DOXOFYLLINE

MAXIVENT®

℞ 200 mg Tablet
400 mg Tablet
BRONCHODILATOR

FORMULATION
Each tablet contains:
Doxofylline ……..…..200 mg
Doxofylline ……..... 400 mg

PRODUCT DESCRIPTION
200mg - White to off white colored plain circular biconvex uncoated tablet.
400mg - White to off white colored, circular biconvex, uncoated tablet with breakline on one side and plain on other side.

PHARMACODYNAMICS
Doxofylline is a novel bronchodilator xanthine that differs from theophylline for the presence of a dioxalane group in position 7. Like theophylline, Doxofylline's mechanism of action is related to the inhibition of phosphodiesterase activities. However, differently from theophylline, Doxofylline appears to have decrease affinities towards adenosine A1 and A2 receptors, which may account for the better safety profile of the drug.

PHARMACOKINETICS
The half-life of Doxofylline is greater than six hours; so as to allow effective constant plasma levels with a t.i.d. dose regimen. Single dose pharmacokinetic studies in man after oral and intravenous administration defined distribution and absorption of the drug.
After i.v. administration of 100 mg to 5 healthy volunteers, distribution of Doxofylline in plasma followed a bi-compartmental model. During the distribution phase the plasma AUC was only a modest portion of the total AUC; plasma clearance was somewhat high, ranging from 444 mL/min to 806 mL/min; apparent volume of distribution was about 1 L/kg. The mean half-life after i.v. administration was about 65 min. (from 40 min to 96 min).
After oral administration (tablets), peak plasma levels were reached after one hour. Absolute bioavailability is about 62.6%; at pH 7.4 plasma proteins binding the compound is about 48%. Less than 4% of an orally administered dose is excreted unchanged in the urine.
Doxofylline is almost completely metabolized in the liver (90% of the total drug clearance).
Hydroxyethyltheophylline is the only detectable circulating metabolite of Doxofylline.
After repeated administrations Doxofylline reaches the steady state in about 4 days; the elimination half-life during long-term treatment is 8-10 hours: this allows a twice-daily dose regimen. No accumulation of the drug was noted after one week of treatment.

INDICATIONS
Doxofylline is indicated for the treatment of bronchial asthma, pulmonary disease with spastic bronchial component and Chronic Obstructive Pulmonary Disease (COPD).

CONTRAINDICATIONS
This product is contraindicated in individuals who have shown hypersensitivity to its components. It is also contraindicated in patients with acute myocardial infarction, hypotension and in lactating women.

ADVERSE DRUG REACTION
After xanthine administration, nausea, vomiting, epigastric pain, headache, cephalalgia, irritability, insomnia, tachycardia, extrasystole, tachypnea, and occasionally hyperglycemia and albuminuria, may occur. If a potential oral overdose is established, the patient may present with severe arrhythmias and seizure; these symptoms could be the first sign of intoxication. Adverse reactions may cause the withdrawal from treatment; a lower dose rechallenge may start only after the advice of physician.

WARNINGS AND PRECAUTIONS
Use with caution in patients with hypertension, heart disease, hypoxemia, hyperthyroidism, chrome right ventricular failure, congestive heart failure, liver disease, renal disease, in those with history of peptic ulcer, and in the elderly.
Frequently, patients with congestive heart failure have markedly prolonged drug plasma levels following discontinuation of the drug.
The half-life of xanthine derivatives is influenced by a number of known variables. It may be prolonged in

patients with liver disease, in patients with congestive heart failure, in those affected with chronic obstructive lung disease or concomitant infections, and in those patients taking certain other drugs (erythromycin, troleandomycin, lincomycin and other antibiotics of the same group, allopurinol, Cimetidine, propranolol, and anti-flu vaccine). In these cases, a lower dose of Doxofylline may be needed.
Phenytoin, other anticonvulsants and smoking may cause an increase in clearance with a short mean half-life: in these cases, higher doses of Doxofylline may be needed.
Laboratory monitoring of plasma concentration of Doxofylline is recommended in all the above situations.

PREGNANCY AND LACTATION
Animal reproduction studies indicate that Doxofylline does not cause fetal harm when administered to pregnant animals nor can affect reproduction capacity. However, since there is limited experience in humans during pregnancy, xanthines should be given to a pregnant woman only if clearly needed. Doxofylline is contraindicated in nursing mothers.

DOSAGE AND ADMINISTRATION
Tablet
Elderly Patients: 200 mg tablet two or three times daily.
Adults: 400 mg tablet two or three times daily.
Or as prescribed by the physician.

DRUG INTERACTIONS
Doxofylline tablets should not be administered together with other xanthine derivatives. Toxic synergism with ephedrine has been documented for xanthine. Like other xanthines, concomitant therapy with erythromycin, troleanodomycin, lincomycin, clindamycin, allopurinol, cimetidine, ranitidine, propranolol and anti-flu vaccine may decrease the hepatic clearance of xanthines causes an increase in blood levels. No evidence of a relationship between Doxofylline serum concentration and toxic events have been reported.

OVERDOSE AND TREATMENT
Although no major arrhythmias have been documented with Doxofylline tablets the occurrence of major cardiac rhythm disturbances cannot be excluded in case of overdosage of xanthine compounds. If a potential oral overdose is established the patient may present with seizures; these symptoms could be the first sign of intoxication. Adverse reactions may cause the withdrawal from treatment. A lower dose-re-challenge may start only after the advice of the physician.
There is no specific antidote. It is suggested that the management principles should be instituted according to a symptomatic relief of cardio circulatory shock. Doxofylline tablets does not cause any risk of tolerance or addiction.

CAUTION: Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

FOR SUSPECTED ADVERSE DRUG REACTION, REPORT TO THE FDA: www.fda.gov.ph
Seek medical attention immediately at the first sign of any adverse drug reaction.

STORE AT TEMPERATURES NOT EXCEEDING 30°C.

AVAILABILITY
Doxofylline (Maxivent®) 200mg Tablet X Alu PVC/PVDC blister pack of 10's, box of 30 tablets
Doxofylline (Maxivent®) 400mg Tablet X Alu PVC/PVDC blister pack of 10's, box of 30 tablets

Maxivent ® is a registered trademark of Ajanta Pharma Philippines, Inc.

REGISTRATION NUMBER
200mg: DR-XY47755
400mg: DRP-11750

DATE OF FIRST AUTHORIZATION
200mg: February 24, 2022
400mg: December 10, 2021

DATE OF REVISION OF PACKAGE INSERT:
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Manufactured by : **Ajanta Pharma Limited**
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