Granisetron Hydrochloride Injection, USP is a serotonin-3 (5-HT3) receptor antagonist indicated for:

1 INDICATIONS AND USAGE

Granisetron Hydrochloride Injection, USP is a serotonin-3 (5-HT3) receptor antagonist indicated for:

1.1 Prevention of Chemotherapy-Induced Nausea and Vomiting

The recommended dosage for granisetron hydrochloride is 10 mg administered intravenously within 30 minutes before initiation of chemotherapy. Granisetron hydrochloride injection has been shown to be stable for at least 24 hours when diluted in parenteral fluids. Parenteral drug products should be inspected visually for particulate matter and discoloration before administration whenever solution and container permit.

1.2 Postoperative Nausea and Vomiting

Granisetron hydrochloride injection is contraindicated in patients with known hypersensitivity to it or any of its components.

2 WARNINGS AND PRECAUTIONS

2.1 Prevention of Chemotherapy-Induced Nausea and Vomiting

Most common adverse reactions:

- Prevention of nausea and/or vomiting associated with initial and repeat courses of emetogenic cancer chemotherapies. (7)

Granisetron hydrochloride injection has been administered safely with benzodiazepines, meperidine, and other antiemetic treatments. Granisetron hydrochloride injection may be administered intravenously either unaltered or over 30 seconds, or diluted with 0.9% Sodium Chloride or 5% Dextrose and given over 5 minutes.

2.2 Postoperative Nausea and Vomiting

Additional adverse events reported in clinical trials were asthenia, somnolence and diarrhea. In over 3,000 patients receiving granisetron hydrochloride injection (2 to 160 mcg/kg) in single-day and multi-day chemotherapy trials, the incidence of granisetron-related adverse events was less than 15%

2.3 Nausea and vomiting in the Elderly

2.4 Pregnancy

2.5 Nursing Mothers

2.6 Geriatric Use

2.7 Overdosage

3 CONTRAINDICATIONS

3.1 Prevention of Chemotherapy-Induced Nausea and Vomiting

3.2 Postoperative Nausea and Vomiting

3.3 Nausea and vomiting in the Elderly

3.4 Pregnancy

3.5 Nursing Mothers

3.6 Geriatric Use

3.7 Overdosage

4 DOSAGE FORMS AND STRENGTHS

Granisetron hydrochloride injection is available for intravenous injection in parenteral drug products and in 10 mL single-use vials. Granisetron hydrochloride injection contains no preservatives.

5 WARNINGS AND PRECAUTIONS

5.1 Prevention of Chemotherapy-Induced Nausea and Vomiting

5.2 Postoperative Nausea and Vomiting

5.3 Nausea and vomiting in the Elderly

5.4 Pregnancy

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5.7 Overdosage

6ADVERSE REACTIONS

6.1 Prevention of Chemotherapy-Induced Nausea and Vomiting

6.2 Postoperative Nausea and Vomiting

6.3 Nausea and vomiting in the Elderly

6.4 Pregnancy

6.5 Nursing Mothers

6.6 Geriatric Use

6.7 Overdosage

7 DRUG INTERACTIONS

7.1 Prevention of Chemotherapy-Induced Nausea and Vomiting

7.2 Postoperative Nausea and Vomiting

7.3 Nausea and vomiting in the Elderly

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7.6 Geriatric Use

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

8.2 Nursing Mothers

8.3 Geriatric Use

9 DRUG INTERACTIONS

9.1 Prevention of Chemotherapy-Induced Nausea and Vomiting

9.2 Postoperative Nausea and Vomiting

9.3 Nausea and vomiting in the Elderly

9.4 Pregnancy

9.5 Nursing Mothers

9.6 Geriatric Use

10 OVERDOSAGE

11 CLINICAL PHARMACOLOGY

11.1 Prevention of Chemotherapy-Induced Nausea and Vomiting

11.2 Postoperative Nausea and Vomiting

11.3 Nausea and vomiting in the Elderly

11.4 Pregnancy

11.5 Nursing Mothers

11.6 Geriatric Use

11.7 Overdosage

12 NONCLINICAL TOXICOLOGY

12.1 Mechanism of Action

12.2 Carcinogenesis, Mutagenesis, Impairment of Fertility

12.3 Toxicity and Treatment of Overdose

12.4 Other Testing

13 CLINICAL STUDIES

13.1 Prevention of Chemotherapy-Induced Nausea and Vomiting

13.2 Postoperative Nausea and Vomiting

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14 CLINICAL STUDIES

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14.2 Postoperative Nausea and Vomiting

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15.2 Postoperative Nausea and Vomiting

15.3 Nausea and vomiting in the Elderly

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16 CLINICAL STUDIES

16.1 Prevention of Chemotherapy-Induced Nausea and Vomiting

16.2 Postoperative Nausea and Vomiting

16.3 Nausea and vomiting in the Elderly

16.4 Pregnancy

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16.7 Overdosage

17 DRUG INTERACTIONS

17.1 Prevention of Chemotherapy-Induced Nausea and Vomiting

17.2 Postoperative Nausea and Vomiting

17.3 Nausea and vomiting in the Elderly

17.4 Pregnancy

17.5 Nursing Mothers

17.6 Geriatric Use

17.7 Overdosage
Granisetron hydrochloride injection, USP, 0.112 mg equivalent to 16 years) to granisetron hydrochloride injection 10, 20 or 40 mcg/kg. Patients were treated with cisplatin

Table 9 Prevention of Chemotherapy-Induced Nausea and Vomiting in Pediatric Patients

<table>
<thead>
<tr>
<th>Patient Age (years)</th>
<th>Number of Patients</th>
<th>Complete Response (no vomiting and no moderate or severe nausea)</th>
<th>No Vomiting (no moderate or severe nausea but with occasional use of rescue antiemetic)</th>
<th>No Nausea (no moderate or severe nausea but with occasional use of rescue antiemetic)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-16</td>
<td>42</td>
<td>29%</td>
<td>56%</td>
<td>38%</td>
<td>0.012</td>
</tr>
<tr>
<td>17-21</td>
<td>41</td>
<td>56%</td>
<td>38%</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>22-25</td>
<td>40</td>
<td>44%</td>
<td>58%</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>&gt;25</td>
<td>46</td>
<td>53%</td>
<td>41%</td>
<td>33%</td>
<td></td>
</tr>
</tbody>
</table>

Response Over 24 Hours

<table>
<thead>
<tr>
<th>Complete Response</th>
<th>No Vomiting</th>
<th>No Nausea</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granisetron</td>
<td>29%</td>
<td>56%</td>
<td>0.012</td>
</tr>
<tr>
<td>Granisetron</td>
<td>29%</td>
<td>56%</td>
<td>0.009</td>
</tr>
<tr>
<td>Placebo</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

No Vomiting 93% 14% <0.001

Complete Response 29% 47% 44% 53% 0.012 0.009 NS

Number of Patients 42 41 40 46

Table 5 Prevention of Chemotherapy-Induced Nausea and Vomiting—Single-Day Moderately Emetogenic Chemotherapy

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Complete Response</th>
<th>No Vomiting</th>
<th>No Nausea</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elderly</td>
<td>14%</td>
<td>29%</td>
<td>56%</td>
<td>0.006</td>
</tr>
<tr>
<td>16-25</td>
<td>29%</td>
<td>56%</td>
<td>38%</td>
<td>0.012</td>
</tr>
<tr>
<td>&gt;25</td>
<td>44%</td>
<td>58%</td>
<td>33%</td>
<td></td>
</tr>
</tbody>
</table>

For the low and high cisplatin dose, the 10, 20, and 30 mcg/kg doses were more effective than the 5 mcg/kg dose in preventing nausea and vomiting within 24 hours of chemotherapy administration. The 40 mcg/kg dose was statistically superior to the 5 mcg/kg dose. However, no significant differences in plasma half-life or area under the curve were observed between the 10, 20, and 30 mcg/kg doses.

Chemotherapy-Induced Nausea and Vomiting

12.2 Mechanism of Action

Granisetron hydrochloride injection was superior to the chlorpromazine regimen in preventing nausea and vomiting induced by cisplatin chemotherapy (see Table 9).

The mechanism of action of granisetron hydrochloride injection was evaluated in a double-blind, randomized study of 93 patients who received cisplatin and granisetron hydrochloride injection or placebo every 3 hours for 2 days. Mean cisplatin dose was 86 mg/m² in the granisetron hydrochloride injection group and 80 mg/m² in the placebo group.

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