INFLUENZA ANTIVIRAL: OSELTAMIVIR

The Disease Control Division of the Malaysian Ministry of Health (MOH) recently held a discussion on the current state of influenza cases in the country. They have concluded that the antiviral Oseltamivir should be prescribed as soon as possible to the high-risk group to prevent the worsening of influenza-like illness (ILI) and to reduce hospitalization. The high-risk populations that should be thoroughly evaluated and considered to be prescribed with Oseltamivir include:

1. individuals with chronic respiratory diseases including asthma, chronic obstructive pulmonary disorder (COPD), and obstructive sleep apnea
2. pregnant women or 2 weeks post-natal women (Pregnancy category: C)
3. obese individuals with body mass index (BMI) of more than 40
4. individuals with comorbidities or chronic illnesses such as chronic heart diseases, diabetes mellitus, chronic kidney diseases and blood disorders
5. individuals with weak immune system including cancer, HIV/AIDS, undergoing chemotherapy/on long-term steroids or organ transplantation
6. geriatric patients of more than 65 years of age with chronic illnesses
7. paediatric patients of less than 6 months of age
8. paediatric patients with comorbidities/chronic illnesses

WHAT IS OSELTAMIVIR?

Oseltamivir belongs to the antiviral group and is prescribed for the treatment of acute, uncomplicated influenza type A (H1N1) or type B illnesses in adults and paediatric patients, including neonates greater than two weeks of age. It is an oral neuraminidase inhibitor (NAI) that acts by stopping the influenza virus from spreading and is active at sites in the body where the virus multiplies. Neonates under two weeks of age may also receive oseltamivir to treat influenza, but the safety and efficacy in this population have not been established.

Oseltamivir was invented and patented by Californian company Gilead Sciences in 1996. Swiss pharmaceutical company Hoffmann-La Roche (Roche) then purchased the rights to develop and market the drug worldwide under the trade name Tamiflu. In 1999 and 2000, Tamiflu was launched commercially in North America (the United States and Canada) and Switzerland, and by 2002–2003, it had reached all main European markets. Tamiflu is licensed for the treatment of influenza in adults and children, and the prevention of influenza in adults and children one year of age and older.

In the MOH drug formulary, Oseltamivir is indicated for the treatment of patients with suspected or confirmed influenza and severe disease (requiring hospitalization or evidence of lower respiratory tract infection) and for the treatment of patients with suspected or confirmed influenza with co-morbidity and associated with increased risk of influenza complications.

Treatment should be started as soon as possible after symptoms onset. The benefits are greatest when administered within 48 hours after symptoms onset. Therefore, prescribers should initiate treatment immediately without waiting for the lab test results. Later initiation of treatment may also be beneficial. However, decisions should be made on a case-by-case basis. If symptoms are improving beyond the first 48 hours, treatment may not be necessary. Clinical benefits of Oseltamivir treatment include reduced risk of pneumonia & reduced need for hospitalization.

The recommended dose in adults and adolescents ≥ 13 years of age and body weight > 40kg is 75mg twice daily for 5 days. The dosing recommendations for children are illustrated in the table below.

Age group	Body weight	Dosing recommendations
Children ≥ 12 months	15kg or less	30mg BD
	16 – 23kg	45mg BD
	24 – 40kg	60mg BD
	More than 40kg	75mg BD

Age group	Dosing recommendations
< 3 months	12mg BD
3 – 5 months	20mg BD
6 – 11 months	25mg BD

For children, if the commercially manufactured Oseltamivir oral suspension (6mg/ml) or pharmacy compounded suspension is not available, Oseltamivir suspension may be prepared at home by following the instructions given by pharmacists. When appropriate capsule strengths are available for the dose needed (e.g. 75mg), the dose is given by opening the capsule and mixing its contents with no more than one teaspoon of a suitable sweetened food product (e.g. chocolate syrup, cherry syrup, sugar water, dessert toppings). The mixture should be stirred and given entirely to the patient. The mixture must be swallowed immediately after its preparation (freshly prepared).

The preparation of the Oseltamivir suspension involves additional steps when doses smaller than 75mg are needed, usually in the cases of young children and infants. For example, when a dose of 30mg is needed, 1 capsule of 75mg is opened and the content (granules) is triturated to fine powder. Then, 5ml of vehicle (a suitable sweetened food product such as chocolate syrup, cherry syrup, sugar water, or dessert toppings) is added and the powder is triturated until a uniform suspension is achieved. The patients or caretakers will be given an instruction to take 2ml of the suspension each time, and a new preparation shall be freshly made whenever the next dose is needed. Any remaining solution must be discarded. It is recommended that this information be provided by affixing an ancillary label to the bottle or adding a statement to the pharmacy label instructions for the patient or caregiver to refer to.

Elevated liver enzymes have been reported in patients with influenza-like illness receiving Oseltamivir. Self-injury and delirium have also been reported in patients receiving Oseltamivir hence patients must be monitored for abnormal behaviour. No dose adjustment is required either for treatment or for prevention in patients with hepatic dysfunction. However, no studies have been carried out on paediatric patients with hepatic disorders. Dose adjustment is recommended for adults and adolescents (13 to 17 years of age) with moderate or severe renal impairment. Recommended doses are detailed in the table below.

Creatinine clearance	Recommended dose
>60 ml/min	75mg BD
>30 to ≤60 ml/min	30mg BD
>10 to ≤30 ml/min	30mg OD
≤10 ml/min	Not recommended
Hemodialysis patients	30mg after each HD session
Peritoneal dialysis patients	30mg single dose

Adverse drug reactions following Oseltamivir have been reported, such as nausea, vomiting, headache, abdominal pain, bronchitis, insomnia, and vertigo. There are also reports on rare cases of anaphylaxis and serious skin reactions including toxic epidermal necrolysis, Steven-Johnson syndrome, and erythema multiforme. The National Pharmaceutical Regulatory Agency (NPRA) has also issued safety alerts regarding the risk of thrombocytopenia on 29 Jan 2021 and the risk of hemorrhages on 8 July 2021 following treatment with Oseltamivir.

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