Table 1

Pharmacologic Properties of Neuraminidase Inhibitors: Oseltamivir,[7-9] Zanamivir,[7] and Peramivir[6]

Pharmacologic Parameter	Oseltamivir (treatment duration is five days)	Zanamivir (treatment duration is five days)	Peramivir (treatment duration is 5-10 days)
Adult Treatment Dose	CrCL > 30mL/min: 75 mg PO BID CrCL 10-30 mL/min: 75 mg PO once daily CrCl < 10 ml/min: not recommended[1]	Two 5-mg inhalations (10 mg total) twice daily. No dose adjustment required for renal dysfunction. Detailed directions on the Diskhaler and a video for proper use can be found at: www.relenza.com/inhaler-step-by-step.html.	CrCL 50-80 mL/min: 600 mg IV over 30 minutes once daily. CrCL 31-49 mL/min: 150 mg IV over 30 minutes once daily. CrCL 10-30mL/min: 100 mg IV over 30 minutes once daily. CrCL < 10ml/min or hemodialysis: 15 mg IV over 30 minutes once daily.
Off-Label Dosing	Per the CDC, some (< 10) severely ill patients from Michigan (most had BMIs in excess of 30 kg/m^2 or 40 kg/m^2) received doses of oseltamivir 150 mg PO BID	Kidd et al[2] used a dosing regimen of 600 mg IV bid in a 22-year-old neutropenic female, for a total of 10 days.	No pediatric patients have received peramivir in clinical trials. However, limited use of peramivir IV in children has been allowed under emergency IND procedures. Dosing in pediatrics is based on modeling. For more dosing information in pediatrics and children, refer to *Table 2*.
Adult Chemoprophylaxis	CrCL > 30mL/min: 75 mg PO Qday CrCL 10-30 mL/min: 75 mg PO every other day or 30 mg PO Qday. CrCL < 10 mL/min: not recommended[1]	Two 5-mg inhalations (10 mg total) once daily.	Not applicable.
Chemoprophylaxis: Children	**Children ≥ 12 Months** 15 kg or less: 30 mg PO Qday; 16-23 kg: 45 mg PO Qday; 24-40kg: 60 mg PO Qday; > 40 kg: refer to adult dose **Children < 12 Months:**[4] < 3 months: not recommended; 3-5 months: 20 mg PO Qday; 6-11 months: 25 mg PO Qday	Children ≥ 5 Years Same as adult dose (see above)	Not applicable.
Resistance	To date, at least 14 cases of H1N1 resistance have been documented in the United States. The mechanism of resistance has been shown to be due to a mutation, H275Y, of the viral neuraminidase gene.	No reports of resistance to zanamivir.	Peramivir IV should not be used for treatment of 2009 H1N1 virus infection in patients with documented or highly suspected oseltamivir resistance. Peramivir IV should be used with caution in patients with documented or highly suspected zanamivir resistance.
Off-Label Formulations	Not applicable	Available as an IV formulation through a compassionate use request to GlaxoSmithKline.[3]	
Common Adverse Effects	Nausea (10%), vomiting (9%), diarrhea (7%) in patients receiving treatment.	≥ 1.5%: sinusitis, dizziness, fever, chills, arthralgia	Diarrhea , nausea, vomiting (composite, 12% with 600-mg dose), psychiatric adverse events (11%), decrease in neutrophil count.

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Pharmacologic Properties of Neuraminidase Inhibitors: Oseltamivir,[7-9] Zanamivir,[7] and Peramivir[6]

Contraindications/ Warnings	Hypersensitivity to oseltamivir. seizures, hallucinations, delirium, and abnormal behavior (especially children)	Lactose/milk protein allergy; hypersensitivity. Avoid using this agent in patients with underlying airway disease.	Hypersensitivty to other neuraminidase inhibitors (oseltamivir or zanamivir) or to any component of peramivir.
Storage Condition for Intravenous Formulation	Not applicable	Not applicable	Available as single-use 10mg/mL, 20 mL vial. Store at 15^{0}C-30^{0}C (59^{0}F-86^{0}F). Diluted product (*see below*) can be stored at 2^{0}C-8^{0}C (36^{0}F-46^{0}F) for 24h.
Dilution of Intravenous Formulation	Not applicable	Not applicable	For patients with normal renal function, transfer 600 mg (60 mL) to an empty sterile container for IV use. Add 40 mL of 0.9% NaCL or 0.45% NaCLl to reach a total volume of 100 mL (maximum concentration, 6 mg/mL). For renally impaired patients, use appropriate volumes based on recommended dosing; final total volume, 100 mL.
Administration of Intravenous Formulation	Not applicable	Not applicable	Once the product is diluted, administer immediately, or if stored in refrigerator, let it come to room temperature. For adults, usual infusion time is 30 minutes; maximum rate, 40 mg/min. Infuse over one hour in pediatric patients.

[1]One study conducted by Robson et al.[8] recommended a dose of oseltamivir 30-mg oral suspension given once weekly in CAPD patients for both treatment and chemoprophylaxis. The investigators proposed a dose of oseltamivir 30-mg oral suspension given after alternate sessions in hemodialysis sessions for both treatment and chemoprophylaxis.

[2]Gastrointestinal side effects are the most likely adverse effects seen with higher doses of oseltamivir. A recent pharmacokinetic study conducted by Wattanagoon and associates[9] used doses up to 675 mg of oseltamivir in healthy volunteers (n = 8), and no major adverse effects were reported. Weight, age, and gender had no effects on the pharmacokinetics of oseltamivir phosphate or oseltamivir carboxylate. The authors proposed that higher doses of oseltamivir may lead to more rapid attainment of therapeutic concentrations. Since obese patients have been shown to be more likely to experience complications from H1N1 infection, perhaps some clinicians may choose higher doses for this patient population.

[3]Compassionate use can be requested by calling 1-888-825-5249. A physician should be expected to provide contact information to the operator so that a GSK physician may call to discuss eligibility criteria. Inclusion criteria (all 4 must be met): 1) hospitalized with severe influenza symptoms, 2) laboratory confirmation of influenza infection, 3) unable to use any other treatment, and 4) ≥ 6 months of age. Exclusion criteria include pregnancy and hypersensitivity.

[4]Treatment of infants younger than the age of 12 months old has been recently approved for Emergency Use Authorization (EUA) by the FDA. When applicable, the FDA may allow the use of unapproved medications or the unapproved use approved agents in times of emergencies with specific products.