (30 seconds).

Maximum dose and duration of treatment:

A total dose of 3 mg of ADCO GRANISETRON given intravenously per day should not be exceeded in patients undergoing anaesthesia for elective surgery.

Special populations:

Care should be exercised when administering ADCO GRANISETRON to the elderly and patients with renal or hepatic impairment.

Paediatric population:

Children:

No data are available for prevention and treatment of postoperative nausea and vomiting in children.

R.Naidoo

Method of administration

Slow intravenous injection or slow intravenous infusion

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

For instructions on preparing the injection and for compatibility of ADCO GRANISETRON with infusion fluids, see section 6.6.

4.3 Contraindications

- Hypersensitivity to granisetron or to any of the ingredients contained in ADCO GRANISETRON
- Children under the age of 2 years.
- Congenital long QT syndrome
- Pregnancy and lactation (see section 4.6).

4.4 Special warnings and precautions for use

As ADCO GRANISETRON may reduce lower bowel motility, patients with signs of sub-acute intestinal obstruction should be monitored following administration of ADCO GRANISETRON. The maximum dose of ADCO GRANISETRON to be administered over 24 hours should not exceed 9 mg (120 µg/kg).

5-HT_3 antagonists, such as ADCO GRANISETRON, may be associated with dysrhythmias or ECG abnormalities including QT interval prolongation. This potentially may have clinical significance in patients with pre-existing dysrhythmias or cardiac conduction disorders or patients who are being treated with anti-dysrhythmic medicines or beta-blockers. Caution should be exercised in patients with cardiac co-morbidities, patients on cardiotoxic chemotherapy and/or with concomitant electrolyte abnormalities (see section 4.5).

Cases of myocardial ischaemia have been reported in patients treated with serotonin receptor antagonists. In some patients, especially in the case of intravenous administration, symptoms appeared

R.Naidoo

immediately after administration of a serotonin receptor antagonist (e.g. ADCO GRANISETRON). Patients should be alerted to the signs and symptoms of myocardial ischaemia.

Cross-sensitivity between 5-HT_3 antagonists (e.g. dolasetron, ondansetron) has been reported.

There have been reports of serotonin syndrome with the use of 5-HT_3 antagonists either alone, but mostly in combination with other serotonergic medicines (including selective serotonin reuptake inhibitors (SSRIs) and serotonin noradrenaline reuptake inhibitors (SNRIs)). Appropriate observation of patients for serotonin syndrome-like symptoms is
advised.

No special precautions are required for the elderly or renally and/or hepatically impaired patients. Owing to kinetics a degree of caution should be exercised in using ADCO GRANISETRON with this category.

Sodium content

ADCO GRANISETRON contains 4,01 mg sodium per ml, equivalent to 0,2 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicines and other forms of interaction

As for other 5-HT_3 antagonists, cases of ECG modifications including QT prolongation have been reported with ADCO GRANISETRON. In patients concurrently treated with medicines known to prolong the QT interval and/or which are dysrhythmogenic, this may lead to clinical consequences (see section 4.4). This may also have clinical significance in patients who are being treated with anti-dysrhythmic medicines or beta-blockers (see section 4.4).

Hepatic enzyme induction with phenobarbital resulted in an increase in total plasma clearance of intravenous ADCO GRANISETRON of approximately one-quarter.

R.Naidoo

ADCO GRANISETRON may be co-administered with benzodiazepines, neuroleptics and anti-ulcer medications commonly prescribed with anti-emetic treatments. Additionally, ADCO GRANISETRON has shown no apparent interaction with emetogenic cancer chemotherapies.

No specific interaction studies have been conducted in anaesthetised patients, but ADCO GRANISETRON has been safely administered with commonly used anaesthetic and analgesic agents.

In vitro, it could be shown that metabolism of ADCO GRANISETRON is inhibited by ketoconazole, a potent CYP3A inhibitor. Co-administration of ADCO GRANISETRON with systemic ketoconazole may, therefore, increase the elimination half-life of ADCO GRANISETRON.

There have been reports of serotonin syndrome following concomitant use of 5-HT3 antagonists and other serotonergic medicines (including SSRIs and SNRIs) (see section 4.4).

4.6 Fertility, pregnancy and lactation

The use of ADCO GRANISETRON during pregnancy and lactation is not recommended as safety and efficacy have not been established (see section 4.3).

4.7 Effects on ability to drive and use machines

There have been reports of somnolence with the use of ADCO GRANISETRON, and this should be taken into account.

4.8 Undesirable effects

a. Summary of the safety profile

The most frequently reported adverse reactions for ADCO GRANISETRON are headache and constipation which may be transient. ECG changes including QT prolongation have been reported with ADCO GRANISETRON (see sections 4.4 and 4.5).

b. Tabulated summary of adverse reactions

Side effects are ranked according to the frequency within each MeDRA System Organ Class (SOC).

R.Naidoo

The following side effects may occur with use of ADCO GRANISETRON:

System Organ Class	**Frequency**	**Adverse Event**
Immune system disorders	Less frequent	Allergic reactions, including anaphylaxis*, shortness of breath*, hypotension*, urticaria*, oedema, facial oedema
Nervous system disorder	Frequent	Headache, somnolence, agitation, anxiety, insomnia, taste disorder
	Less frequent	Extrapyramidal reactions, dystonia, dyskinesia, serotonin syndrome
Eye disorders	Less frequent	Abnormal vision
Ear and labyrinth disorders	Frequent	Dizziness
Cardiac disorders	Less frequent	Dysrhythmias and chest pain, sinus bradycardia, atrial fibrillation, AV-block, ventricular ectopy, non-sustained tachycardia, ECG abnormalities, QT interval prolonged
	Frequency not known	**Myocardial ischaemia (see section 4.4)**
Vascular disorders	Frequent	Hypertension
	Less frequent	Hypotension
Gastrointestinal disorders	Frequent	Constipation, diarrhoea, anorexia

R.Naidoo

Hepatobiliary disorders	Frequent	Raised transaminase levels
	Less frequent	Abnormal hepatic function
Skin and subcutaneous tissue disorders	Less frequent	Allergic reactions, including minor skin rashes, local irritation at administration site**
General disorders and administrative site conditions	Frequent	Fever, asthenia

*Hypersensitivity reactions

**After repeated intravenous administration

c. Description of selected adverse events

As for other 5-HT_3 antagonists, ECG changes including QT prolongation have been reported with ADCO GRANISETRON (see sections 4.4 and 4.5).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

For reporting of side effects directly to the Holder of the Certificate of Registration, contact +27 11 635 0134 or email Adcock.aereports@adcock.com

4.9 Overdose

Headache may occur. There is no specific antidote for ADCO GRANISETRON. In the case of overdosage, symptomatic treatment should be given.

R.Naidoo

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiemetics and antinauseants, Serotonin (5-HT_3) antagonists

ATC code: A04AA02

Mechanism of action:

Granisetron is a selective antagonist of 5-hydroxytryptamine (5-HT_3)-receptors with anti-emetic properties. Radioligand binding studies have demonstrated that granisetron has negligible affinity for other receptor types including 5-HT and dopamine D_2 binding sites.

5.2 Pharmacokinetic properties

Absorption

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 %.

Distribution

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.

Biotransformation

Granisetron is metabolised primarily by 7-hydroxylation.

Elimination

The elimination half-life is reported to be approximately 3 to 4 hours in healthy individuals and about 9 to 12 hours in cancer patients. Less than 20 % of a dose is recovered unchanged in urine; 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.

R.Naidoo

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Sodium chloride
- Sodium citrate dihydrate
- Citric acid anhydrous
- Water for injections
- Nitrogen gas

6.2 Incompatibilities

As a general precaution, ADCO GRANISETRON should not be mixed in solution with other medicines.

No interactions with ADCO GRANISETRON have been recorded with multiple chemotherapy regimens, including cisplatin up to 120 mg/m^2.

6.3 Shelf life

Unopened: 24 months

After dilution: Ideally, intravenous infusions of ADCO GRANISETRON should be prepared at the time of administration. However, recommended solutions of ADCO GRANISETRON have been shown to be stable for at least 24 hours in the following solutions when stored at room temperature: 0,9 % *m/v* sodium chloride, 5 % *m/v* dextrose (glucose), and Ringer's Lactate.

6.4 Special precautions for storage

Store at or below 25 °C. Protect from light.

Store the ampoules in the carton until required for use.

Do not freeze.

R.Naidoo

6.5 Nature and contents of container

ADCO GRANISETRON 1 mg/1 ml

Packed in 1 ml, clear, closed, easy breakable glass ampoules for intravenous injection, available in packs of 5 ampoule trays containing 5 ampoules per tray (pack of 25 ampoules).

ADCO GRANISETRON 3 mg/3 ml

Packed in 3 ml, clear, closed, easy breakable glass ampoules for intravenous injection, available in packs of 5 ampoule trays containing 5 ampoules per tray (pack of 25 ampoules).

Not all strengths and/or pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

ADCO GRANISETRON is compatible with the following infusion fluids:

0,9 % *m/v* sodium chloride

5 % *m/v* dextrose (glucose)

Ringer's Lactate.

Preparing the infusion:

Adults:

To prepare the dose of ADCO GRANISETRON 3 mg/3 ml, the contents of one ampoule (3 mg) or 40 µg/kg is withdrawn from the ampoule and diluted with infusion fluid, to a total volume of 20 to 50 ml in any of the following solutions: 0,9% m/v sodium chloride, 5% *m/v* dextrose, or Ringer's Lactate.

Children:

To prepare the dose of 10 to 40 µg/kg, the appropriate volume (up to 3 ml) from the 3 mg ampoule, or up to 1 ml from the single use ampoule, is withdrawn and diluted with infusion fluid (as for adults) to a total volume of 10 to 30 ml.

R.Naidoo

7 HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Critical Care (Pty) Ltd

1 Sabax Road

Aeroton

Johannesburg, 2013

Tel: +27 11 494 8000

8 REGISTRATION NUMBERS

ADCO GRANISETRON 1 mg/1 ml: 41/5.7.2/1079

ADCO GRANISETRON 3 mg/3 ml: 41/5.7.2/1080

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12 June 2009

10 DATE OF REVISION OF THE TEXT

14 July 2025

R.Naidoo