**Submission to the**
**Medicines Classification Committee**
**for:**

# oseltamivir

**(Tamiflu® powder filled capsules, 75mg)**

**Review of the exemption to allow Pharmacy Prescribing of oseltamivir for treatment of influenza in adults and adolescents during the influenza season in New Zealand.**

**January 2008**

**Sponsor:** **Roche Products (New Zealand) Limited**

# Executive Summary

## Introduction

In January 2005 Roche Products (New Zealand) Limited applied to the Medicines Classification Committee (MCC) to reclassify Tamiflu from a Prescription Only Medicine to a Pharmacist Only Medicine. In August 2006 the MCC determined that oseltamivir would remain a prescription only medicine but be exempt from this status to allow sale by a registered pharmacist during the influenza season. During the 2007 influenza season the exemption came into effect.

With the benefit of the seasonal experience in 2007 Roche Products (New Zealand) Limited would now like to provide further information to the MCC to consider a review of the current conditions of the exemption.

## Part A

The International Birth Date for Oseltamivir was the 21st of September 1999 in Switzerland and has subsequently been approved in over 100 countries world-wide.

Tamiflu is a well tolerated medicine with a favourable risk/benefit profile. As a prescription medicine in New Zealand Tamiflu is indicated for the treatment and prevention of infection by influenza A and B for people aged 1 year and older. In New Zealand exemption status for Tamiflu allows a registered pharmacist to supply the medicine to adults and adolescents without a prescription for the treatment of influenza between the months of May and September.

The mechanism of supply under the seasonal exemption is unique to New Zealand. The only country with a similar mechanism of supply is the United Kingdom (UK). In the UK oseltamivir is available via the NHS Patient Group Directions (PGD). A PGD allows an accredited pharmacist to supply Tamiflu to "at-risk" individuals during influenza outbreaks.

## Part B

### Classification Issue

At the 34th meeting of the MCC, June 2006, the committee made the recommendation that pharmacists should be able to sell oseltamivir between the months of May and September for the treatment of influenza. The decision was made acknowledging the management of seasonal influenza as an important public health initiative. Pharmacy access to oseltamivir ensures that a patient can have rapid access to medication. The granting of the exemption was a significant decision and New Zealand is the only country in the western world to put such a mechanism in place. It is therefore important to review the exemption to ensure it remains an appropriate and effective mechanism for management of seasonal influenza. On the basis of experienced gained during the 2007 influenza season Roche Products (New Zealand) Ltd would like the MCC to review the following restrictions to pharmacy dispensing of oseltamivir:

- The requirement for a face to face consultation; and
- The restrictions to sale between May and September.

Given the unique situation relating to the exemption for dispensing Tamiflu in New Zealand, a team of senior pharmacists from Pharma Projects Ltd and Auckland University led a study to review the acceptability, benefits and difficulties of the unique classification system for pharmacists and whether the system led to inappropriate use of Tamiflu. Roche Products (New Zealand) Ltd supplied funding to conduct the research.

Overall the mechanism of supply was viewed positively by most pharmacists. The specific restrictions that led to most frustration were the need for a face to face consultation and the restriction to sale between May and September. Most pharmacists interviewed expressed a desire to remove these restrictions to dispensing.

The face to face presentation poses the largest problem for pharmacists. The symptoms of influenza are often so debilitating they prevent the sufferer from presenting for treatment. A face to face consultation is particularly disadvantageous to people in rural communities. In addition the requirement to present to the pharmacist is inconsistent with the information provided by the Ministry of Health to those who have influenza. The key messages relating to seasonal influenza instruct a patient to "stay at home if you are unwell to prevent spreading the virus". Similarly, in the pandemic context the messages relating to influenza include social distancing and the prevention of spread. It is important that the public health messages are consistent.

Pharmacy protocols can easily be adapted to ensure that the same case definition and reference to surveillance information that applies to a face to face consultation can be applied to the carer that presents on behalf of a patient. Most carers presenting on behalf of a patient would describe the most predictive symptoms which include fever, fatigue and cough .

The original restriction also occurred at a time when the social environment relating to the supply of Tamiflu was quite different. Fears about a pending pandemic were at very high levels and demand for Tamiflu was also very high. Clear Government communication about pandemic preparedness, government stockpiling and changes to manufacturing capacity to ensure both seasonal and pandemic supply can be satisfied, have all served to alleviate fears and the need to obtain a personal stockpile. As indicated in the structured interviews conducted by the research team there was very little evidence of pressure to supply from consumers wanting to stockpile Tamiflu for pandemic purposes. In 2007 the volume of sales in New Zealand also reflected the fact that New Zealand experienced a very mild influenza season and inappropriate sales did not occur.

The review also highlighted the seasonal restriction as somewhat of a concern for pharmacists. Whilst the vast bulk of patients would undoubtedly present between May and October, exceptions do occur. In addition travellers arriving from the Northern hemisphere may also present with influenza. For patients that present to a general practitioner outside of the influenza season May to September, the doctor will still apply the same criteria to diagnose influenza as the pharmacist.

Given that there are few concerns about the safety of the product it is unlikely that removal of the above restrictions will lead to inappropriate use. The study team evaluating the first season of oseltamivir supply through pharmacy came to the following conclusions:

- No serious safety concerns were observed with the mechanism of supply;
- Barriers to access still exist (namely the face to face prescribing requirement and the seasonal restriction) preventing full realisation of the public health benefits of access to the medication through pharmacy;
- A further relaxing to the conditions of the exemption for supply would not present a safety concern to the public

**2. Benefits of Tamiflu as a Pharmacist Only Medicine**

As detailed in the original application, pharmacy supply of Tamiflu provides a number of important public health benefits including a reduction in morbidity and viral infection in the community, a reduction in antibiotic use for influenza related complications, a reduction in the burden to primary care during outbreaks and a reduction in mortality, particularly from secondary complications.

New data continues to demonstrate the effectiveness of using Tamiflu for appropriate management of seasonal influenza. Retrospective analyses using health insurance claims data in the US have demonstrated that in adults and adolescents, treatment with oseltamivir for influenza reduced the incidence of secondary complications and hospitalisation (Blumentals and Schulman, 2007) and for diabetic patients the incidence of influenza associated respiratory illness and hospital admission were both reduced (Orzeck et al., 2007). A recent prospective cohort study was conducted to investigate the impact of treatment with Tamiflu on outcomes for patients hospitalised due to influenza infection. Treatment with Tamiflu for influenza infection was associated with a significant reduction in mortality (McGeer et al, 2007).

There is an additional benefit in removing the face to face consult and seasonal restriction which relates to the ease of availability of Tamiflu in the event of an influenza pandemic. Pharmacies could play a vital role in ensuring fast access to carers both in rural and urban areas who have correctly followed Ministry of Health advice for social distancing and the prevention of spread. Easing of restrictions surrounding conditions of sale will indirectly provide an important access channel should the country be faced with a pandemic scenario. Finally, the best way to prepare for a pandemic is in fact to use antiviral

medication in the inter-pandemic period. It will ensure that health care professionals and patients alike know how to use them and have confidence in the fact there is a class of medicine that can protect against infection.

**3. Suitability of Tamiflu as a Pharmacist only Medicine**

**3.1 Resistance**

The neuraminidase inhibitors are key tools for the management of seasonal influenza and have a critical role as part of pandemic preparedness. One of the concerns during the original review by the MCC was the potential for resistance to occur in the community if Tamiflu was more widely available. A number of mechanisms have been put in place globally to monitor resistance to the neuraminidase inhibitors, including the Neuraminidase Inhibitor Susceptibility Network (NISN), the European Surveillance Network for Vigilance against Viral Resistance/ European Influenza Surveillance Scheme (VIRGIL/EISS), monitoring by the CDC in the US, monitoring by a number of WHO influenza regional laboratories and other local laboratories that collaborate with the WHO reference laboratories like the Environmental Science and Research (ESR) unit in New Zealand.

Recent surveillance data has indicated that isolates tested of the influenza A H1N1 virus currently circulating in Europe carries a mutation which confers resistance to Tamiflu. It would seem that the mutation has not been induced by oseltamivir use. At present the W H O, the European Centre for Disease Control and the CDC in the US have not changed the recommendations for the use of oseltamivir in seasonal and avian influenza.

In New Zealand influenza surveillance data is collected by the Institute for Environmental Science and Research (ESR). Given the unique situation relating to supply and in collaboration with the WHO Collaborating Centre for Reference and Research in Influenza in Melbourne, the ESR have put in place a mechanism to monitor the prevalence of Tamiflu resistance in New Zealand. Viral isolates from the New Zealand population were collected during the 2006 and 2007 influenza season. No significant anti-viral resistance to Tamiflu was detected in New Zealand.

**3.2 Safety of Tamiflu**

Tamiflu continues to satisfy the requirements for an appropriate Pharmacist Only Medicine. Tamiflu has low abuse potential, low potential for harm from inappropriate use, a low incidence of severe adverse events or side effects, minimal known drug-drug interactions and a wide therapeutic index.

Recently media focus has been directed toward patients who take Tamiflu and experience neuropsychitaric events. As reviewed by the FDA Pediatric Advisory Committee in November 2007, a growing body of data shows no evidence of a causal relationship between Tamiflu and the reported events. The data show that these neuropsychiatric adverse events also occurred in influenza

patients who were not taking Tamiflu. The Committee "expressed an increasing level of comfort in the evidence that NP events may be more likely a manifestation of influenza than of drug or the interaction of drug and disease, although uncertainty still exists".

**4. Conclusion**

Pharmacy supply of Tamiflu to consumers for treatment of influenza is an important public health initiative unique to New Zealand. It is important that the conditions relating to the supply mechanism are reviewed to fully realise the potential public health benefit. On the basis of an independent review of the 2007 influenza season in New Zealand, Roche Products (New Zealand) Ltd is requesting the restrictions around supply are relaxed, namely the requirement for a face to face consultation and the restriction to prescribing between May and September only. It is unlikely the relaxation to the conditions of the exemption pose any additional safety concerns to the public. The amendment to the exemption will in fact ensure patients are able to access a safe and effective treatment option for influenza infection.