

Prophylactic Use of Tamiflu Bad Idea, Leading Virologist Says

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Tuesday, 10 June 2008

'Early treatment is the only way to go'

The US government's new proposal to use drugs like Tamiflu and Relenza as a prophylaxis to prevent infection by a pandemic strain of influenza is wrongheaded, says Dr. Graeme Laver, a former professor of biochemistry and molecular biology at the John Curtin School of Medical Research at the Australian National University in Canberra.

Laver, who played a key role in the development of both drugs, has been studying influenza viruses for nearly 40 years. He and Dr. Robert Webster (another world-renowned virologist at St. Jude Children's Research Hospital) are credited with having first found the link between human flu and bird flu. In the 1960's, both received world acclaim when they developed a new and innovative generation of vaccines for flu viruses.

Laver told HSToday.us that 'prophylaxis with Tamiflu in a pandemic is wrong. Early treatment is the only way to go.'

But the US government proposes to use Tamiflu and Relenza prophylactically to prevent infection, including giving guidelines to businesses that may want to buy the drugs in advance to treat or protect employees.

The Department of Health and Human Services' (HHS) pandemic plan calls for 'targeted antiviral prophylaxis of disease clusters, administration of antiviral treatment to persons with confirmed or suspected cases of pandemic influenza, and provision of drug prophylaxis to all persons in [an] affected community.'

Similarly, should clusters of humans be found infected with a virulent strain of influenza like H5N1, the World Health Organization's plan of attack is to flood the regions with Tamiflu in the hope that it will quell further spread of the virus.

Dr. Ben Schwartz, a pandemic planner at HHS who wrote most of the new guidelines, told Reuters that "for prophylaxis of health care and emergency services workers, the responsibility for purchasing and stockpiling the drugs would primarily be on the health care organizations ... or on the emergency organizations that would be protecting their workforce.'

Meanwhile, HSToday.us has learned that there also are discussions within HHS about making Tamiflu and Relenza 'push packets' available to people to have on hand in the event of a pandemic.

Laver also has problems with that notion.

"Personal stockpiles of Tamiflu or Relenza are not a good idea," Laver told HSToday.us, explaining, "personal stockpiles are wrong for two reasons. First, nothing might happen and the stockpiles will be wasted and, second, if the stockpiles are used, it will be on the basis of self-diagnosis, and that is not a great idea."

"Widespread prophylaxis to control a pandemic before any vaccine is available, is totally wrong," Laver continued. "It would be a wicked waste of a valuable resource! Australia had a policy (long since abandoned) to provide essential workers with Tamiflu prophylaxis for six weeks at the start of the pandemic."

But "what happens then?" Laver mused. "Apart from the difficulty in identifying the essential workers, and keeping the Tamiflu stockpile safe from desperate people who would do anything to get the drug, at the end of six weeks all those people who had been taking Tamiflu for prophylaxis would be left without protection. And the stockpile would have vanished."

Laver explained to HSToday.us that it is "much better to use Tamiflu only for early treatment. If people with flu symptoms take Tamiflu immediately, say within six or so hours after symptom onset, the infection should be rapidly terminated, the person should recover, and then, and this is important, should then be immune to reinfection for the rest of the pandemic. Much better than any vaccine. This has been called "Aborted-infection Immunization," and to use Tamiflu in this way would allow many health care workers and so on to go about their business without fear of reinfection."

"People will, of course, say, "but Aborted-infection Immunization has never been shown to work,"" Laver said. "Of course not, but then neither has long-term prophylaxis or the use of pre-pandemic vaccines. But my bet is that it will!"

To work, Tamiflu must be taken in proper doses within 6 to 12 hours after onset of symptoms.

"Forty-eight hours is about the limit the drug is effective," Laver said.

Laver does believe that "prophylaxis with Tamiflu should be used in some circumstances. For example, Tamiflu should be taken by poultry workers culling H5 or H7 infected chickens," he said.

Prior to HHS's release of its new proposals Laver expressed his concerns in a letter to Dr. Bruce Gellin, director of the department's National Vaccine Program Office and chairman of HHS Secretary Michael Leavitt's Task Force on Influenza Preparedness.

“I believe this is completely wrong,” Laver wrote Gellin, explaining that “as soon as prophylaxis is stopped, the person taking Tamiflu is just as susceptible to infection as before. Early treatment would be so much better.” Laver told Gellin “Tamiflu should be available over-the-counter [OTC] in pharmacies now, where flu victims can get it without the time-wasting need to first get a prescription from a doctor. There is no need for a prescription and the time taken to get one can render Tamiflu pretty well useless.

“To have people familiar with the correct use of Tamiflu (and Relenza) for seasonal influenza infections would mean the community would be “trained” in the correct use of these drugs in the event of a pandemic. I imagine that, in this case, there would be much less panic than would occur otherwise.”

Laver told HSToday.us that it would be “much better to hold stocks of the drugs in every pharmacy in the country where it can be got quickly after diagnosis by a trained pharmacist or other health care worker.”

Laver also said “using a rapid flu test to assist this would be a good idea, so that people who think they have the flu can be properly diagnosed quickly and take the drugs very soon after symptom onset. This rapid procedure of “test and treat” would mean that the infection should be immediately terminated and the flu victim experience a quick recovery. Seems quite simple, really!”

In late 2006, the Centers for Disease Control and Prevention awarded \$11.4 million in contracts to four companies working to develop new diagnostic tests that doctors and field epidemiologists could eventually use to quickly and accurately test patients for avian influenza H5N1 and other emerging influenza viruses, as well as more common influenza viruses.

Brit Oiulfstad, pandemic influenza coordinator for the County of Los Angeles, had earlier expressed concern to HSToday.us about the prophylactic use of Tamiflu.

Oiulfstad said she and other authorities “are concerned about “the current push for community-wide antiviral prophylaxis when the effectiveness for such long-term use (several times the duration of the recommended treatment period) has not been evaluated.”

Continuing, Oiulfstad told HSToday.us that “planning for antivirals is very complex as we are not certain that the current antivirals will be effective in whatever viral strain will be circulating. However, planning for any pharmaceutical dispersal is good for other future events. In Los Angeles County, planning for antiviral use and distribution is going well as our overall goal is to use antivirals in medical settings to reduce serious illness and death among cases, not general prophylaxis.”

Oiulfstad added: “We do not know the effects of long-term antiviral use in a prophylactic setting. Therefore, we always consider that we must do no harm, and until we have some more answers, we proceed on those recommendations for prophylaxis with great caution. Until the science is in that shows that these drugs prevent illness,

this seems to be the only reasonable way to approach the problem.”;

The Infectious Diseases Society of America (IDSA) said in an October 2005 statement that "personal stockpiling would likely lead to inappropriate use and wastage," adding, "institutions should not stockpile drug for prophylaxis of health care workers, as this strategy requires much greater drug supplies than early treatment, and could deplete the reserve necessary for treatment on a national level.";

IDSA and the Society for Healthcare Epidemiology of America (SHEA) said local health care institutions ought to have sufficient stockpiles to treat sick people and maintain the health care system in the event of a pandemic.

The group advised health care facilities to have enough supply of the drugs to reduce hospitalizations and mortality and maintain social order and function in the event of a severe pandemic.

"Hospitals will need to be able to treat those who are sick and keep their own doors open," said Dr. Kathleen Neuzil, chair of IDSA's Pandemic Influenza Task Force.

IDSA and SHEA do not recommend institutions stockpile enough drugs to prevent illness among health care workers because this strategy requires much greater drug supplies than early treatment and could deplete the reserve necessary for treatment on a national level.

"This recommendation could change if drug supplies increase in the future," Dr. Neuzil said. "When one considers the cost and loss of workers caused by illness among nurses and doctors, it may make sense for hospitals to have adequate supplies to use the drug to prevent illness among health care workers who are seeing patients with flu.";

HHS's goal is to have 81 million doses (10 capsules per dose) of Tamiflu, Relenza and Rimantidine available for the US population. Of this 81 million, 50 million are to be stored in the Strategic National Stockpile (SNS). Of this, approximately 44 million courses are to be held for emergency pandemic usage by states and 6 million reserved for domestic containment efforts at the onset of localized outbreaks.

Of the 50 million doses the government plans to put into the SNS, though, HHS says only 37.4 million have been procured and 29.8 million treatment courses put into the SNS, and the remaining 7.6 million treatment courses are due by the end of calendar year 2007. The balance, HHS says, is expected this year.

The Department of Defense has stockpiled many millions less, and less than half the states have stockpiled only 13 million of the 31 million doses HHS is supposed to help states buy, largely because the remaining states have had difficulty coming up with their share of the money for purchases. HHS is authorized to subsidize 25 percent of the procurement costs states incur, apportioned based on population.

Oklahoma is among the states that haven't yet stockpiled Tamiflu because of the cost. Even with manufacturer F. Hoffmann-La Roche giving states an 80-percent discount on the medication, states still must fork up \$14.43 per dose. Oklahoma would have to spend \$10 million to stockpile enough of the drug to treat a massive outbreak.

States without stockpiles shouldn't count on having supplies earmarked for them in the SNS. According to the HHS pandemic plan, "should the military stockpile be exhausted and additional antiviral medication required to ensure national defense or continued support to civil authorities, use of antiviral drugs from the national stockpile may also be required."

There's another problem with Tamiflu. It has a shelf life of approximately five years, which means stockpiles must be replenished. Existing mass stockpiles will have to be replaced in order to ensure there are adequate stores beyond 2010, but according to F. Hoffmann-La Roche, new orders for future batches have dwindled, and there's a lag time in making the drug. The company has, though, entered into agreements with other countries to allow them to manufacture Tamiflu themselves.

The Food and Drug Administration manages a Shelf Life Extension Program, but only products in the federal SNS are eligible to receive an extended expiration date if a drug meets specific conditions. When states' stockpiles expire, they will have to buy new supplies - without additional federal assistance.

This problem, combined with those states that have yet to procure their own stockpiles, means there could be a widespread national shortage of antivirals. Thus, as Laver pointed out, using Tamiflu to treat, rather than trying to prevent, infections, is necessary to prevent the valuable stockpiles of these drugs from being wasted.