OMIFLU CAPSULE 75MG

DESCRIPTION:
A size '2' capsule, yellow / white colour, with 'DUO 861' marking. Capsule content is white to off white crystalline powder.

COMPOSITION:
Each capsule contains: Oseltamivir Phosphate equivalent to Oseltamivir 75mg.
Capsule Source: Bovine source.

PHARMACODYNAMICS:
Oseltamivir phosphate is a pro-drug of the active metabolite, oseltamivir carboxylate. The active metabolite is a selective inhibitor of influenza virus neuraminidase enzymes, which are glycoproteins found on the virion surface. Viral neuraminidase enzyme activity is essential for the release of recently formed virus particles from infected cells and the further spread of infectious virus in the body.

PHARMACOKINETICS:
Absorption: Oseltamivir is absorbed from the gastrointestinal tract after oral administration of oseltamivir phosphate and is converted predominantly by hepatic esterases to the active metabolite. At least 75% of an oral dose reaches the systemic circulation as the active metabolite. Exposure to the pro-drug is less than 5% relative to the active metabolite. Plasma concentrations of the active metabolite are unaffected by co-administration with food.
Distribution: The active metabolite reaches all key sites of influenza infection as shown by studies in the ferret, rat and rabbit. In these studies, anti-viral concentrations of the active metabolite were seen in the lung, bronchoalveolar lavage, nasal mucosa, middle ear and trachea, following oral administration of oseltamivir phosphate. The mean volume of distribution (Vss) of the active metabolite is approximately 23 L in humans. The binding of the active metabolite to human plasma protein is negligible (approximately 3%).
Metabolism: Oseltamivir is extensively converted to the active metabolite by esterases located predominantly in the liver. Neither oseltamivir nor the active metabolite is a substrate for, or an inhibitor of, the major cytochrome P450 isoforms. Thus interactions mediated by competition for these enzymes are unlikely.
Elimination: Absorbed oseltamivir is primarily (> 90%) eliminated by conversion to the active metabolite. Peak plasma concentrations of the active metabolite decline with a half-life of 6 hours to 10 hours in most subjects. The active metabolite is not further metabolised and is eliminated entirely (> 99%) by renal excretion. Renal clearance (18.8 L/hr) exceeds glomerular filtration rate (7.5 L/hr) indicating that tubular secretion (via the anionic pathway) in addition to glomerular filtration occurs.

INDICATIONS:
Treatment of Influenza: OMIFLU is indicated for the treatment of influenza in adults and adolescents 13 years of age or older. Treatment should commence as soon as possible but no later than forty-eight hours after the onset of the initial symptoms of infection.
Prevention of Influenza: OMIFLU is indicated for post exposure prevention in adults and adolescents 13 years of age or older following contact with a clinically diagnosed influenza case when influenza virus is circulating in the community.

RECOMMENDED DOSAGE:
OMIFLU may be taken with or without food. However, OMIFLU taken with food may enhance tolerability in some patients.
Standard dosage:
Treatment of influenza: Treatment should begin within the first or second day of onset of symptoms of influenza.
Adults and adolescents: The recommended oral dose of OMIFLU capsules in adults and adolescents 13 years of age or older is a 75mg capsule twice daily, for 5 days.
Prevention of Influenza:
Post exposure prevention in adults and adolescents 13 years or older: The recommended dose for prevention of influenza following close contact with infected individual is 75mg oseltamivir once daily for at least 7 days. Therapy should begin as soon as possible within two days of exposure to an infected individual.
Prevention during an influenza epidemic in the community: The recommended dose for prevention of influenza during a community outbreak is 75mg oseltamivir once daily for up to six weeks. The safety and efficacy of OMIFLU for the prevention of influenza in children 12 years or younger have not been established.
Special dosage instructions:
Patients with renal impairment: *Treatment of influenza:* No dose adjustment is necessary for patients with creatinine clearance above 30 ml/min. In patients with creatinine clearance of 10-30 ml/min, it is recommended that the dose be reduced to 75mg of OMIFLU once daily for 5 days. No dosing recommendation is available for patients undergoing routine hemodialysis and continuous peritoneal dialysis with end stage renal disease and for patients with creatinine clearance 10ml/min or less.
Prevention of influenza: Dose adjustment is recommended for adults with severe renal impairment as detailed in the table below:

Creatinine clearance	Recommended dose for prevention
>30 (ml/min)	75 mg once daily
>10 to 30 (ml/min)	75 mg every second day
<10 (ml/min)	Not recommended
Dialysis patients	Not recommended

Patients with hepatic impairment: No dose adjustment is required for patients with hepatic dysfunction.
Elderly: No dose adjustment is required for elderly patients.
Children: The safety and efficacy of OMIFLU for prophylaxis in paediatric patients younger than 13 years of age have not been established. The safety and efficacy of OMIFLU for treatment in paediatric patients younger than 1 year of age have not been established.

CONTRAINDICATIONS: Oseltamivir is contraindicated in patients with known hypersensitivity to any component of the product.

ROUTE OF ADMINISTRATION: Oral

WARNING & PRECAUTIONS:
There is no evidence for efficacy of Oseltamivir in any illness caused by agents other than influenza viruses types A and B. Dose adjustment is recommended for patients with creatinine clearance of 10–30 mL/min for the treatment of influenza and the prevention of influenza. No dosing recommendation is available for patients undergoing haemodialysis and continuous peritoneal dialysis with end stage renal disease and for patient with creatinine clearance of ≤ 10mL/min. Oseltamivir is a specific treatment for infections due to influenza A or B viruses. Use should be limited to patients who have characteristic symptoms of influenza when influenza A or B virus infections have been documented locally.

Data on the treatment of Influenza B are limited. Efficacy has not been established in patients who begin treatment after 40 hours of symptoms. There is no current evidence for the safety or efficacy of Oseltamivir in the treatment of influenza in persons with underlying respiratory or cardiac disease, or in persons with complications of an acute influenza episode such as viral or bacteria pneumonia. Such patient may require extensive supportive and adjunctive care. Antiviral therapy has not been shown to reduce the need for such care and monitoring. Safety and efficacy of repeated treatment courses have not been studied.

INTERACTION WITH OTHER MEDICATIONS:
Oseltamivir phosphate is rapidly converted to the active metabolite by esterases, located predominantly in the liver. Drug 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 drug displacement interactions.
In vitro studies demonstrated that neither oseltamivir phosphate nor the active metabolite is a good substrate for P450 mixed-function oxidases or for glucuronyl transferases. There is no mechanistic basis for an interaction with oral contraceptives.
Cimetidine, a non-specific inhibitor of cytochrome P450 isoforms and competitor for renal tubular secretion of basic or cationic drugs has no effect on plasma levels of Oseltamivir or its metabolite.
Clinically important drug interactions involving competition for renal tubular secretion are unlikely, due to the known safety margin for most of these substances, the elimination characteristics of the active metabolite (glomerular filtration and anionic tubular secretion) and the excretion capacity of these pathways. Co-adminstration of probenecid results in approximate two fold increase in exposure to the active metabolite due to a decrease in active tubular secretion in the kidney. However, due to the wide safety margin of the active metabolite, no dose adjustment are required when co-administering with probenecid.
Co-administration with amoxicillin does not alter plasma levels of either compound, indicating that competition for the anionic pathway is weak.
Co-administration with paracetamol does not alter plasma levels of oseltamivir, its active metabolite, or paracetamol.
No pharmacokinetic interactions between oseltamivir or its major metabolite have been observed when co-administering oseltamivir with paracetamol, acetyl-salicylic acid, cimetidine or with antacids (magnesium and aluminium hydroxides and calcium carbonates).

USE IN PREGNANCY & LACTATION:
Use in Pregnancy: At present, insufficient data are available in pregnant women taking the drug to enable an evaluation of the potential for Oseltamivir to cause fetal malformations or fetal toxicity. Oseltamivir should therefore be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Use in Lactation: OMIFLU should be used only if the potential benefit for the lactating mother justifies the potential risk for the nursing infant.

SIDE EFFECTS:
The most commonly reported adverse effects associated with Oseltamivir are nausea and vomiting, abdominal pain, bronchitis, insomnia, and vertigo. Diarrhoea, dizziness, headache, cough, and fatigue may occur, but many adverse effects may be difficult to distinguish from the symptoms of influenza. Other adverse effects occurring less commonly have included unstable angina, anaemia, pseudomembranous colitis, pneumonia, pyrexia, and peritonsillar abscess. There have been occasional reports of skin rash and, rarely, elevated liver enzymes and hepatitis.
Convulsion, depressed level of consciousness, abnormal behaviour, hallucinations and delirium have been reported during Oseltamivir administration, leading in rare cases to accidental injury. Patients especially children and adolescents should be closely monitored and their healthcare professional should be contacted immediately if patients show any signs of unusual behaviour.
Blood and lymphatic system disorders
Frequency 'Rare': Thrombocytopenia

SYMPTOMS AND TREATMENT OF OVERDOSE:
There is no experience with overdose. However, the anticipated manifestations of acute overdose would be nausea, with or without accompanying emesis. Single doses of up to 1000mg of Oseltamivir have been well tolerated apart from nausea and/or vomiting. Patients should discontinue the treatment in the event of overdose. No specific antidote is known.

STORAGE CONDITIONS: Store below 30°C. Protect from light. Keep out of reach of children. *Jauhkan daripada kanak-kanak.*

PACK SIZE: Blister of 1 x 10's.

SHELF LIFE: Please refer outer package.

PRODUCT REGISTRATION HOLDER & MANUFACTURER:
DUOPHARMA (M) SDN BHD
Lot 2599 Jalan Seruling 59 Kawasan 3,
Taman Klang Jaya, 41200 Klang, Selangor, MALAYSIA.