5-HT<sub>3</sub> Receptor antagonist antiemetic
Nasea OD Tablet 0.1 mg
<Ramosetron hydrochloride>
Powerful drug, Designated drug, and Prescription-only drug

**DESCRIPTION**

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Nasea OD Tablet 0.1 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingredient/content</td>
<td>Ramosetron hydrochloride 0.1 mg</td>
</tr>
<tr>
<td>Dosage form</td>
<td>Orally disintegrating tablet</td>
</tr>
<tr>
<td>(mm) diameter</td>
<td>8.5</td>
</tr>
<tr>
<td>Color</td>
<td>Curved side: light reddish-yellow</td>
</tr>
<tr>
<td></td>
<td>Plain side: dark reddish-yellow</td>
</tr>
<tr>
<td>Thickness (mm)</td>
<td>4.0</td>
</tr>
<tr>
<td>Weight (g)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

This product appears as a hemispherical tablet with a flat top. Aspartame (L-phenylalanine compound) is contained as an inactive ingredient.

**INDICATIONS**

Prophylaxis of Gastrointestinal symptoms (nausea and vomiting) associated with carcinostatics (such as cisplatin)

**DOSEAGE AND ADMINISTRATION**

The recommended adult oral dosage is 0.1 mg of ramosetron hydrochloride once a day. Dosage may be adjusted depending on the patient's age and symptoms.

**PRECAUTIONS**

1. **Important Precautions**
   (1) Swallow with saliva or water: Nasea OD Tablet is not absorbed from the mucosa of the oral cavity, although it disintegrates in the oral cavity.
   (2) Nasea OD Tablet should only be used to treat severe nausea and vomiting associated with carcinostatics (such as cisplatin).
   (3) Nasea OD Tablet should be used mainly for preventing nausea and vomiting when carcinostatics (such as cisplatin) that causes these reactions are administered. Nasea Injections should be used for antiemetic therapy in patients who have already developed nausea and vomiting.
   (4) Nasea OD Tablet should be administered for 1 hr before administration of anticancer drugs.
   (5) Nasea OD Tablet should be administered for 5 days or less with each course of cancer chemotherapy.
   (6) When nausea and vomiting occur after administration of carcinostatics due to insufficient efficacy of Nasea OD Tablet, other antiemetic therapies (such as administration of Nasea Injections) should be considered.

2. **Adverse Reactions**

   During the safety evaluation for the product’s approval, adverse reaction with Nasea OD Tablet were observed in 6 (2.2%) of 278 patients. The most frequently observed adverse events were headache, headache dull, etc.

   (1) **Clinically significant adverse reactions**
       **Shock and anaphylactoid symptoms** (Incidence unknown): Shock or anaphylactoid symptoms (such as ill feeling, feeling of chest distress, dyspnea, wheezing, hot facial flushes, redness, itching, cyanosis, and hypotension) may occur. Patients therefore should be carefully observed, and if such reactions develop during treatment with Nasea OD Tablet, discontinue treatment and institute appropriate medical therapy.

   (2) **Clinically significant adverse reactions (analog)**
       **Epileptiform attacks**: Epileptiform attacks have been reported with other 5-HT3 receptor antagonist antiemetics in foreign countries.

   (3) **Other adverse reactions**
2% > ≥ 0.1% Incidence unknown

Hypersensitivity (note)
- Rash

Nervous system/psychiatric
- Headache, dull headache, and sleepiness

Gastrointestinal
- Constipation

Renal
- Increase BUN

Hepatic
- Increased GPT, increased GOT, increased LDH

Hepatic function disorders

Others
- Fever

Note) If such a reaction develops, discontinue treatment.

3. Geriatric Use
It is advisable to cautiously administer the drug under careful observation of the patient's condition. If any adverse reaction develops, discontinue treatment and institute appropriate medical therapy. [The elderly are more likely to have a physiological hypofunction].

4. Pregnancy and Nursing Mothers
(1) Nasea OD Tablet should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. [The safety in pregnancy has not been established].
(2) Caution should be exercised when ramosetron hydrochloride is administered to nursing mothers. [It has been reported that ramosetron hydrochloride is excreted in the milk of lactating rats].

5. Pediatric Use
Safety in pronaties, newborns, sucklings, infants, and children has not been established. [no clinical experience].

6. Precautions concerning Use
(1) Caution in Dispensing
1) Patient should be instructed to press the tablet out of a press-through package (PTP) and take it. [It has been reported that, if the PTP sheet is swallowed, the sharp corners of the sheet may puncture the esophageal mucosa, resulting in severe complications such as mediastinitis].
2) When Nasea OD Tablet is taken out from a PTP sheet, the edge of the tablet may be chipped or damaged. However, there is no problem with quality. When the Tablets are chipped, patients are requested to take the whole Tablets. It is desirable to push the tablet out with the cushion of the finger without digging the nails in when removing the drug from a PTP blister.

(2) Caution in Taking
Nasea OD Tablet can be swallowed with saliva alone after placing the tablet on the tongue, wetting it, mashing it slightly with the tongue, and then letting it disintegrate.

PHARMACOKINETICS
<Absorption, metabolism and excretion>
When 0.4 to 1.6 mg of Nasea OD Tablet was orally administered to healthy volunteers, the concentration of the unchanged drug in plasma exhibited its C_max at approximately 2 hr after administration, and the half-life was about 5 hr thereafter. The C_max and AUC were proportional to dose and linearity was shown for the pharmacokinetics. The effective bioavailability for oral dose was 50% or higher based on the plasma concentration after intravenous administration. Between 8% and 13% of the dose was excreted as unchanged drug in the urine in the 24 hr after dosing. The demethylated compound, hydroxylated compound and their conjugates were also detected in the urine as metabolites, as well as the unchanged drug. The pharmacokinetic profile remained unaltered and there was no evidence of accumulation in healthy volunteers receiving repeated doses.

<Pharmacokinetic parameters after oral administration to healthy adults >

<table>
<thead>
<tr>
<th>Dosage (mg)</th>
<th>Tmax (hr)</th>
<th>Cmax (ng/mL)</th>
<th>Half-life (hr)</th>
<th>AUC (ng.hr/mL)</th>
<th>Bio-availability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.4</td>
<td>2.17</td>
<td>1.37</td>
<td>5.52</td>
<td>11.58</td>
<td>53.0</td>
</tr>
<tr>
<td>0.8</td>
<td>2.50</td>
<td>2.77</td>
<td>5.35</td>
<td>25.77</td>
<td>59.0</td>
</tr>
<tr>
<td>1.6</td>
<td>2.67</td>
<td>3.63</td>
<td>4.93</td>
<td>48.05</td>
<td>55.0</td>
</tr>
</tbody>
</table>

(Average from 6 volunteers)

CLINICAL STUDIES
<Clinical Efficacy>
Double-blind comparative studies and open clinical studies were conducted in a total of 284 patients at 90 institutions in Japan who were administered this product 1 hr prior to administration of cisplatin for the nausea and vomiting that develops with administration of antineoplastic drug such as cisplatin. Summaries of these clinical studies are provided below.
The usefulness of Nasea OD Tablet has been demonstrated by double-blind comparative studies in patients with nausea
and vomiting caused by anticancer chemotherapies such as cisplatin

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Effectiveness rate of single oral administration for nausea and vomiting induced by administration of carcinostatics (such as cisplatin)</th>
<th>Effectiveness rate of oral administration for 5 consecutive days for nausea and vomiting induced by administration of carcinostatics (such as cisplatin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1 mg</td>
<td>77.9% (106 cases out of 136)</td>
<td>80.0% (12 cases out of 15)</td>
</tr>
</tbody>
</table>

**PHARMACOLOGY**

**<Pharmacological actions>**

1. **5-HT₃ receptor antagonistic effect**
   In a serotonin-induced constriction experiment in the colon isolated from guinea pigs, a potent and selective 5-HT₃ receptor antagonistic effect was observed. In addition, in a serotonin-induced bradycardic reflex (Bezold-Jarisch reflex) experiments in rats and ferrets, a potent and sustained 5-HT₃ receptor antagonistic effect was shown after oral administration.

2. **Efficacy of antiemetic vomiting induced by a carcinostatics**
   Vomiting induced by administration of cisplatin in ferrets was suppressed by oral administration of this product. The effect was potent and sustained.

**<Mechanism of action>**

Carcinostatics drugs such as cisplatin cause enterochromaffin cells in the gastrointestinal tract to release serotonin. The released serotonin binds to 5-HT₃ receptors present in the afferent vagal nerve-endings in the gastrointestinal mucosa, and the stimulation that is evoked induces emesis via the vomiting center. Ramosetron hydrochloride is considered to exert its antiemetic action by blocking 5-HT₃ receptors.

**PHYSICOCHEMISTRY**

**Nonproprietary name:**

Ramosetron hydrochloride

**Chemical Name :**

\((-\)-(R)-5-[(1-methyl-1H-indol-3-yl)carbonyl]-4,5,6,7-tetrahydro-1H-benzimidazole monohydrochloride\)

**Molecular formula :**

C₁₇H₁₇N₃O.HCl

**Molecular weight:**

315.80

**Structural formula :**

![Structural formula of Ramosetron hydrochloride](image)

**Description :**

Ramosetron hydrochloride occurs as a white to pale yellowish white crystalline powder. It is freely soluble in water or in methanol, soluble in ethanol and in glacial acetic acid, very slightly soluble in acetonitrile or in acetic anhydride, and practically insoluble in tetrahydrofuran or in ether. Ramosetron hydrochloride is hygroscopic. It is affected by light.

**PACKAGING**

Nasea OD Tablet 0.1 mg :

1 Box @ 10 sachets @ 1 blister @ 1 tablet

Store below 25°C, protect from light.

Approved shelf life : 36 months
“Harus dengan resep dokter”

Imported by P.T. Yamanouchi Indonesia, Jakarta from Yamanouchi Pharmaceutical Co., Ltd., Japan