Study design

- Randomized, double-blind, multicenter, placebo-controlled trial conducted in Japan between December 2007 and April 2008
- A total of 300 previously healthy adults aged 20 to 64 years were recruited within 48 hours of the onset of influenza symptoms
- Patients randomized to receive:
  - Placebo (n = 100)
  - 300 mg peramivir (n = 99)
  - 600 mg peramivir (n = 97)

Conclusions

- Rapivab is a single IV dose of peramivir, a selective inhibitor of viral neuraminidase, which is indicated for the treatment of acute uncomplicated influenza in patients 18 years and older who have been symptomatic for no more than 2 days
- Efficacy of Rapivab was based on clinical trials in which the predominant influenza virus strain was the A/H1 subtype
- Patients with influenza may be at an increased risk of hallucinations, delirium, and abnormal behavior early in their illness. There have been postmarketing reports of delirium in patients who were treated with Rapivab. However, the relationship of this condition to Rapivab is not established.

**Important Safety Information**

Rapivab® (peramivir injection) is indicated for the treatment of acute uncomplicated influenza in patients 18 years and older who have been symptomatic for no more than 2 days.

**Warnings and Precautions**

- **Serious skin reactions:** Rare cases of serious skin reactions, including erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported with Rapivab in clinical studies and postmarketing experience. Cases of erythema multiforme and Stevens-Johnson syndrome have been reported in postmarketing experience. Cases of toxic epidermal necrolysis have not been reported with Rapivab.
- **Drug interactions:** No significant drug interactions were noted with Rapivab in clinical studies.
- **Laboratory abnormalities:** Lab abnormalities (incidence ≥2%) occurring more commonly with Rapivab included elevated ALT 2.5 times the upper limit of normal (17% vs 10%), elevated AST at least 6 times the upper limit of normal (3% vs 2%), elevated serum glucose >160 mg/dL (5% vs 3%), and decreased WBC count (12% vs 8%).

**Contraindications**

- Rapivab is contraindicated in patients with known serious hypersensitivity or anaphylaxis to peramivir or any component of the product.
- Rapivab is contraindicated in patients with severe influenza requiring hospitalization.
- Patients with influenza may be at an increased risk of hallucinations, delirium, and abnormal behavior early in their illness. There have been postmarketing reports of delirium in patients who were treated with Rapivab. However, the relationship of this condition to Rapivab is not established.

**ADVERSE REACTIONS**

- **Most common adverse reactions** were diarrhea (8% Rapivab vs 7% placebo), headache (19% vs 14%), and rash (6% vs 4%).
- **Less common adverse reactions** included asthenia (19% vs 11%), nausea (10% vs 4%), vomiting (10% vs 3%), and abdominal pain (7% vs 2%).
- **Laboratory abnormalities** (incidence ≥2%) occurring more commonly with Rapivab included elevated ALT 2.5 times the upper limit of normal (17% vs 10%), elevated AST at least 6 times the upper limit of normal (3% vs 2%), and decreased WBC count (12% vs 8%).
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**Concurrent Use With Live Attenuated Influenza Vaccine**

- Concurrent use of Rapivab with LAIV is not recommended. Features of the seasonal influenza vaccines inactivated and live attenuated vaccines are not expected to influence the efficacy of Rapivab.

**References**

Peramivir afforded significant reduction in time to alleviation of symptoms compared with placebo.

Shortened time to alleviation of symptoms by 21 hours:

- **RAPIVAB 600 mg**
- **PLACEBO**

<table>
<thead>
<tr>
<th>Hours, median</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>59.9</td>
<td>P = 0.0092</td>
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<tr>
<td>81.8</td>
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</table>

**Time to resolution of fever by 12 hours**

Peramivir recipients reported shorter times to resumption of their usual activities:

- **300 mg Peramivir**
- **600 mg Peramivir**
- **Placebo**

<table>
<thead>
<tr>
<th>Time to resumption of normal activities, median (h)</th>
<th>Difference vs placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>125.6 (95% CI: 113.8–148.1)</td>
<td>43.6 hours earlier</td>
<td>P = 0.007</td>
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<tr>
<td>127.4 (95% CI: 120.1–133.1)</td>
<td>41.7 hours earlier</td>
<td>P = 0.013</td>
</tr>
<tr>
<td>168.3 (95% CI: 142.0–194.0)</td>
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</tbody>
</table>

Peramivir has a demonstrated safety profile:

The incidence of all adverse events was comparable to that for placebo. In clinical trials, the most common adverse events were gastrointestinal in nature, including diarrhea and nausea.

Please see Important Safety Information on back cover and enclosed U.S. Full Prescribing Information for Rapivab.

Peramivir recipients reported shorter times to resumption of their usual activities:

- **300 mg Peramivir**
- **600 mg Peramivir**
- **Placebo**

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A single IV dose of peramivir:*

- Significantly reduced the time in alleviation of symptoms
- Allowed patients to get back to their normal activities sooner
- Decreased the duration of illness
- Has a demonstrated safety profile

Study objective:
To investigate the efficacy and safety of a single intravenous dose of peramivir, a selective inhibitor of influenza virus neuraminidase, for the treatment of uncomplicated influenza virus infection in the outpatient setting.

Study design:
- Randomized, double-blind, multicenter, placebo-controlled trial conducted in Japan between December 2007 and April 2008
- A total of 300 previously healthy adults aged 20 to 64 years were recruited within 48 hours of the onset of influenza symptoms
- Patients randomized to receive:
  - 600 mg peramivir (n = 97)
  - 300 mg peramivir (n = 99)
  - Placebo (n = 100)
- Predominant influenza virus strain was the A/H1 subtype
- Patients randomized to receive: intravenous dose of peramivir, a selective inhibitor of influenza virus neuraminidase
- Randomized, double-blind, multicenter, placebo-controlled trial in Japan between December 2007 and April 2008
- A total of 300 previously healthy adults aged 20 to 64 years were recruited within 48 hours of the onset of influenza symptoms
- 300 mg peramivir (n = 99)
- Placebo (n = 100)
- Predominant influenza virus strain was the A/H1 subtype
- Patients randomized to receive: 300 mg peramivir or placebo
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- Randomized, double-blind, multicenter, placebo-controlled trial conducted in Japan between December 2007 and April 2008
- A total of 300 previously healthy adults aged 20 to 64 years were recruited within 48 hours of the onset of influenza symptoms
- Predominant influenza virus strain was the A/H1 subtype

**Other Efficacy End Points:**
- Change from baseline in composite symptom scores at 24, 36, 48, and 72 hours after start of treatment
- Time to recovery to normal temperature
- The proportion of viral subtypes (A/H1, A/H3, A/H5, and B) seen in postmarketing experience with Rapivab

**Safety Evaluation:**
- Advance notice, physical findings, vital signs, and laboratory data were assessed for duration, severity, and frequency of the study medication

**Primary Efficacy End Point:**
- Time to alleviation of symptoms defined as the time to recovery to normal temperature

**Efficacy and safety of intravenous peramivir for treatment of seasonal influenza virus infection**


**References:**

**Visit www.fda.gov/medwatch or call 1-800-FDA-1088.**
You are encouraged to report negative side effects of prescription drugs to the FDA. There are several ways to report a problem with a prescription drug, including the website of the FDA’s MedWatch Adverse Event Reporting Program. Please see enclosed Prescribing Information for Rapivab for more information.
Efficacy and safety of intravenous peramivir for treatment of seasonal influenza virus infection

**Study objective**

To investigate the efficacy and safety of a single intravenous dose of peramivir, a selective inhibitor of neuraminidases produced by influenza A and B viruses, for patients with uncomplicated influenza virus infection in the outpatient setting.

**Study design**

- Randomized, double-blind, multicenter, placebo-controlled trial conducted in Japan between December 2007 and April 2008
- A total of 300 previously healthy adults aged 20 to 65 years were recruited within 48 hours of the onset of influenza symptoms
- Patients randomized to receive:
  - Placebo (n = 100)
  - 300 mg peramivir (n = 99)
  - 600 mg peramivir (n = 97)
- Randomized, double-blind, multicenter, placebo-controlled trial
- 600 mg peramivir (n = 97)
- 300 mg peramivir (n = 99)

**Study objective**

1. To investigate the efficacy and safety of a single intravenous dose of peramivir, a selective inhibitor of neuraminidases produced by influenza A and B viruses, for patients with uncomplicated influenza virus infection in the outpatient setting.

**Primary Efficacy End Point**

Time to alleviation of symptoms defined as the time from initiation of treatment to recovery

**Other Efficacy End Points**

- Change from baseline in composite symptom scores at day 3
- Change from baseline in composite symptom scores at day 5
- Change from baseline in composite symptom scores at day 7
- Change from baseline in composite symptom scores at day 9
- Change from baseline in composite symptom scores at day 11

**Safety Evaluation**

Adverse events, physical findings, vital signs, and laboratory data were assessed for severity, frequency, and causality of the study medication

**Efficacy and safety of intravenous peramivir for treatment of seasonal influenza virus infection**

A single IV dose of peramivir:

- Significantly reduced the time to alleviation of symptoms
- Allowed patients to get back to their normal activities sooner
- Decreased the duration of illness
- Has a demonstrated safety profile

**Efficacy**

Rapivab® (peramivir injection) is indicated for the treatment of acute uncomplicated influenza in patients 18 years and older who have been symptomatic for 1 to 2 days. Efficacy of Rapivab has been based on clinical trials in which the predominant influenza virus strain was the A/H1 subtype.

**Contraindications**

Rapivab is contraindicated in patients with known serious hypersensitivity or anaphylaxis to peramivir or any component of the product. Severe allergic reactions have included anaphylaxis, erythema multiforme, and Stevens-Johnson syndrome.

**Warnings and Precautions**

- Rapivab is contraindicated in patients with known serious hypersensitivity or anaphylaxis to peramivir or any component of the product. Severe allergic reactions have included anaphylaxis, erythema multiforme, and Stevens-Johnson syndrome.
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**Adverse Reactions**

The most common adverse reactions were diarrhea (5% vs 3%), elevated CPK at least 6 times the upper limit of normal (5% vs 3%), elevated serum glucose >160 mg/dL (5% vs 3%), pruritus (4% vs 2%), and dyspnea (4% vs 3%).

**Concurrent Use With Live Attenuated Influenza Vaccine**

Concurrent use of Rapivab with LAIV has not been evaluated. Because of the potential for interference between Rapivab and LAIV, concurrent use is contraindicated. Rapivab should not be used within 2 weeks after or 48 hours before administration of LAIV unless medically indicated.

**References**


**Visit www.fda.gov/medwatch or call 1-800-FDA-1088.**

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