Efficacy and safety of intravenous peramivir for treatment of seasonal influenza virus infection[1]

Kohno S et al. *Antimicrob Agents Chemother.* 2010;54(11):4568-4574.

Timely administration of peramivir
(within 48 hours of influenza-like illness)

was shown to **REDUCE THE TIME TO ALLEVIATION OF SYMPTOMS**

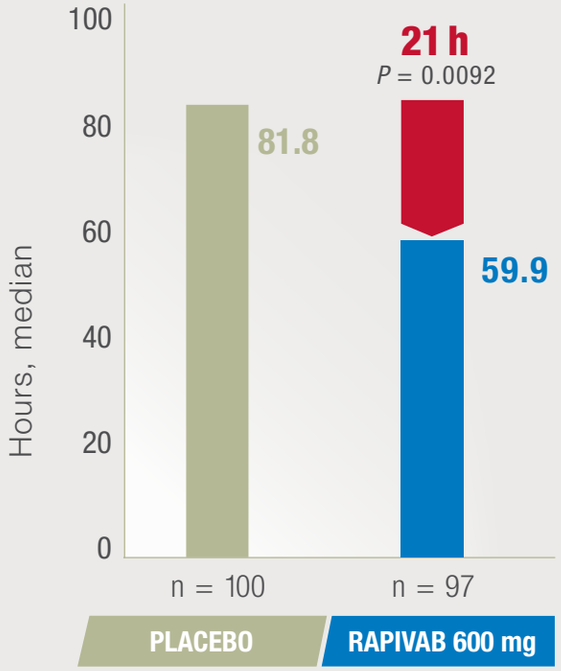
and **HELP PATIENTS GET BACK TO THEIR DAILY ACTIVITIES SOONER** compared with placebo[1]

Please see Important Safety Information on back cover and enclosed US full Prescribing Information for Rapivab.

Rapivab®
peramivir injection

Peramivir afforded significant reduction in time to alleviation of symptoms compared with placebo[1]

Shortened time to alleviation of symptoms by 21 hours[1]



REDUCED TIME TO **resolution** OF FEVER BY **12** HOURS[2]

Peramivir recipients reported shorter times to resumption of their usual activities[1]

	300 mg Peramivir	600 mg Peramivir	Placebo
Time to resumption of normal activities, median (h)	125.6 (95% CI, 103.8-148.5)	127.4 (95% CI, 122.1-153.1)	169.1 (95% CI, 142.0-180.0)
Difference vs placebo	43.6 hours earlier	41.7 hours earlier	
***P* value**	*P* = 0.0367	*P* = 0.0152	

Peramivir has a demonstrated safety profile[1]

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 US full Prescribing Information for Rapivab.

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

Study design[1]

- 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:
  - 300 mg peramivir (n = 99)
  - 600 mg peramivir (n = 97)
  - Placebo (n = 100)
- Predominant influenza virus strain was the A/H1 subtype

Primary Efficacy End Point[1]

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

Safety Evaluation[1]

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

Other Efficacy End Points[1,2]

- Change from baseline in composite symptom scores at 24, 36, 48, and 96 hours after start of treatment
- Time to recovery to normal temperature
- The proportion of afebrile subjects (<37°C; axillary)
- Change in influenza virus titer from baseline
- Time to resumption of usual activities
- Incidence of influenza-related complications

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Rapivab®
peramivir injection

A single IV dose of peramivir[1]:

- 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

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.

Efficacy of Rapivab was based on clinical trials in which the predominant influenza virus type was influenza A; a limited number of subjects infected with influenza B virus were enrolled.

Influenza viruses change over time. Emergence of resistance substitutions could decrease drug effectiveness. Other factors (for example, changes in viral virulence) might also diminish clinical benefit of antiviral drugs. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use Rapivab.

Efficacy could not be established in patients with serious influenza requiring hospitalization.

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

- Rare cases of serious skin reactions, including erythema multiforme, have been reported with Rapivab in clinical studies and in postmarketing experience. Cases of anaphylaxis and Stevens-Johnson syndrome have been reported in postmarketing experience with Rapivab. Discontinue Rapivab and institute appropriate treatment if anaphylaxis or a serious skin reaction occurs or is suspected. The use of Rapivab is contraindicated in patients with known serious hypersensitivity or anaphylaxis to Rapivab.
- Patients with influenza may be at an increased risk of hallucinations, delirium, and abnormal behavior early in their illness. There have been postmarketing reports (from Japan) of delirium and abnormal behavior leading to injury in patients with influenza who were receiving neuraminidase inhibitors, including Rapivab. Because these events were reported voluntarily during clinical practice, estimates of frequency cannot be made, but they appear to be uncommon. These events were reported primarily among pediatric patients. The contribution of Rapivab to these events has not been established. Patients with influenza should be closely monitored for signs of abnormal behavior.
- Serious bacterial infections may begin with influenza-like symptoms or may coexist with or occur as complications during the course of influenza. Rapivab has not been shown to prevent such complications.

Adverse Reactions

The most common adverse reaction was diarrhea (8% Rapivab vs 7% placebo).

Lab abnormalities (incidence ≥2%) occurring more commonly with Rapivab than placebo were elevated ALT 2.5 times the upper limit of normal (3% vs 2%), elevated serum glucose >160 mg/dL (5% vs 3%), elevated CPK at least 6 times the upper limit of normal (4% vs 2%), and neutrophils <1.0 x 10^9/L (8% vs 6%).

Concurrent Use With Live Attenuated Influenza Vaccine

Antiviral drugs may inhibit viral replication of a live attenuated influenza vaccine (LAIV). The concurrent use of Rapivab with LAIV intranasal has not been evaluated. Because of the potential for interference between these two products, avoid use of Rapivab within 2 weeks after or 48 hours before administration of LAIV unless medically indicated.

Please see enclosed Prescribing Information for Rapivab.

You are encouraged to report negative side effects of prescription drugs to the FDA.

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

References: 1. Kohno S et al. *Antimicrob Agents Chemother.* 2010;54(11):4568-4574. **2.** Rapivab [package insert]. Durham, NC: BioCryst Pharmaceuticals, Inc; 2016.

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December 2016

US/RIV/1016/0082(1)