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Executive Summary

This application seeks approval for the reclassification of oseltamivir (Tamiflu®) 75mg powder filled capsules from Prescription Only Medicine to Pharmacist Only Medicine for the treatment and prophylaxis of influenza in adults and adolescents.

Tamiflu efficacy against acute influenza is most effective when administered within 48 hours of symptom onset, with earlier treatment likely to lead to better outcomes.[1] The requirement of a doctor's prescription makes it difficult for potential influenza sufferers to access Tamiflu in time to commence treatment, particularly given that during the influenza season demand for a GP consultation also increases.[2] Tamiflu has an excellent safety profile that is consistent and stable with few adverse characteristics making it appropriate for use as a Pharmacist Only medicine. Improved access to Tamiflu will complement the vaccination program in an inter-pandemic situation and provide healthcare workers and patients experience with the product in the event of an influenza pandemic.

Roche has consistently maintained that requiring a visit to a doctor to obtain a prescription is a barrier to access for a medicine required to be taken within 48 hours of symptom onset. Indeed, in 2007 the Medicines Classification Committee (MCC) granted an exemption which allowed pharmacist to prescribe and sell Tamiflu for the treatment of influenza during the influenza season (May to September). Since 2007, minor amendments have been made to the exemption to widen access as many of the initial concerns relating to pharmacy supply of Tamiflu have been addressed as both pharmacists and the community have gained experience with the product.[3] The classification exemption period has been widened to include the months between April and November. In addition, some criteria have been eased whereby a patient no longer has to present in person to the pharmacy in order to receive a treatment course of Tamiflu. Pharmacists have been educated and provided with protocols to assess the suitability of Tamiflu for a consumer. The reference to allowing access only to New Zealand residents has also been addressed by the MCC; currently, a person who does not reside in New Zealand is also eligible to obtain Tamiflu when in New Zealand. This has provided simpler access for Tamiflu to the wider patient community. Given the experience over some 5.5 years and the important role that the pharmacist has been able to play in the management of influenza, Roche now considers enough evidence exists to support the full reclassification of Tamiflu to a Pharmacist Medicine for treatment and prophylaxis of influenza.

Part A

1. International Non-proprietary Name of the medicine (or British Approved name or US Adopted Name)

Oseltamivir, as oseltamivir phosphate

2. Proprietary Name

Tamiflu

3. Name of Company requesting Reclassification

Roche Products (New Zealand) Limited
8 Henderson Place
Onehunga
Auckland 1061

Phone: (09) 635 1557
Fax: (09) 635 1522

4. Dose Form and Strength for which a change is sort

75mg powder filled capsules

5. Pack Size and other Qualifications

Blister Pack: 10 capsules packaged into a carton with an accompanying patient information leaflet in CMI format.

6. Indications for which change is sought

The proposed Pharmacist Only medicine classification is intended for the following indication:

- For treatment and prophylaxis of influenza in adults and adolescents aged 13 years and older

7. Present Classification of Medicine

Prescription Only Medicine

8. Classification Sought

Pharmacist Only Medicine

9. Classification in other Countries (especially Australia, UK, USA and Canada)

Tamiflu is a Prescription Only medicine in all markets.

In the United Kingdom, the Pharmacist Only category does not exist, therefore Tamiflu can be supplied via the NHS Patient Group directions (PGD). NHS PGD allow accredited pharmacists and registered nurses to supply Tamiflu to "at-risk" individuals. PGD are designed to relieve the pressure on primary care services in the event of a pandemic/epidemic. PGD's are used in situations where there is "*an advantage for patient care without compromising patient safety, and where it is consistent with appropriate professional relationships and accountability*". The use of PGDs for the supply of Tamiflu in the UK has been limited.

Two applications in Australia to the NDPSC to reclassify Tamiflu to a Pharmacist Only medicine have been rejected. The committee highlighted concerns relating to resistance, potential for misdiagnosis, reduced uptake of vaccination, as well as the possible impact upon pandemic preparedness.

10. Extent of Usage in New Zealand and elsewhere (e.g. Sales Volumes) and dates of original consent to distribute

New Zealand

Tamiflu was granted consent in New Zealand on 27th January 2000 for the treatment of influenza in adults and adolescents. Roche Products (NZ) Limited launched the product to the New Zealand market in March 2000. On 5th February 2004, Tamiflu was approved for the prevention of influenza in adults and adolescents.

Sales of Tamiflu have remained fairly consistent with approximately 1200 packs of Tamiflu being sold in New Zealand during non-pandemic years.

World-wide

Since it was first marketed in Switzerland in September 1999, Tamiflu has been approved in over 100 countries world-wide with an estimated total cumulative patient exposure of more than 90 million patients, demonstrating significant exposure.

11. Labelling or draft labelling for the proposed new presentation

The following indication for Tamiflu is currently registered:

- *Tamiflu is indicated for the treatment of influenza in adults and children ≥1 year of age.*
- *Tamiflu is indicated for the prophylaxis of influenza in adults and children ≥ 1 year of age.*
- *Vaccination is the preferred method of routine prophylaxis against infection with influenza virus.*

The proposed indication for Tamiflu as a Pharmacist Only medicine will be as follows:

- *Tamiflu is indicated for the treatment of influenza in adults and adolescents ≥13 years of age.*
- *Tamiflu is indicated for the prophylaxis of influenza in adults and adolescents ≥13 years of age.*
- *Vaccination is the preferred method of routine prophylaxis against infection with influenza virus.*

Roche considers it appropriate that management of influenza in the paediatric population continues to be carried out by a physician, therefore Tamiflu as a Pharmacist Only medicine will only be available to those aged 13 years and older.

Following reclassification, the Tamiflu carton, data sheet and consumer medicine information (CMI) will be updated.

Carton –

- The classification statement will be changed from "Prescription Medicine Only" to "Pharmacist Medicine Only"
- The purpose of treatment with Tamiflu, as well as directions for use for both treatment and prophylaxis will be added to the carton
- The statement "If symptoms persist see your doctor" will be added to the carton

Data Sheet and CMI –

- The package insert will continue to be a CMI. Currently the oral suspension and the 30 mg, 45 mg (not marketed) and 75 mg capsules have a common Data Sheet and CMI. Following reclassification of Tamiflu, the 75 mg capsule presentation will have a separate Data Sheet and CMI to the oral suspension, which will remain a prescription medicine. If the 30 mg and 45 mg capsules were to be marketed at some point in the future, these would also have a prescription only Data Sheet and CMI.

Roche Products (New Zealand) Limited assures the MCC that the New Zealand Pharmacist Only Medicine labelling will be submitted to Medsafe shortly following approval of the reclassification.

12. Proposed warning statements if applicable

Tamiflu is a well-tolerated medicine that currently requires few warnings in order to be safely used.

The following warning statements are proposed for the labelling of the Tamiflu Pharmacist Only Medicine pack:

Please consult your doctor for treatment in children.

Check with your doctor or pharmacist before using Tamiflu if you:

*** are pregnant or may become pregnant**
*** are breastfeeding or**
*** suffer from kidney problems**

These warnings will be included in the Data Sheet.

13. Other products containing the same active ingredient(s) and which would be affected by the proposed change

A generic version of oseltamivir was registered in New Zealand in December 2011, however Roche Products (New Zealand) Limited hold exclusive rights to market oseltamivir in New Zealand until June 2015. Therefore this application for classification change will not initially affect any other product in the New Zealand market.

Part B

1. Statement of the benefits to both the consumer and to the public expected from the proposed change

1a) The proposal

Tamiflu (oseltamivir) has been marketed in New Zealand for over 12 years. During that time it has been well established that Tamiflu has low abuse potential, low potential for harm from inappropriate use, low incidence of severe adverse events or side effects, minimal known drug-drug interactions and a wide therapeutic index, all criteria which make the medicine a suitable candidate for a pharmacist only medicine. For the current submission we seek to reclassify Tamiflu 75 mg capsules to a pharmacist only medicine; for the treatment of a consumer who is in New Zealand, is 13 years of age or more, and currently has the symptoms of influenza or is at risk of contracting influenza.

1b) General Background.

Roche has previously made the case to the Medicines Classification Committee (MCC) that requiring a visit to a doctor to obtain a prescription is a barrier to access for a medicine required to be taken within 48 hours of symptom onset. In New Zealand and since 2007, Tamiflu has remained as a prescription medicine with an exemption to allow pharmacists to supply Tamiflu without prescription between the months of May and September for the treatment of influenza but not for prophylaxis. Since 2007, minor amendments have been made to the exemption to widen access as many of the concerns relating to pharmacy supply of Tamiflu have been addressed.[3] Currently, the exemption period has been widened to between April and November and a patient no longer has to present in person to the pharmacy to receive a treatment course. The reference to allowing access only to New Zealand residents has also been discussed by the MCC to allow supply to a person in New Zealand who may not be a resident. Given the experience over the last 5.5 years and the important role that the pharmacist has been able to play in the management of influenza, Roche now considers enough evidence exists to support the full reclassification of Tamiflu to a pharmacist only medicine for treatment and prophylaxis of influenza.

The reclassification also seeks to maintain the restriction to patients 13 years and over. The management of influenza in the paediatric population is still best carried out by a physician. This also allows for the reclassification to be separated according to medicine presentation. The 75 mg capsules would be a pharmacist only medicine and the suspension formulation, more suitable for use in children, would be a

prescription only medicine. Although not currently marketed, the 30mg and 45mg capsules will also remain prescription only.

1c) Benefits to the consumer and the public expected from the proposed change

Previous applications and comment have established the benefits of having Tamiflu available as a pharmacist only medicine for the treatment of influenza during the southern hemisphere influenza season. The "hands-on" experience over the past 5.5 years also supports the decision by the MCC to effectively trial pharmacy supply under the conditions of the exemption. Expanding the access to a pharmacist only medicine will also allow for the prophylaxis of influenza and for supply all year round. This application will therefore focus on the benefits of the wider access full reclassification will allow.

1d) Prophylaxis of influenza

The benefit of allowing supply for the prophylaxis on influenza should focus on the timely access of the medicine for a person at risk of exposure to an infected person, that is, post exposure prophylaxis (PEP).

The benefit of Tamiflu use in the PEP setting is well established[4,5] (also see current Data Sheet, Appendix 1). The protective efficacy of Tamiflu against influenza may be as high as 90%.[4,6]

The potential for resistance to be an issue in the PEP setting is also reduced. As per the Data Sheet, "in clinical studies conducted in post-exposure (7 days), post-exposure within household groups (10 days) and seasonal (42 days) prophylaxis of influenza in immunocompetent persons, there was no evidence for emergence of drug resistance associated with the use of Tamiflu" (see page 16 of 21). The most recent Product Safety Update Report (PSUR)[7] for Tamiflu also highlights that prior to the 2009-10 pandemic there had been no reported cases of resistance selection from prophylaxis or PEP use of Tamiflu in seasonal influenza virus infections. Post 2009-10 pandemic, resistance as a consequence of PEP use remains a small proportion of what is overall, a low incidence of resistance during treatment with Tamiflu in seasonal influenza and highly pathogenic virus infection settings. During 2010 the WHO reported that 6% of resistance cases reported were observed when analyzing samples from otherwise healthy patients receiving Tamiflu as prophylaxis.[6]

The MCC has highlighted the potential for Tamiflu to be seen as a replacement for vaccination if reclassification for prophylaxis was successful. Roche agrees that vaccination is the gold standard for prevention of influenza and this is reiterated in the approved indication in the New Zealand Data Sheet for Tamiflu:

Tamiflu is indicated for the treatment of influenza in adults and children ≥1 year of age.

Tamiflu is indicated for the prophylaxis of influenza in adults and children ≥ 1 years of age.

Vaccination is the preferred method of routine prophylaxis against infection with influenza virus.

Distribution and claims data since 2007 suggests that uptake of the influenza vaccination has increased despite Tamiflu being readily available for treatment of influenza[3,8]. In addition cost would be prohibitive if a consumer were to take Tamiflu for an extended period of time to prevent influenza infection relative to routine prophylaxis through vaccination. Roche will also ensure that educational material and pharmacist treatment algorithms will emphasize the message that Tamiflu is not a replacement for routine influenza vaccination (see section 2). This is also noted on the Tamiflu website, which states that "Tamiflu is not a substitute for the influenza vaccine (the vaccine acts to prevent certain strains of influenza). For further information on the influenza vaccine please ask your health professional or visit www.influenza.org.nz".

Roche does not see a widening of the access to Tamiflu to facilitate personal stockpiling or for travel medicine. In the context of personal stockpiling we still strongly advocate that medicine should not be taken without the advice of a healthcare professional. Access to Tamiflu for travel medicine does not require "timely access" and reclassification does not prevent a consumer from seeking the advice of a doctor for travel medicine purposes.

As highlighted in the minutes from the 47th meeting of the MCC, "prevention advice was considered more appropriate than treatment advice and a pharmacist would be well placed to give such advice". Roche supports this position and agrees that the discussion around PEP is relatively straight forward. If the pharmacist has made the decision that a person has influenza and would benefit from antiviral treatment, it is a natural extension to offer a caregiver likely to be exposed to the virus a PEP course. It would be extremely unlikely that a caregiver would seek a course of Tamiflu for PEP via the prescription route after obtaining a treatment course for an infected person from a pharmacy. As mentioned above and detailed in section 2, educational material and the treatment algorithm will provide direct guidance with respect to PEP use.

1e) Supply all year around.

Influenza is the most common travel related infection preventable by a universal vaccine, and particularly in the tropics for example, influenza occurs throughout the year.[9,10] Although we anticipate frequency to be low, both New Zealand nationals

returning from overseas and visitors to New Zealand could benefit from being able to access Tamiflu in the community setting and outside the typical Southern Hemisphere influenza season.

2. Ease of self-diagnosis or diagnosis by a pharmacist for the condition indicated

Roche Products (New Zealand) Limited produces and makes available Tamiflu promotional material for both healthcare professionals (namely pharmacists) and consumers (patients). Promotional material available includes a prescribing protocol for pharmacists, a patient information leaflet distributed through pharmacies, and a consumer website containing information about influenza and Tamiflu.

The pharmacist protocol details the symptoms of influenza versus the common cold. The protocol contains a flowchart that aids the pharmacist in the diagnosis of influenza. It allows the pharmacist to ascertain whether Tamiflu treatment is suitable for the consumer (see Appendix 2). Following a positive recommendation by the MCC committee for reclassification of Tamiflu, the Tamiflu pharmacist protocol will be updated to include information about the use of Tamiflu for post exposure prophylaxis. Updated information will include vaccination as the preferred method of routine prophylaxis against infection with influenza virus, and emphasize that prophylaxis with Tamiflu is only appropriate where the consumer has had close contact (for example a caregiver) with a patient with influenza. The protocol also describes situations where the pharmacist should advise at-risk patient groups or patients with other symptoms when it is more appropriate to see their doctor. The pharmacist will be in the position to recommend alternative symptomatic relief should the consumer have cold symptoms and not symptoms of influenza. The current patient information leaflet details vaccination as being the preferred method of routine prophylaxis against influenza, and following reclassification this leaflet would be updated to include a statement regarding the appropriateness of post-exposure prophylaxis.

Consumer information is also available (www.tamiflu.co.nz) detailing the difference between symptoms of influenza versus the common cold, and includes a statement that the use of Tamiflu should not affect a consumers decision to have an annual influenza vaccination.

3. Relevant comparative data for like compounds

The influenza anti-virals fall into two classes – the M2 inhibitors or the neuraminidase inhibitors. The two classes are distinguished by the mechanism by which they inhibit viral replication.

The M2 inhibitors interfere with the un-coating of viral nucleoprotein by blocking the ion channel activity of the viral M2 protein in Type A influenza virus strains. In New Zealand, amantadine (trade name Symmetrel) is the only M2 inhibitor available. In other countries the M2 inhibitor rimantadine is also available. The use of amantadine is limited in that it is only effective against the Influenza A virus; also its safety profile limits its use, particularly in the elderly, in whom a number of CNS effects such as delirium, hallucinations and seizures have been reported following amantadine treatment. Resistance to amantadine also develops rapidly.

Zanamivir (Relenza) is the only other approved neurominidase inhibitor on the market in New Zealand. Viral neurominidase enzymes are glycoproteins which are found on virion surfaces that promote the release of the virus from the infected cell. Neuorominidase enzymes are vital for the replication of both Influenza A and B viruses. Neurominidase inhibitors prevent the release of the virus and promote viral aggregation reducing the virus available to infect other cells. The neurominidase inhibitors are well tolerated, have fewer adverse events that amantadine and are active against both Influenza A and B viruses. Due to the mechanism of action, neuraminidase inhibitors do not impair the natural immune response to influenza infection.

Both amantadine and zanamivir are prescription only.

4. Local data or special considerations relating to New Zealand

The exemption to allow pharmacy supply of Tamiflu in New Zealand in general can be considered a special consideration. New Zealand is the only country that has a dedicated mechanism to allow a pharmacist to supply Tamiflu for seasonal influenza. Over 5 years of experience has allowed the pharmacy profession and the community to become comfortable with the mechanism of supply in New Zealand.

During the review of several applications from Roche to reclassify Tamiflu in Australia and New Zealand, the committees responsible for evaluating the proposal have raised a number of issues. These issues have included:

- the potential for antiviral resistance to increase;
- the potential for consumers to stockpile medicine;
- a potential for inappropriate supply and,
- the potential for easier access to Tamiflu to impact upon the rates of vaccination for influenza.

Gauld et al.[3] sought to determine whether the concerns raised about the reclassification of Tamiflu had been realized over the five year period from January 2007 to September 2011 using a structured interview of pharmacists matched to printed reports of Tamiflu supply and records of resistance data for New Zealand during the same period. Gauld et al.[3] concluded that the pharmacy profession had

done a very good job of managing seasonal supply of Tamiflu, even during a global pandemic. A number of findings deserve further comment:

- Overall supplies for Tamiflu in the pharmacy setting were low during the non-pandemic years
- Oversupply did not occur and even during the 2009-10 pandemic pharmacy supply was far less than supply via a prescription.
- Patterns for the supply of Tamiflu from pharmacy were well matched to virus circulation
- The commercial imperative for a pharmacy to make money out of supplying a comparatively expensive item in the cold and flu space did not drive additional sales.
- There were no significant changes to the pattern of resistance other than those that also occurred at a global level (e.g. resistance to AH1N1 during the 2008 and 2009 seasons).

Kelly et al[11], (manuscript in prep) assessed the barriers to supply in the reclassification situation. During structured interviews the biggest pharmacy related barrier to supply was lack of confidence stemming from limited experience with the product and doubts regarding efficacy, again highlighting that clinical concerns took precedent over commercial returns. Comments also reflected the belief that Tamiflu was only really useful to treat severe influenza, like highly pathogenic avian influenza or in the pandemic situation. In reality the bulk of clinical trials have actually been conducted in the seasonal setting and in otherwise healthy individuals (see Data Sheet).These findings confirms that for this class of medicine to be best utilized in the seasonal setting, and even more so the pandemic setting, healthcare professionals need to have the experience of administering these medicines.[12]

Interestingly, some countries (e.g. Australia and Norway) see supply via pharmacy a useful distribution mechanism during a pandemic. NDPSC, the Australian Committee responsible for making scheduling decisions in 2008, highlighted (as documented in the Record of Reasons) that the need to reclassify Tamiflu was not necessary because legislative mechanisms allowed pharmacy supply of Tamiflu during a pandemic for all States and Territories. However, in light of the above mentioned discussion, it would appear that a lack of experience and confidence with the product may still be a barrier for pharmacy supply, should a pandemic occur.

5. Interactions with other Medicines

Information derived from pharmacology and pharmacokinetic studies of oseltamivir phosphate suggest that clinically significant interactions with other medicines are unlikely. All interactions are listed in the Data Sheet (see Appendix 1).

Oseltamivir phosphate is extensively converted to the active compound by esterases, located predominately in the liver. Interactions involving competition for esterases have not been extensively reported in the literature. Low protein binding of oseltamivir and the active metabolite do not suggest the probability of displacement interactions.

In vitro studies have demonstrated neither oseltamivir phosphate nor the active metabolite is a good substrate for P450 mixed-function oxidases or for glucuronyl transfers. There is no mechanistic basis for an interaction with oral contraceptives.

6. Contraindications

As per the Data Sheet (see Appendix 1), Tamiflu is contraindicated in patients with hypersensitivity to oseltamivir phosphate or any component of the product.

No further contraindications for the use of Tamiflu are proposed with the proposed change in classification.

7. Possible resistance

The risk of emergence of drug resistance during treatment of influenza virus infection with oseltamivir has been extensively examined in Roche sponsored clinical trials. The emergence of oseltamivir resistant virus during treatment has not been associated with clinically significant consequences in immunocompetent individuals to date, as the resistant virus appears only transiently and is subsequently cleared from the infected individual similar to wild-type virus. None of the subjects with detectable oseltamivir resistant virus selected during treatment had any clinical evidence of recrudescence of fever or an increase in symptom severity. This is consistent with complete resolution of the acute infection.[13]

Five sets of data have been evaluated for the emergence of resistance:

- Data from Roche sponsored clinical trials in seasonal influenza
- Data from published literature on treatment outcomes in patients following H1N1 and H5N1 infection
- Published information on naturally occurring resistance mutations
- Public information from WHO and published information for pandemic H1N1 resistance
- Data from Roche sponsored global resistance investigation study (NV20237)

There were no reported cases of resistance selection from prophylaxis or post-exposure prophylaxis use of oseltamivir in seasonal influenza virus infections prior to the 2009-2010 pandemic. Cases of resistant pandemic H1N1 virus have been observed in persons on post-exposure prophylaxis. The overall incidence of resistance during treatment of influenza virus infection is low in the

management of seasonal and highly pathogenic virus infection, including pandemic H1N1 2009. There has been no evidence of any substantial or sustained community level resistance in the recent pandemic H1N1. Resistance has been limited to small clusters and limited person to person accounts of transmission of resistance.
Influenza A/H1N1 virus variants naturally resistant to oseltamivir have appeared in the 2007/2008 season. The overall prevalence of resistant virus infections between 2007 and 2009 varied widely by season and geographic regions.
The clinical significance of oseltamivir resistance appears modest in most immunocompetent individuals, however in the severely immunocompromised individuals studies are ongoing to better define clinical implications for these immunocompromised individuals.

The Institute of Environmental Science and Research Limited (ESR) provides national influenza monitoring in New Zealand. Oseltamivir resistance is also included in the monitoring program. During 2006-2007, all influenza viruses tested were sensitive to oseltamivir.[8] In 2008, only six seasonal A(H1N1) viruses (0.8%) were detected, of which, only four were available for antiviral susceptibility testing and were all resistant to oseltamivir. Initial assays indicated that the four viruses showed highly reduced sensitivity to oseltamivir. Further genetic analysis confirmed that the four viruses had the H275Y mutation, conferring resistance to oseltamivir. None of the patients or their close contacts had received oseltamivir prior to sample collection. In 2009, 25 seasonal A(H1N1) virus were phenotypically tested and all were resistant to oseltamivir. However, all influenza A(H1N1)pdm09 isolates tested between 2009 and 2011 were sensitive to oseltamivir.During 2011, 261 influenza viruses were tested. All showed sensitivity to oseltamivir.
The monitoring undertaken by ESR shows that there has been no increase in resistance directly attributable to the Pharmacist Only exemption granted for Tamiflu since 2007.[3]

8. Adverse Events – nature, frequency etc

There is a low incidence of severe adverse events or side effects which are likely to require medical intervention. The safety profile for Tamiflu supports the use for both the treatment of influenza and for prophylactic therapy.

Tamiflu has an excellent safety profile with few side effects. In adult/adolescent treatment studies the most frequently reported adverse events were nausea, vomiting and headache. The majority of these AEs were reported on a single occasion, occurred on either the first or second treatment day, and resolved spontaneously within 1-2 days. In adult/adolescent prophylaxis studies, the most frequent AEs reported were nausea, vomiting, headaches and pain.

The Data Sheet provides additional information on adverse events that were observed in clinical trials. Post marketing experience has shown to be consistent with that reported in clinical trials.

9. Potential for abuse or misuse

Tamiflu has very low potential for abuse.

Reports of overdose with Tamiflu have been received from clinical trials and during post-marketing experience. In the majority of cases reporting overdose, no adverse events were reported. Any adverse events reported following overdose were similar in nature and distribution to those observed with therapeutic doses of Tamiflu.

Tamiflu specifically targets the influenza virus and selectively inhibits the influenza neurominidase enzymes (viral cell surface glycoproteins) preventing the release of newly formed virus cell particles to other cells. Tamiflu is absorbed from the GI tract after oral administration and is extensively converted to the active form (carboxylate) via hepatic esterases. Approximately 3% of the active metabolite is plasma protein bound. More than 90% of oseltamivir is converted to the active metabolite of which more than 99% of the active ingredient is eliminated by renal excretion. There is no preclinical evidence to show that the active metabolite affects the central nervous system (CNS) and any CNS effect due to oseltamivir itself occurs at extremely high plasma concentrations, approximately 4000 fold higher than the average peak human plasma levels. Periodic Safety reports have been issued since 1999, and there have been no reports of abuse, misuse, dependency or withdrawal in association with Tamiflu treatment.

Conclusion

Tamiflu is a safe and effective medicine for the prevention and treatment of influenza. Tamiflu efficacy against acute influenza is most effective when administered within 48 hours of symptom onset, with earlier treatment likely to lead to better outcomes. The requirement of a doctor's prescription makes it difficult for potential influenza sufferers to access Tamiflu in time to commence treatment. In 2007 the MCC granted an exemption which allowed pharmacist prescribing and selling of Tamiflu for the treatment of influenza during the flu season (May to September). Since 2007, minor amendments have been made to the exemption to widen access as many of the concerns relating to pharmacy supply of Tamiflu had been addressed. Pharmacists have had experience in prescribing Tamiflu for the treatment of influenza, and training education and protocols have been provided by Roche for this purpose. Roche now believe there is evidence to include year round pharmacist

prescribing for the treatment and prophylaxis of influenza. In addition, pharmacists are well placed to dispense Tamiflu for prophylaxis of influenza where a consumer may be at risk of contracting influenza. The ability of pharmacists to supply Tamiflu for both treatment and prophylaxis of influenza will reduce the burden on the healthcare system during a seasonal epidemic, as consumers will more readily be able to access Tamiflu within the 48 hour window.

The major concerns initially leveled at the reclassification of Tamiflu as a Pharmacist Only medicine have not been realized.[3] With some 12 years of marketed experience and over 5 years' experience in the community pharmacy setting with the seasonal exemption, Roche makes the case that Tamiflu has clearly demonstrated its suitability as a Pharmacist Only Medicine.