Factsheet Tamiflu

Roche

Tamiflu in brief

- Tamiflu (oseltamivir) is an oral antiviral treatment (not a vaccine!) for influenza, and belongs to a class of medicines called neuraminidase inhibitors (NAI). These medicines prevent the influenza virus from spreading inside the body. Because of the way it works, it is designed to be active against all clinically relevant influenza virus strains. Tamiflu can be used both for prophylaxis and treatment of influenza.

- Tamiflu is proven to be effective in the treatment of influenza in adults and in children 1 year and older and for the prevention of influenza in adults and adolescents 13 years of age or older.

- Tamiflu is given orally, as a convenient capsule (75 mg), enabling it to reach all key sites in the body where the virus multiplies. The dose for the adult treatment of influenza is a 75 mg capsule, taken twice daily for five days. One pack of Tamiflu contains a full treatment course of 10 capsules. Treatment must commence within 48 hours of the onset of symptoms for full efficacy. For post exposure prophylaxis the dosage is one 75 mg capsule daily for up to 6 weeks.

- In 1996 Roche acquired from Gilead the worldwide rights to develop and market the drug

- Tamiflu was launched in North America (US and Canada) and Switzerland during 1999/2000. In all key European markets, it was launched by 2002/2003.

- Over 33 million patients have been treated with Tamiflu in about 80 countries worldwide including United States, Japan, Canada, Australia, the EU, Switzerland and Latin America.

- Tamiflu is patent protected until 2016.

Tamiflu efficacy data

- When administered according to its approved dosage (75 mg twice daily for 5 days), Tamiflu delivers a 38 per cent reduction in the severity of symptoms, a 67 per cent reduction in secondary complications such as bronchitis, pneumonia and sinusitis in otherwise healthy individuals and a 37 per cent reduction in the duration of influenza illness. These data were derived from seasonal outbreaks of influenza.

- As with any antiviral, a theoretical potential exists for an influenza virus to emerge with decreased sensitivity to a drug. Data collected from around 4000 treated with Tamiflu demonstrate an overall incidence of resistant virus of 0.4% in adults and 4% in children aged one to 12. The greatest use of Tamiflu today is in Japan. To illustrate this, there were an estimated 16 million influenza infections in Japan over the 2004/2005 influenza season.

Roche estimates that around 6 million of those individuals infected with the influenza virus received Tamiflu. Even with this high degree of usage, resistance appears very infrequent. This is supported by recent data compiled by the neuraminidase inhibitor susceptibility network (NISN) which surveyed resistance amongst virus isolated from 1180 influenza patients in Japan. Only four of the 1180 isolates showed reduced susceptibility to Tamiflu, highlighting the low frequency of resistance to Tamiflu.

Influenza pandemics

- Influenza, commonly called – the 'flu'- is a serious disease caused by influenza A and B viruses, which usually occurs seasonally in the autumn and winter months.

- According to the World Health Organisation (WHO) an influenza pandemic occurs when a new strain of influenza A virus appears, against which the human population has no immunity resulting in several, simultaneous epidemics worldwide with enormous numbers of deaths and illness. Influenza pandemics have occurred around 3 times in each century, when a new strain of the influenza virus caused simultaneous deaths worldwide.

For further information concerning pandemics and avian influenza, such as how it is different to seasonal influenza, and how it is transmitted, please visit the following WHO website:

http://www.who.int/csr/disease/avian_influenza/avian_faqs/en/index.html

Influenza pandemics and Tamiflu

- Tamiflu is designed to be active against all clinically relevant influenza virus strains therefore should be effective against any pandemic strain.

- Key international research groups have evaluated the therapies available to fight the H5N1 avian and human virus strain using animal models of influenza demonstrating that Tamiflu is effective against these avian strains. Roche recommends that approved dose and duration of treatment/chemoprophylaxis represents the minimum required for the management of pandemic influenza. In the absence of a vaccination against this virus strain, Tamiflu will prove an important management option.

- Roche is funding additional animal studies to further evaluate the antiviral activity of Tamiflu against the H5N1 avian influenza virus. In addition, Roche is in discussions with WHO on clinical studies which may provide additional clinical data.

Manufacturing of Tamiflu

- The manufacturing of Tamiflu is complex and involves 10 main steps, some of which have been identified as complicated (e.g. azide chemistry). Manufacturing takes approximately 6-8 months once all the raw materials have been sourced however, our assumption is that for any party starting from scratch it would take 2-3 years to produce Tamiflu.

- The starting material of the Tamiflu production process, shikimic acid, is extracted from the star anise. Further to extraction from anise Roche also developed a fermentation process in order to produce shikimic acid.

Roche's action to respond to heightened demand for Tamiflu

- In support of the global effort to fight a potential pandemic, Roche is prepared to discuss collaborations with additional third parties to increase the manufacturing of Tamiflu, provided such parties can realistically produce substantial amounts of medicine for emergency pandemic use, in accordance with appropriate quality specifications, safety and regulatory guidelines.

- Roche can confirm that it is currently receiving requests from many companies and governments to support Roche in scaling up production or requests to receive a sub-license to manufacture Tamiflu. Roche cannot however disclose the names of these companies or governments.

- Roche believes that it is not the patent that is the concern but the production capacities. Roche is working with a collaborative production network to expand those and is open to negotiate with any partner about granting a license under these patents at equitable conditions.

- Roche initially doubled production at its own risk before any governmental pandemic orders were received and we will have increased production by 8 – 10 fold by mid 2006. To rapidly expand production capacity for Tamiflu, Roche is working in collaboration with an increasing number of partners. More than a dozen manufacturing facilities worldwide network for Tamiflu production, more than half of which are with third party manufacturers. The different raw materials and excipients needed for the manufacture of Tamiflu are provided by about 50 external suppliers today. In summary Roche is mobilising a substantial supply chain across the industry and continents to address the issue.

- Roche is aware that the heightened interest in avian influenza in the last few weeks has resulted in increased demand for Tamiflu, particularly by individuals and institutions. Roche's priority is to ensure Tamiflu will be available for seasonal use to patients and to fulfil government pandemic orders. It is important to note that there is no influenza currently circulating and the threat of the pandemic has not been realized. We are asking people to act responsibly so that Tamiflu is available to patients who need it once the influenza season starts.

Tamiflu pandemic orders

- Roche has agreed quantities and delivery schedules with around 40 countries to date for stockpiling of Tamiflu.

- Because of the high demand and long manufacturing lead times for Tamiflu Roche has made clear that it is highly unlikely to fulfill large Tamiflu orders at short notice. This is why Roche has been encouraging governments over the last three years to stockpile in advance.

- The API (Active pharmaceutical ingredient) is available at a significantly reduced price and Tamiflu capsules purchased by governments for pandemic use are at a significant discount compared to the seasonal price.

Tamiflu donations for rapid deployment

- The co-ordination of pandemic plans for third world countries is the responsibility of the WHO. Roche is working with the WHO to develop a central stockpile of Tamiflu for distribution at the discretion of the WHO to countries in need, and initially donated 125,000 packs of Tamiflu to the stockpile last year. Furthermore, Roche recently donated another 3 million treatment courses of Tamiflu to the WHO for rapid deployment at the epicentre of the pandemic. The WHO will decide who receives the antiviral when a pandemic occurs. 3 million treatment courses is the quantity indicated by modelling (Science, Nature) that will reduce morbidity and mortality and help delay its spread in an affected nation. This stockpile is not a substitute for national preparedness and stockpiling by individual markets.

- In October 2005 Roche donated 5000 packs to Turkey and 2400 packs to Romania following the emergence of the H5N1 avian influenza virus in birds in these countries. These donations were made to protect highly exposed emergency workers collecting birds in farms close to location of the outbreak.

Counterfeit Tamiflu

- Tamiflu is a prescription medicine and as with any prescription medicine, Roche does not advocate the purchase of Tamiflu via the internet. Patients should always gain a diagnosis from a healthcare professional before buying Tamiflu and ensure they obtain it from a reliable source.

Roche Photolibrary for Media

Roche Group
27 October 2005