MICRO LABS LIMITED, BANGALORE, INDIA			
1	Product Name	Microphylline	Colours Used
2	Strength	400 mg	BLACK
3	Component	Leaflet	
4	Category	Expot - Philippines	
5	Dimension	120 (L) x 240 (H) mm	
6	Artwork Code	EXG-ML01I-1035/B	
7	Pharma Code	N/A	
8	Reason for Change	Size & New Regulation	

	Prepared by (DTP)	Checked by (PD)	Approved by			
			Head CQA	Head Production/ Packing (Site)	Head QC (Site)	Head QA (Site)
Sign	Kantharaju L.					
Date	14-06-2018					

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DOXOPHYLLINE

MICROPHYLLINE

400 mg Tablet

BRONCHODILATOR

PRODUCT DESCRIPTION:
White, flat, circular, bevel edged uncoated tablets with breakline on one surface

FORMULATION/COMPOSITION:
Each tablet contains
Doxophylline ..... 400 mg

PHARMACODYNAMICS/PHARMACOKINETICS:
Pharmacodynamics:
(7-(1, 3-dioxalan-2-ylmethyl)theophylline) is a methyl xanthine derivative characterized by the presence of a dioxalane group in position 7. It has potent bronchodilator activity equal or superior to theophylline.
Doxophylline activity is due to its ability to inhibit phosphodiesterase enzyme followed by an increase in cyclic-3'-5'-adenosine monophosphate (cAMP) resulting in smooth muscle relaxation. The decreased affinity of Doxophylline for adenosine A_1 and A_2 receptors has been suggested to account for its better safety profile compared to theophylline.

Pharmacokinetics:
After oral administration of Doxophylline 400 mg twice daily for 5 days, the peak serum Doxophylline concentration at steady-state was 5.78-20.76 mcg/mL
(mean ± SD 15.21±1.73 mcg/mL), with time to reach maximum concentration of 1.19±0.19 hrs.
The total clearance was 555.2±180.6 L/min and the mean elimination $t_{½}$ was 7.01±0.8 hrs.
The absolute bioavailability of Doxophylline was reported to be 63±25% after oral administration at a dose of 400 mg given in healthy subjects, with only 1 metabolite
(β-hydroxymethyltheophylline), which was devoid of any significant pharmacological activity, being detected in the serum and urine.

INDICATIONS:
Doxophylline is indicated for the treatment of chronic obstructive pulmonary disease(COPD), bronchial asthma and pulmonary disease with spastic bronchial component.

DOSAGE AND MODE / ROUTE OF ADMINISTRATION:
Elderly Patients: 1/2 tablet two or three times daily.
Adults: 1 tablet two or three times daily. Or as prescribed by a physician

CONTRAINDICATIONS &PRECAUTION(S), WARNING(S)
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.

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 Doxophylline may be needed. Phenytoin, other anticonvulsants and smoking may cause an increase in clearance with a shorter mean halflife: in these cases higher doses of Doxophylline may be needed. Use with caution in patients with hypoxemia, hyperthyroidism, liver disease, renal disease, in those with history of peptic ulcer and in elderly. Frequently, patients with congestive heart failures have markedly prolonged drug serum levels following discontinuation of the drug.

PREGNANCY AND LACTATION:
Animal reproduction studies indicate that Doxophylline 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. Doxophylline is contraindicated in nursing mothers.

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INTERACTIONS:
Doxophylline should not be administered together with other xanthine derivatives, including beverages and foods containing caffeine.
Toxic synergism with ephedrine has been documented for xanthines. Concomitant therapy with erythromycin, troleandomycin, Lincomycin, clindamycin, allopurinol, cimetidine, propranolol and anti-flu vaccine may decrease the hepatic clearance of xanthine's causing an increase in blood levels.

ADVERSE EFFECTS:
After xanthine administration, nausea, vomiting, epigastric pain, Cephalalgia, irritability, insomnia, tachycardia, extra systole, 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 rechallenged may start only after the advice of physician.

OVERDOSAGE AND TREATMENT:
Common clinical manifestations of xanthine over dosage include nausea, vomiting gastrointestinal bleeding, metabolic acidosis, hypokalemia, hypotension, cardiac arrhythmias and seizures, often ending in death.
Treatment of xanthine over dosage is symptomatic and supportive. It includes withdrawal of the drug. If seizures have not occurred following acute over dosage, the stomach should be emptied immediately by inducing emesis or by gastric lavage, followed by administration of activated charcoal and cathartic. If the patient is having seizures, an adequate airway should 1st be established and maintained. Seizures may be treated with intravenous diazepam, phenobarbital or in combination. There is no adequate evidence to support the use of dialysis in the treatment of Doxophylline overdose.

STORAGE CONDITION:
Store at temperatures not exceeding 30°C.

DOSAGE FORMS AND PACKAGING AVAILABLE:
Doxophylline Tablets 400 mg are Packed in Alu/PVC Blister Pack of 10's(Box of 30's)

INSTRUCTIONS AND SPECIAL PRECAUTIONS FOR HANDLING AND DISPOSAL (IF APPLICABLE):
Not Applicable

NAME AND ADDRESS OF MARKETING AUTHORIZATION HOLDER:
Marketing Authorization Holder
Brown & Burk Philippines Inc
U-501, 5/F., SEDCCO 1 Bldg., 120 Rada cor.,
Legaspi Sts., Legaspi Village, Makati City, Philippines

NAME AND ADDRESS OF MANUFACTURER:
MICRO LABS LIMITED
92, Sipcot Industrial Complex,
Hosur – 635 126, India.

CAUTION STATEMENT:
FOODS, DRUGS, DEVICES, AND COSMETICS ACT PROHIBITS DISPENSING WITHOUT PRESCRIPTION.

ADR REPORTING STATEMENT:
"FOR SUSPECTED ADVERSE DRUG REACTION, REPORT TO THE FDA: www.fda.gov.ph
Seek medical attention immediately at the first sign of Adverse Drug Reaction.

REGISTRATION NUMBER:
DRP-5703

DATE OF FIRST AUTHORIZATION:
3 Dec.2014

DATE OF REVISION OF PACKAGE INSERT:
Oct. 2016

EXG-ML01I-1035/B

Size: 120 x 240 mm