Granisetron
(solution, tablets)

Core Safety Profile

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use
As granisetron may reduce lower bowel motility, patients with signs of sub-acute intestinal obstruction should be monitored following its administration.

As for other 5-HT3 antagonists, ECG changes including QT interval prolongation have been reported with granisetron. In patients with pre-existing arrhythmias or cardiac conduction disorders this might lead to clinical consequences. Therefore caution should be exercised in patients with cardiac co-morbidities, on cardiotoxic chemotherapy and/or with concomitant electrolyte abnormalities (see section 4.5).

Cross-sensitivity between 5-HT3 antagonists (e.g. dolasteron, ondansetron) has been reported.
Patients with rare hereditary problems of galactose intolerance, lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Paediatric population ***(text valid for tablets only)***
There is insufficient clinical evidence to recommend administration of these tablets to children.

4.5 Interaction with other medicinal products and other forms of interaction
As for other 5-HT3 antagonists, cases of ECG modifications including QT prolongation have been reported with granisetron. In patients concurrently treated with medicinal products known to prolong QT interval and/or which are arrhythmogenic, this may lead to clinical consequences (see section 4.4).

In studies in healthy subjects, no evidence of any interaction has been indicated between granisetron and benzodiazepines (lorazepam), neuroleptics (haloperidol) or anti-ulcer medicinal products (cimetidine). Additionally, granisetron has not shown any apparent medicinal product interaction with emetogenic cancer chemotherapies.

No specific interaction studies have been conducted in anaesthetised patients.

4.6 Fertility, pregnancy and lactation
Pregnancy
There is limited amount of data from the use of granisetron in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure**,** it is preferable to avoid the use of granisetron during pregnancy.

Breastfeeding

It is unknown whether granisetron or its metabolites are excreted in human milk. As a precautionary measure, breast-feeding should not be advised during treatment with granisetron.

Fertility
In rats, granisetron had no harmful effects on reproductive performance or fertility.

4.7 Effects on ability to drive and use machines

Granisetron has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile
The most frequently reported adverse reactions for Granisetron are headache and constipation, which may be transient. ECG changes including QT prolongation have been reported with Granisetron (see sections 4.4 and 4.5).

Tabulated list of adverse reactions
The following table of listed adverse reactions is derived from clinical trials and post-marketing data associated with Granisetron and other 5-HT3 antagonists. Frequency categories are as follows:

Very common: ≥1/10;
Common ≥1/100 to <1/10;
Uncommon ≥1/1,000 to <1/100
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)

Immune system disorders	
Uncommon	Hypersensitivity reactions e.g. anaphylaxis, urticaria
Psychiatric disorders	
Common	Insomnia
Nervous system disorders	
Very common	Headache
Uncommon	Extrapyramidal reactions
Cardiac disorders	
Uncommon	QT prolongation
Gastrointestinal disorders	
Very common	Constipation
Common	Diarrhoea
Hepatobiliary disorders	
Common	Elevated hepatic transaminases*
Skin and subcutaneous tissue disorders	
Uncommon	Rash

*Occurred at a similar frequency in patients receiving comparator therapy

Description of selected adverse reactions

As for other 5-HT3 antagonists, ECG changes including QT prolongation have been reported with granisetron (see sections 4.4 and 4.5).

4.9 Overdose

There is no specific antidote for Kytril. In the case of overdose with the tablets, symptomatic treatment should be given. Doses of up to 38.5 mg of Kytril as a single injection have been reported, with symptoms of mild headache but no other reported sequelae.