

Support for a Personal Tamiflu Stockpile

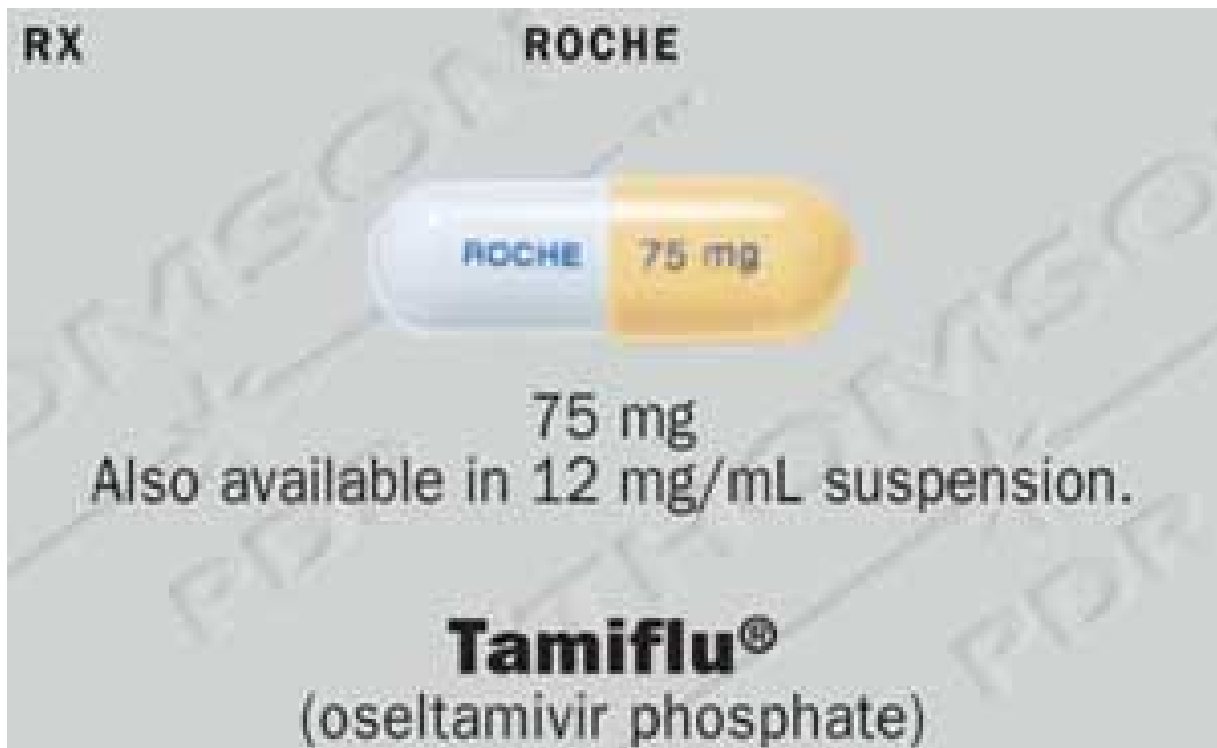
By Grattan Woodson, MD, FACP

It is responsible and ethical for physicians to prescribe Tamiflu for their patients to stockpile and use later during pandemic bird flu. Presently the risk of an influenza pandemic is high. Roche and its licensees have significantly ramped up production of Tamiflu beginning in the spring of 2006. This has alleviated the severe supply shortage seen in 2005. There will not be an effective H5N1 pandemic influenza vaccine until about 6 months after the pandemic strain first emerges. Even then supplies of the vaccine will be limited with only enough for about 10% of the population. There is doubt regarding the ability of the US Government and organized medicine to respond effectively to an emergency on the scale of a severe influenza pandemic. These factors are those that have led me to support the practice of helping my patients establish a Tamiflu stockpile for use during the pandemic. Nationally there is a woeful lack of preparation to respond to this serious public health issue. My position differs from most government and medical bodies who have expressed an opinion. In this brief essay, I provide the rationale for why I think it is both a good medical practice and ethical for doctors to prescribe and patients to obtain Tamiflu prior to the pandemic.

The Tamiflu shortage

The World Health Organization (WHO) has recommended that every country establish a stockpile of enough drugs to treat 20% of its citizens in preparation for a possible avian influenza pandemic.¹ Most of the developed nations followed the WHO

recommendations except for the US who hesitated placing their order in the fall of 2005. The CBO stated in a recent study of the macroeconomic effect of influenza pandemic on the US, that by the end of 2005, the US Strategic National Stockpile would contain enough Tamiflu for 4 million five-day treatment courses and 84,000 Relenza treatment courses.² This is enough for about 1.4% of the US population assuming that the standard treatment regimen will be effective for bird flu. This dose and the length of treatment with Tamiflu for bird flu is currently under review by infectious disease and public health experts. There is a good chance that they will recommend that the dose and course of therapy both be doubled.³ If so, this would reduce the coverage by 75%.



When the US finally placed an order for 12 million additional treatment courses from Roche, the company informed the US

that Roche was already at full manufacturing capacity worldwide and the orders were to be filled on a first come first serve basis. Since the US was one of the last countries to order the drug, Roche informed the US Department of Health and Human Services (US DHHS) in October 2005 that it would not even begin to fill the US order until late 2007.²

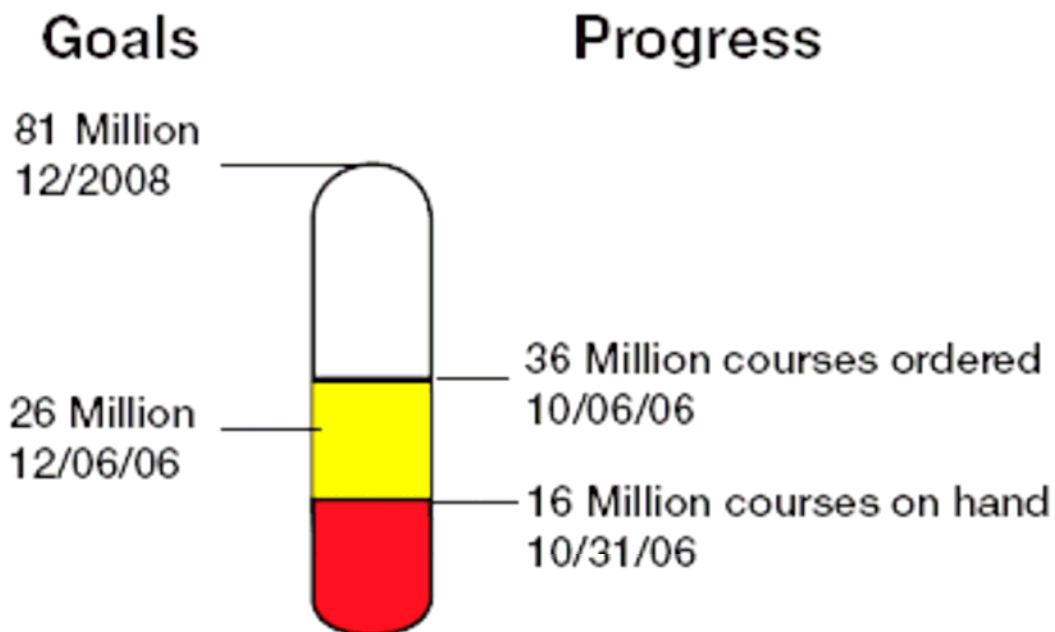
This resulted in pressure being applied by various stakeholders, both political and commercial. In response, Roche addressed this problem in November 2005 by issuing licenses to manufacture Tamiflu to pharmaceutical companies worldwide. Roche also found a synthetic substitute for the main and most expensive ingredient of the drug, star anise, which is a botanical grown only in China. It took the Roche licensees 6 months to retool and begin Tamiflu production. Since the spring of 2006 these new supplies began to be shipped. The US DHHS announced in November 2006 that the US National Strategic Stockpile of Tamiflu stood at 16 million effective 5-day courses with 20 million more expected by March 2007, enough for 11% of the US population.⁴

The US States have ordered 31 million courses of Tamiflu as well. By December 2008, 81 million courses of the drug are projected to be on hand, enough to cover 25% of the US population.

Today supplies of the drug for present use and that destined for the national stockpiles are being met around the world. While more drug is needed, the supply of Tamiflu is now sufficient to allow for limited individual stockpiling to occur without there being any concern about causing shortages for present use or

interfering with the national authorities desire to fill their stockpiles.

Antiviral Stockpile



The lack of a pandemic flu vaccine



The pandemic strain of H5N1 has yet to emerge. Until it does so, only prototype vaccines, of unforeseeable efficacy, can be made using viral isolated samples obtain earlier human cases of bird flu isolated in Viet Nam and Indonesia. When the actual pandemic virus begins to spread, there will not be any vaccine doses available for anyone for at least six months. Using current technology with some luck thrown in, it is estimated that supplies will be limited to only 30 million effective doses being available at 6-month intervals. This quantity is enough to vaccinate no more than

10% of the US population. If the pandemic lasts for 18 months, vaccination will be an option for about 30% of Americans. During this period, Tamiflu (and Relenza) will be the only option for effective medical treatment of pandemic flu available to most people.

Would personal stockpiles Tamiflu be properly used?

In the December 22, 2005 issue of the *New England Journal of Medicine*, Anne Moscona, M.D. argued “personal stockpiling of oseltamivir is likely to lead to the use of insufficient doses or inadequate courses of therapy. Shortages during a pandemic would inspire sharing of personal supplies, resulting in inadequate treatment. Such under-treatment is of particular concern in children — the main source for the dissemination of influenza within the community, since they usually have higher viral loads than adults and excrete infectious virus for longer periods. The habit of stopping treatment prematurely when symptoms resolve (a well established tendency with antibiotic therapy) could also lead to sub-optimal treatment of influenza and promote the development of drug resistance.” Her conclusion is “Improper use of personal stockpiles of oseltamivir may promote resistance, thereby lessening the usefulness of our frontline defense against influenza, and should be strongly discouraged.” These sentiments are being widely supported in the public health and infectious disease community.^{5,6,7}

I disagree with these assumptions for several reasons. First, the idea that people who use Tamiflu out of their private stockpile will misuse it is an unwarranted generalization. While there are segments of the population that may be unable to self-administer drugs properly, these are probably not the same people who are

interested in obtaining a personal Tamiflu stockpile. In my experience, the people who have requested a Tamiflu prescription from me for the purpose of establishing a personal stockpile have researched the issue thoroughly and are very clear on the



indications for use, timing of the dose, and treatment course. They probably know these things better than most doctors who rarely prescribe Tamiflu. Interestingly, this lack of experience prescribing Tamiflu is often due to the fact that by the time most patients seek treatment for the flu, it is too late in the course of the illness to start it. To be effective, Tamiflu must be initiated within a 48-hour therapeutic window after the onset of symptoms.

For the administration of the Tamiflu in a timely manner, I can hardly think of a better place for the drug to be stored than in the house of the person coming down with the flu. With respect to being able to take the drug within 2 days of the beginning of symptoms, what could be better? It is important that the person deciding when to start the Tamiflu have a good grasp of what flu symptoms are so they don't waste their precious drug. I provide this information to my patients and find that similar information is available in many places on the Internet today.

I advocate physicians prescribe drugs for their patients that will be useful for the management of influenza before they become scarce, an event likely to accompany the pandemic as it emerges. Specifically, I think it is prudent for patients to have

Tamiflu, over-the-counter and other prescription drugs stored at home for personal use during a pandemic. As is the case any time we prescribe drugs, a key responsibility of the prescribing physician is to ensure that the patient is provided with specific advice on how to use these medications properly and when to do so. An influenza pandemic could begin at any time now. Under these circumstances and considering the inadequate national pandemic preparedness, I think it is both prudent and

responsible for practicing physicians to give patients access to Tamiflu if they want it. This is especially so since it is well understood that once the pandemic starts, most people will have no chance at all of getting



any or for that matter even getting in to see their doctor whose office is likely to be overwhelmed by patients sick with flu. For these reasons, the only way I see that a patient with pandemic flu has any chance of benefiting from Tamiflu within the therapeutic window is if they already have it on hand.

Bird flu resistance to Tamiflu

One of the arguments used by opponents of patient stockpiles of Tamiflu is that their misuse or even their use of the drug could result in higher rates of oseltamivir resistant H5N1 bird flu. Based on our experience with all other anti-infective agents, this is a true statement and will happen irrespective of whether it is

used properly or not. *A unique and truly interesting fact concerning Tamiflu resistant strains of influenza is that they are less infective and have lower virulence and lethality compared with non-resistant strains.* This means that inducing Tamiflu resistance in the pandemic bird flu strain could have beneficial effect. In fact, I think it might give us something we can exploit to lower the severity of bird flu infections. This finding has to do with the way the virus has to alter the neuraminidase receptor to avoid Tamiflu. While making this change allows the flu to escape the effect of Tamiflu it also partially cripples itself by making it much harder for it to enter and leave the cell. In other words, bird flu without the Tamiflu resistance mutation is much more deadly than those with it. So, this may mean that Tamiflu could be useful for treatment of bird flu even if there is a high prevalence of Tamiflu resistant avian influenza strains in the community. The drug would be useful by selecting out the weaker members of the viral family as the ones that got through the Tamiflu defense while screening out the stronger members.

In summary, the facts that support the establishment of personal Tamiflu stockpiles by individuals who desire to do so include:

- A) The increase in Tamiflu supplies now allow for limited personal stockpiles of the drug to be obtained without the risk that this will cause shortages of the drug for current use or interfere with the US Government's efforts to obtain a supply of the drug for the National Strategic Stockpile.
- B) The unavailability of an efficacious pandemic vaccine for a least 6 months after the beginning of the pandemic that will

be adequate for no more than 30% of the population during the course of the pandemic.

- C) The probability that during the pandemic, patients with influenza will have great difficulty gaining timely access to their physician sufficient to receive a prescription for Tamiflu to begin it within the 48-hour therapeutic window required.
- D) That Tamiflu resistance may not be as bad a problem as it is being made out to be and in fact may improve the chances of survival for some patients.
- E) Lack of confidence in the US, state, and local government's ability to distribute Tamiflu and vaccine in an efficient and timely manner during the chaos expected during a severe pandemic.
- F) Lastly, I think patients have a right to make this decision for themselves and that those who chose to obtain a personal supply of Tamiflu will use it responsibly.

I support the practice of prescribing drugs for the treatment of influenza for patients to stockpile in anticipation of a pandemic as long as practitioners writing these prescriptions fulfill their obligation to ensure that the patient has thorough instructions on how and when to employ these agents including Tamiflu.

For more information on pandemic influenza visit www.BirdFluManual.com.

¹ WHO Global Influenza Pandemic Preparedness Plan, July 2005

² A Potential Influenza Pandemic: Possible Macroeconomic Effects and Policy Issues. The Congress of the US, The Congressional Budget Office, December 8, 2005, US Government Printing Office.

³ Moscona, A., Tamiflu Resistance — Disabling Our Influenza Defenses N Engl J Med 2005: 353; 25

⁴ Pandemic Planning Update US DHHS 13Nov2006

⁵ Joint Position Statement of the Infectious Diseases Society of America and Society for Healthcare Epidemiology of America on Antiviral Stockpiling for Influenza Preparedness October 31, 2005; <http://www.idsociety.org>

⁶ Brett AS, et al., Run on Tamiflu NEJM 2005 353,25

⁷ Harvard Vanguard Medical Associates. Avian influenza (bird flu): frequently asked questions. (Accessed November 17, 2005, at <http://www.harvardvanguard.org/flu/avian.asp>)