Zanamivir Aqueous Solution For The Treatment of Serious Influenza Illness

Zanamivir aqueous solution is not an approved product. It is currently under investigation in clinical trials and is available globally on a compassionate use basis for the treatment of serious influenza illness. The Zanamivir aqueous solution formulation can be administered intravenously or by nebulization (**WARNING:** the zanamivir lactose powder formulation contained in the approved RELENZA DISKHALER® device cannot be nebulized as the lactose can cause clumping and obstruction of plastic tubing; only the aqueous solution of zanamivir can be safely nebulized).

There are currently two ways to obtain Zanamivir aqueous solution; enrollment in a clinical trial at a participating clinical trial site or through a compassionate use request made to GlaxoSmithKline (GSK) along with FDA approval.

GSK Sponsored Clinical Trials (NAI113678 and NAI114373)

For information about potential enrollment in an ongoing Zanamivir aqueous solution clinical trial, see:

NAI113678 (Pediatric Clinical Trial) - ClinicalTrials.gov Identifier: NCT01014988

NAI114373 (Adult Clinical Trial) - ClinicalTrials.gov Identifier: NCT01231620

Zanamivir Aqueous Solution for Compassionate Use

Compassionate Use may be considered for hospitalized influenza patients who meet the following criteria: not responding to either oral or inhaled approved antiviral medicinal products *OR* drug delivery by a route other than IV (e.g., oral oseltamivir or inhaled zanamivir) is not expected to be dependable or appropriate *OR* patients infected with documented influenza virus resistant to other antiviral agents and not suitable for therapy with inhaled zanamivir.

To request Zanamivir aqueous solution for compassionate use, the requesting clinician should first contact the **GSK Clinical Support Help Desk** at:

Phone: 1-877-626-8019 or 1-866-341-9160

Email: gskclinicalsupportHD@gsk.com

Availability is 7 days a week, 24 hours/day, including holidays

The GSK Clinical Support Help Desk will provide information and instructions on obtaining Zanamivir aqueous solution (i.e., EIND process), assess eligibility for clinical trials, and provide the Request for Patient Information Form that needs to be completed for FDA review and approval.

FDA Contact Information

During normal business hours (8:00 AM - 4:30 PM Eastern Standard Time), please call DAVP at 301-796-1500 or email DAVPEINDREQUEST@fda.hhs.gov.

After normal business hours (weekdays after 4:30 PM or before 8:00 AM Eastern Standard Time; weekends or holidays), please call the FDA Emergency Coordinator at 1-866-300-4374 or 301-796-8240 or the CDER Emergency Coordinator at 301-796-9900.

Selected References for Zanamivir Aqueous Solution

Calfee D, Peng A, Cass L, et al. Safety and Efficacy of Intravenous Zanamivir in Preventing Experimental Influenza A Virus Infection. *Antimicrob Agents Chemother* 1999; 43(7): 1616-1620.

Cass LMR, Efthymiopoulos C, Bye A. Pharmacokinetics of Zanamivir After Intravenous, Oral, Inhaled or Intranasal Administration to Healthy Volunteers. *Clin Pharmacokinet* 1999a; 36(Suppl 1): 1-11.

Cass LMR, Efthymiopoulos C, Marsh J, Bye A. Effect of Renal Impairment on the Pharmacokinetics of Intravenous Zanamivir. *Clin Pharmacokinet* 1999b; 36(Suppl 1): 13-19.

Da Dalt L, Calistri A, Chillerri C, Cusinato R, Franchin E, Salata C, et al. Oseltamivir-Resistant Pandemic (H1N1) 2009 Treated with Nebulized Zanamivir [letter]. Emerg Infect Dis [serial on the Internet]. 2010 Nov [*date cited*]. http://www.cdc.gov/EID/content/16/11/1813.htm

Dohna-Schwake C, Schweiger B, Felderhoff-Műser U. Severe H1N1 Infection in a Pediatric Liver Transplant Recipient Treated with Intravenous Zanamivir: Efficiency and Complications. *Transplantation* 2010; 90(2):223-224

Dulek DE et al. Use of Intravenous Zanamivir After Development of Oseltamivir Resistance in a Critically Ill Immunosuppressed Child Infected with 2009 Pandemic Influenza A (H1N1) Virus. *Clin Inf Dis* 2010; 50(11): 1493–1496.

EMEA. Document EMA/CHMP/32815/2010; 2010

Gaur A, et al. Intravenous Zanamivir for Oseltamivir-Resistant 2009 H1N1 Influenza. N Engl J Med 362;1 nejm.org January 7, 2010. Available at: http://content.nejm.org/cgi/content/full/NEJMc0910893

Härter G et al. Intravenous Zanamivir for Patients with Pneumonitis Due to Pandemic (H1N1) 2009 Influenza Virus. *Clin Inf Dis* 2010; 50(9): 1249–1251.

Kidd MI, Down J, Nastouli E, et al. Case Report: H1N1 Pneumonitis Treated with IV Zanamivir. *The Lancet*. Published online at www.thelancet.com/infection; Sept 4, 2009

Pukrittayakamee S, Jittamala P, Stepniewska K, et al. An Open-Label Crossover Study to Evaluate Potential Pharmacokinetic Interactions Between Oral Oseltamivir and Intravenous Zanamivir in Healthy Thai Adults. *Antimicrob Agents Chemother* 2011; 55(9): 4050-4057.

Ridwan BU, Goekoop GJD, Muijsken MA, Tacx AN, van de Visse EP. Intravenous Zanamivir Treatment of an Obese Patient with Severe Pandemic H1N1 2009 Influenza. Scientific Spring Meeting of the Dutch Society for Medical Microbiology. 19th – 21st April 2010; Papendal, the Netherlands. (Poster 058).

Shelton MJ, Lovern M, Ng-Cashin J, et al. Zanamivir Pharmacokinetics and Pulmonary Penetration into Epithelial Lining Fluid Following Intravenous or Oral Inhaled Administration to Healthy Adult Subjects. *Antimicrob Agents Chemother* 2011, 51(11): 5178-5184.

Speers DJ et al. Oseltamivir-resistant pandemic (H1N1) 2009 Influenza in a Severely Ill Patient: The First Australian Case. *Med J Australia* 2010; 192(3): 166-168. Available at: http://www.mja.com.au/public/issues/192_03_010210/spe11148_fm.html

Van der Vries E, Stelma FF and Boucher CA. Emergence of a Multi-Drug Resistant Pandemic Influenza A (H1N1) Virus. *New Engl J Med* 2010; 363 (14); 1381-82.

Weller S, Jones LS, Lou Y, Peppercorn A, Ng-Cashin J. Pharmacokinetics of Intravenous Zanamivir in Subjects with Renal Impairment. Infectious Diseases Society of America 48th Annual Meeting. Oct 2010. Presentation #767.

Wolfe C, Greenwald I, and Chen L. Pandemic (H1N1) 2009 and Oseltamivir Resistance in Hematology/ Oncology Patients. Emerging Infectious Diseases. www.cdc.gov/eid. Vol. 16, No. 11, November 2010.

Wolfe C, Turner D, Rudd C, Pham J, Cheifetz I. Intravenous Zanamivir for Critical Illness Due to Pandemic H1N1 Influenza. Society of Critical Care Medicine 40th Critical Care Congress. Jan 2011. Posters #777.