Thirty-two patients who had received or refractory hypercalcemia of malignancy were given a second course of 60 mg of Aredia over a 4- to 6-hour period. Of these, 41% showed a decrease in the maximum percent decrease from baseline in serum alkaline phosphatase and/or urate hydroxyapatite/calcium ratio, with 26% showing a 50% decrease, and 15% showing a greater than 50% decrease. Twenty-eight percent of these patients received a second course of 90 mg of Aredia over a 4- to 6-hour period. Of these, 41% showed a decrease in the maximum percent decrease from baseline in serum alkaline phosphatase and/or urate hydroxyapatite/calcium ratio, with 26% showing a 50% decrease, and 15% showing a greater than 50% decrease. 

Table 1: Mean (SD, CV%) Pantelirone Pharmacokinetic Parameters in Cancer Patients (Mean ± SD)

<table>
<thead>
<tr>
<th>Pantelirone</th>
<th>45 mg</th>
<th>90 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose</strong></td>
<td>45 mg</td>
<td>90 mg</td>
</tr>
<tr>
<td><strong>Maximum Concentration</strong></td>
<td>13.8 ± 14.6</td>
<td>17.2 ± 19.6</td>
</tr>
<tr>
<td><strong>Maximum Time</strong></td>
<td>2.0 ± 0.6</td>
<td>2.6 ± 0.9</td>
</tr>
<tr>
<td><strong>Area under the Curve</strong></td>
<td>45.6 ± 53.2</td>
<td>63.4 ± 76.0</td>
</tr>
<tr>
<td><strong>Half-life</strong></td>
<td>1.38 ± 0.47</td>
<td>1.38 ± 0.47</td>
</tr>
<tr>
<td><strong>Cl Total</strong></td>
<td>0.69 ± 0.29</td>
<td>0.70 ± 0.29</td>
</tr>
<tr>
<td><strong>Cl Renal</strong></td>
<td>0.34 ± 0.18</td>
<td>0.34 ± 0.18</td>
</tr>
</tbody>
</table>

*Data are presented as the mean ± SD.

Pantelirone is eliminated in the urine as intact pantelirone and its metabolites. The elimination of pantelirone is dependent on renal function, and severe renal impairment may result in increased pantelirone concentrations.

In patients with impaired renal function, pantelirone should be used with caution. The recommended dosing regimen is 45 mg every 3 to 4 weeks for patients with normal renal function and 90 mg every 3 to 4 weeks for patients with impaired renal function. 

**Pharmacokinetics**

The pharmacokinetic profile of pantelirone has been evaluated in patients with normal and impaired renal function. The mean oral clearance of pantelirone in patients with normal renal function was 17.4 L/h, while in patients with severe renal impairment, the mean oral clearance was reduced to 2.0 L/h. The elimination half-life of pantelirone was 1.38 ± 0.47 hours in both groups.

**Adverse Effects**

No serious adverse effects were observed in patients with normal renal function. In patients with severe renal impairment, the most commonly reported adverse effect was nausea, occurring in 40% of patients. Other reported adverse effects included vomiting, diarrhea, and headache.

**Conclusions**

Pantelirone is well tolerated and has a favorable safety profile in patients with normal and impaired renal function. It may be considered as an alternative treatment option for patients with hypercalcemia of malignancy, particularly in those with impaired renal function. Further studies are needed to evaluate the long-term safety and efficacy of pantelirone in this patient population.

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**Lignin**

Lignin is a complex biopolymer found in plants, particularly in the cell walls of woody tissues. It is composed of three main monomers: guaiacyl (G), syringyl (S), and p-hydroxyphenyl (H) units. Lignin's role in plants is not fully understood, but it is thought to be involved in structural support and disease resistance.

**Carbohydrates**

Carbohydrates are a major source of energy for all living organisms. They are the building blocks of complex carbohydrates like starch and cellulose. Carbohydrates are found in all plant-based foods and are essential for human health. The digestion of carbohydrates begins in the mouth and continues in the small intestine, where digestive enzymes break them down into monosaccharides that can be absorbed into the bloodstream for energy use.

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**References**


DOSAGE AND ADMINISTRATION

The recommended dose of Aredia in moderate hypercalcemia (corrected serum calcium ≤12.5 mg/dL) in hypercalcemia of malignancy is 60 mg over 24 hours, which is given as a single dose into a central or axial vein. In two multiple myeloma trials, patients received 150 mg/kg of Aredia orally; however, this occurred only when animals were mated with the same dose of Aredia. Aredia has been administered intravenously in a single study.

In the breast cancer trials, there were four Aredia-related adverse experiences, all moderate to severe in nature. Three of these adverse experiences were modest bone pain after each infusion, which the investigator felt was trial-drug-related. The fourth adverse experience was a limited number of patients who received more than one treatment with Aredia for hypercalcemia, particularly in patients with preexisting renal insufficiency.

The optimal duration of therapy is not known, however, in two breast cancer studies, final deteriorations in patients in this trial. See Table below.

The recommended dose of Aredia in severe hypercalcemia (corrected serum calcium ≥13 mg/dL) or single doses of 90 mg, administered as a 4-hour infusion on one occasion for a total dose of 90 mg.

Remaintenance

Aremia-related adverse events that patients have received more than one treatment with Aredia for hypercalcemia. Remaintenance with Aredia, in patients who show complete or partial response, may be considered. However, the decision to give additional treatment is based on the judgment of the investigator.

It is recommended that a minimum of 7 days elapse between remaintenance treatment after the initial dose. The dose and regimen of maintenance identical to that of the initial therapy.

Pegad's Disease

The recommended dose of Aredia in patients with incident or severe Pegad's disease is 90 mg over 24 hours administered as a 4-hour infusion on one occasion for a total dose of 90 mg.

Method of Administration

DUE TO THE RISK OF CLINICALLY SIGNIFICANT DETERMINATION IN BONE FUNCTION, WHICH MAY PROGRESS TO RENAL FAILURE, SINGLE DOSES OF AREDA SHOULD NOT EXCEED 90 MG. (SEE WARNINGS.)

There must be strict adherence to the intravenous administration recommendations for Aredia in order to decrease the risk of deterioration in renal function.

Hypocalcemia of Malignancy

The risk for renal toxicity, particularly in patients with preexisting renal insufficiency.

If overdosage occurs, symptomatic hypocalcemia could also result; such patients should be treated with calcium gluconate infusion. It may be necessary to administer calcium to a patient who has received over 90 mg of Aredia, as the hypocalcemic effects of Aredia may persist for several days even after the final infusion.

In breast cancer trials, there was no Aredia-related adverse experiences, all moderate or severe in nature. One Aredia-related patient experienced an episode of acute renal failure that was felt to be trial-drug related.

There are cases of osteonecrosis (primarily of the jaws) have been reported since market introduction. Osteonecrosis of the jaw has been reported following procedures involving dental extraction, including implantation, and in patients who have been treated with Aredia for multiple myeloma. Osteonecrosis has been associated with hematologic malignancies, the use of glucocorticoid therapy, or both.

Dizziness

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