PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

Grantryl 1 mg/1 ml

Grantryl 3 mg/3 ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

GRANTRYL 1 mg/1 ml: Ampoules containing granisetron 1 mg (as hydrochloride) in 1 ml aqueous solution

GRANTRYL 3 mg/3 ml: Ampoules containing granisetron 3 mg (as hydrochloride) in 3 ml aqueous solution

Sugar free.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Injection

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

GRANTRYL is indicated for the management of nausea and vomiting induced by chemotherapy and radiotherapy. GRANTRYL is also indicated for the prevention and treatment of post-operative nausea and vomiting.

4.2. Posology and method of administration

Chemotherapy induced nausea and vomiting (CINV):

Posology

Adults

Prevention: A dose of 1-3 mg (10 – 40 µg/kg) of GRANTRYL should either be administered either as a slow intravenous injection (over 30 seconds), or as an intravenous infusion diluted in 20 – 50 mℓ infusion fluid (see Preparation of dosage form) and administered over 5 minutes, prior to the start of chemotherapy.

Treatment: A dose of 1-3 mg (10 – 40 µg/kg) of GRANTRYL should be administered either as a slow intravenous injection (over 30 seconds), or as an intravenous infusion diluted in 20–50 mℓ infusion fluid (see Preparation of dosage form) and administered over 5 minutes. Further maintenance doses of GRANTRYL may be administered, if required, at least 10 minutes apart. The maximum dose of GRANTRYL to be administered over 24 hours should not exceed 9 mg.

Paediatrics

GRANTRYL is contra-indicated in children under 2 years of age (see CONTRA-INDICATIONS).

A dose of 10 – 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 prior to the start of chemotherapy.

One additional dose may be administered within a 24 hour period if required. This additional dose should not be administered until at least 10 minutes after the initial infusion.

Radiotherapy induced nausea and vomiting (RINV):

Adults

Prevention: A dose of 1-3 mg (10 – 40 µg/kg) of GRANTRYL should be administered either as a slow intravenous injection (over 30 seconds) or as an intravenous infusion diluted in 20-50 mℓ infusion fluid and administered over 5 minutes, prior to the start of radiotherapy.

Paediatrics

Due to lack of data, GRANTRYL is not recommended for prevention and treatment of RINV in children.

Post-operative nausea and vomiting (PONV):

Adults

Prevention: A dose of 1 mg (10 µg/kg) of GRANTRYL should be administered as a slow intravenous injection (over 30 seconds) prior to induction of anaesthesia

Treatment: A dose of 1 mg (10 µg/kg) of GRANTRYL should be administered as a slow intravenous injection (over 30 seconds). The maximum dose for patients undergoing anaesthesia for surgery is a total dose of 3 mg of GRANTRYL intravenous in one day.

Paediatrics

Due to lack of data, GRANTRYL is not recommended for prevention and treatment of PONV in children.

Special dosage instructions:

Elderly patients (65 yers of age or older)

No dosage adjustments required.

Renal impairment

No dosage adjustment required

Hepatic impairment

There is no evidence to date for an increased incidence of adverse events in patients with hepatic disorders. On the basis of its kinetics, whilst no dosage adjustment is necessary, GRANTRYL should be used with a certain amount of caution in this patient group. See Pharmacokinetics.

Method of administration

Preparation of dosage form:

Use immediately after reconstitution. Solutions should not be stored for longer than 24 hours at a temperature of 2 – 8 °C unless prepared under controlled aseptic conditions.

Adults:

GRANTRYL may be diluted with 20 to 50 ml of the following infusion fluids:

- 0,9 % m/v sodium chloride
- 0,18 % m/v sodium chloride and 4 % m/v glucose
- 5 % m/v glucose
- Hartmann's solution
- Sodium lactate
- 10 % m/v mannitol

Children (>2 years):

GRANTRYL may be diluted with 10 to 30 ml of the following infusion fluids:

- 0,9 % m/v sodium chloride
- 0,18 % m/v sodium chloride and 4 % m/v glucose
- 5 % m/v glucose
- Hartmann's solution
- Sodium lactate
- 10 % m/v mannitol

4.3. Contraindications

Hypersensitivity to any of the ingredients contained in GRANTRYL.

Children under the age of 2 years.

Pregnancy and lactation (see PREGNANCY AND LACTATION).

Congenital long QT- syndrome.

4.4. Special warnings and precautions for use

As GRANTRYL may reduce lower bowel motility, patients with signs of sub-acute intestinal obstruction should be monitored following administration of GRANTRYL.

The maximum dose of GRANTRYL to be administered over 24 hours should not exceed 9 mg (120 µg/kg).

GRANTRYL may be associated with dysrhythmias or ECG abnormalities. This may have clinical significance in patients with pre-existing dysrhythmias or cardiac conduction disorders and/or patients with concomitant electrolyte disturbances, or in patients who are being treated with antidysrhythmic medicines, beta-blockers and medicines that prolong the QT-interval.

Cases of myocardial ischemia have been reported in patients treated with granisetron. In some patients, especially in the case of intravenous administration, symptoms appeared immediately after administration of granisetron. Patients should be alerted to the signs and symptoms of myocardial ischaemia.

4.5. Interactions with other medicines and other forms of interaction

Hepatic enzyme induction with phenobarbital resulted in an increase in total plasma clearance of intravenous GRANTRYL of approximately one-quarter. GRANTRYL may be co-administered with benzodiazepines, neuroleptics and anti-ulcer medications commonly prescribed with anti-emetic treatments. No apparent interaction with emetogenic cancer chemotherapies has been shown. No specific interaction studies have been conducted in anaesthetised patients, but GRANTRYL may be administered with commonly used

anaesthetic and analgesic agents. In addition, in vitro human microsomal studies have shown that the cytochrome P450 subfamily 3A4 (involved in the metabolism of some of the main narcotic analgesic agents) is not modified by granisetron.

4.6. Fertility, pregnancy and lactation

The use of GRANTRYL during pregnancy and lactation is contra-indicated as safety and efficacy have not been established (see CONTRA-INDICATIONS).

4.7. Effects on ability to drive and use machines

GRANTRYL may cause somnolence and transient visual disturbances. Patients should be advised not to drive or handle machinery if these side effects occur.

4.8. Undesirable effects

The following side effects may occur with use of GRANTRYL:

Infections and infestations

Frequency not known: Infection, urinary tract infection

Blood and lymphatic system disorders

Frequency not known: Anaemia, leukocytosis

Immune system disorders

Less frequent: Hypersensitivity reactions, including skin rashes and anaphylaxis.

Psychiatric disorders

Less frequent: Anxiety, insomnia, somnolence.

Nervous system disorders

Less frequent: Headache, dizziness, seizures, oculogyric crisis.

Eye disorders

Frequency not known: Transient visual disturbances such as blurred vision.

Cardiac disorders

Less frequent: Angina pectoris, dysrhythmias, atrial fibrillation, chest pain, fainting, tachycardia, bradycardia, ECG abnormalities, QT-prolongation.

Frequency unknown: myocardial ischemia (see section 4.4)

Vascular disorders

Less frequent: Hypertension, hypotension, flushes.

Gastrointestinal disorders

Frequent: Abdominal pain, constipation, diarrhoea, hiccups

Less frequent: Dyspepsia, unusual taste in mouth.

Musculoskeletal disorders

Frequency not known: Dystonia and dyskinesia

Hepato-biliary disorders

Less frequent: A rise in hepatic transaminases.

General disorders and administration site disorders

Frequent: Asthenia/fatigue

Less frequent: Fever, injection site reactions.

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. Health care provders are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reactions Reporting Form”, found online under SAHPRA’s publications:

https://www.sahpra.org.za/Publications/Index/8

Acino Pharma (Pty) Ltd: E-mail: drugsafety_za@acino.swiss Tel: 060 998 7896

By reporting side effects, you can help provide more information on the safety of GRANTRYL.

4.9. Overdosage

Headache may occur. There is no specific antidote for granisetron. In the case of over-dosage, symptomatic and supportive treatment should be given.

5. PHARMACOLOGICAL PROPERTIES

A 5.7.2 Anti-emetics and anti-vertigo preparations

ATC code: A04AA02

5.1. Pharmacodynamic properties

Granisetron is a selective 5-HT3 receptor-antagonist with anti-emetic properties. Chemotherapeutic agents and radiotherapy may cause release of 5-HT in the small intestine initiating a vomiting reflex by activating vagal afferents via 5-HT3 receptors. The initiation of this reflex is blocked by granisetron. Activation of vagal afferents may also cause a release of 5-HT in the area postrema, located on the floor of the fourth ventricle, and this may also promote emesis through a central mechanism.

5.2. Pharmacokinetic properties

Granisetron has an apparent volume of distribution of about 3 litres/kg. Plasma protein binding is approximately 65 %.

The pharmacokinetics of granisetron exhibit considerable inter-individual variation. The elimination half-life after an intravenous dose is reported to be around 4 to 5 hours in healthy subjects but about 9 to 12 hours in cancer patients. It is metabolised in the liver, primarily by N-demethylation, with less than 20 % of a dose 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.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Citric acid monohydrate, Sodium citrate, Sodium chloride, water for injection and Nitrogen

6.2. Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store in the original packaging (in the carton) at or below 30 °C. Protect from light.

Diluted solution: Use immediately after reconstitution. Solutions should not be stored for longer than 24 hours at a temperature of 2 – 8 °C unless prepared under controlled aseptic conditions. Any unused solution should be discarded after 24 hours.

KEEP MEDICINE OUT OF THE REACH OF CHILDREN.

6.5. Nature and contents of container

Identification

GRANTRYL 1 mg/1 ml: A clear Type 1 glass ampoule containing a clear colourless solution. The content allows withdrawal of 1 ml.

GRANTRYL 3 mg/3 ml: A clear Type 1 glass ampoule containing a clear colourless solution. The content allows withdrawal of 3 ml.

Presentations

GRANTRYL 1 mg/1 ml: Packs of 5 x 1 ml Type I glass ampoules, packed in a PVC tray, contained in a cardboard carton

GRANTRYL 3 mg/3 ml: Packs of 5 x 5 ml Type I glass ampoules, packed in a PVC tray, contained in a cardboard carton.

6.6. Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Acino Pharma (Pty) Ltd

106 16th Road

Midrand,

1686

8. REGISTRATION NUMBERS

GRANTRYL 1 mg/1 ml: 44/5.7.2/0892

GRANTRYL 3 mg/3 ml: 44/5.7.2/0893

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Registration date: 27 November 2014

10. DATE OF REVISION OF THE TEXT

28 November 2022