Neuraminidase inhibitors are most effective for acute uncomplicated influenza when administered within 48 hours of onset of symptoms. Rapivab, specifically, has been clinically shown to reduce the total time to alleviation of symptoms of influenza by a median of 21.5 hours sooner and resolution of fever a median of 12 hours sooner when compared with placebo. Rapivab also has a demonstrated safety profile.

The single-dose, IV delivery of Rapivab makes it optimal for patients presenting to the ED with symptoms precluding them from taking oral antiviral therapy or for patients requiring IV hydration. Additionally, a high percentage of patients do not adhere to oral, multiday, neuraminidase inhibitor treatment making a one-dose option like Rapivab the most fitting choice.

## 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 $<1.0 \times 10^9$/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 accompanying full 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.

Seqirus

**Seqirus USA Inc.**
King of Prussia, Pennsylvania 19406

December 2016 US/RIV/1116/0085a

Rapivab® peramivir injection

# Case study: Focus on IV administration

## One-dose intravenous neuraminidase inhibitor in patients unable to tolerate conventional antiviral influenza therapy

### THE CHALLENGE:

Between the months of December and March, healthcare professionals see an increase in patients presenting with symptoms associated with influenza such as cough, fatigue, fever, headache, myalgia, nasal congestion, and sore throat. To help treat the flu, healthcare professionals commonly prescribe an oral or inhaled multidose antiviral neuraminidase inhibitor that can alleviate the symptoms, on average, about a day sooner than standard of care. However, oral (e.g., capsule, oral suspension) and inhaled antiviral influenza therapies may not be appropriate for all patients.

Patients who have difficulty swallowing (e.g., dysphagia), those who present with nausea, vomiting, or diarrhea, or those on a ventilator may have difficulty with orally administered medications. It is estimated that dysphagia affects up to 68% of elderly nursing home residents, up to 30% of elderly patients admitted to the hospital, and 13% to 38% of elderly patients who live independently. Similarly, patients with enteral feeding tubes may also benefit from intravenous (IV) administration. Whereas these patients may be treated with oral medications delivered through a feeding tube, this method of administration may increase the risk of errors and problems such as tube occlusion, incorrect administration techniques, and inappropriate dosage selection. Patients with underlying airway diseases, such as asthma or COPD, are not recommended to receive inhaled antiviral influenza therapy due to serious risk of bronchospasm. Intravenously administered peramivir provides an alternative for this subgroup of patients who cannot tolerate oral or inhaled antiviral therapy.

### THE CASE:

A 38-year-old female with a medical history of gastroesophageal reflux disease (GERD) and asthma presented with a headache, muscle aches, cough, and a fever as well as heartburn. She described developing a headache and cough the previous day, followed by progressive symptoms of “feeling hot.” The patient also reported recent GERD episodes as heartburn irritating her throat and causing difficulty swallowing liquids and solids. As a busy working professional, she expressed worry about catching the flu because she could not afford to miss work. She stated she was not able to tolerate food or fluids for the past 2 days and was taken to the emergency department (ED) by her husband.

Upon presentation to the ED, the patient denied tender nodes, sputum production, chest pain, and wheezing, and reported she had forgotten to get her flu shot this year because she had been traveling for the past month. The patient also reported that she had run out of her esomeprazole a couple days ago. The patient’s vital signs were as follows: temperature: 101°F, HR: 80 bpm, RR: 18/min, BP: 88/58 mm Hg. Her examination was notable for high fever, cough, and dysphagia associated with heartburn.

### THE RESULTS:

The patient was treated with one dose of Rapivab® (peramivir injection), a complete treatment course for uncomplicated influenza. IV administration was deemed preferable due to her inability to swallow an oral antiviral regimen, a history of asthma, and an established IV access from her IV proton pump inhibitor and hydration therapy. Hydration therapy was necessary, as the patient has not been able to tolerate liquids or solid foods for the past 48 hours and exhibited symptoms of dehydration including dry mucous membranes and dizziness. The patient was also treated for her GERD exacerbation and then observed for the next 20 hours. Once she was able to ambulate and oral intake was initiated, the patient was discharged from the ED with instructions to call her outpatient physician should symptoms not resolve completely over the next few days.

### THE CONCLUSION:

Rapivab is a neuraminidase inhibitor against influenza A and B viruses that has been shown in clinical trials to reduce the time to alleviation of fever by 12 hours and symptoms by 21 hours compared with placebo. Rapivab is completely bioavailable and has a well-demonstrated safety profile. IV administration provides an alternative for patients unable to take medications via the oral or inhalation routes.

IV administration of Rapivab:

- Avoids any issues related to oral administration such as nausea, vomiting, or difficulty swallowing
- Offers complete bioavailability unlike oral treatment’s dependency on absorption
- Offers an alternative for those patients not recommended to receive inhaled antiviral influenza treatments such as patients with lung diseases and lactose allergies
- Ensures compliance (which may be a challenge for certain patients); is given under professional supervision; and there is no further action required of the patient

**Please see Important Safety Information on back cover and accompanying full Prescribing Information for Rapivab.**

Rapivab
peramivir injection