ROFLAST

Roflumilast 500 mcg

COMPOSITION

Each film coated tablet contains Roflumilast INN 500 mcg.

PHARMACOLOGICAL INFORMATION

Therapeutic class

Phosphodiesterase 4 (PDE4) Inhibitor

Mechanism of action

Roflumilast is a selective and long acting PDE4 inhibitor, a non-steroid, anti-inflammatory agent designed to target both the systemic and pulmonary inflammation associated with COPD. The mechanism of action is the inhibition of PDE4, a major cyclic adenosine monophosphate (cAMP) - metabolizing enzyme found in structural and inflammatory cells important to the pathogenesis of COPD. This mechanism of action and the selectivity also apply to roflumilast N-oxide, which is the major active metabolite of Roflumilast.

Pharmacodynamic effects

In COPD patients, 4 week treatment with Roflumilast 500 mcg oral once daily reduced sputum neutrophils and eosinophils by 31% and 42%, respectively. In a pharmacodynamic study in healthy volunteers, Roflumilast 500 mcg once daily reduced the number of total cells, neutrophils and eosinophils found in bronchoalveolar lavage fluid following segmental pulmonary lipopolysaccharide (LPS) challenge by 35%, 38% and 73%, respectively.

Pharmacokinetic properties

A	Approximately 80% absorbed
	t_{max} ~ 1 hr
D	V_d ~ 2.9 L/kg
	Plasma protein binding of 97% (Active metabolite)
M	Extensively metabolized via Phase I (cytochrome P450) and Phase II (conjugation) reactions to the active metabolite Roflumilast N-oxide
E	Urine 70% (Inactive metabolite)
	Faeces 20% (Inactive metabolite)
	$t_{1/2}$ ~ 10-20 hrs (Active metabolite)

CLINICAL INFORMATION

Indications

Roflumilast is indicated for the maintenance treatment of severe COPD associated with chronic bronchitis with a history of frequent exacerbations as an add-on to bronchodilator treatment.

Dosage and Administration

The recommended dose of Roflumilast is one 500

microgram (mcg) tablet once daily. The tablet should be swallowed with water and can be taken with or without food.

Side effects

The majority of side effects was mild or moderate occurring within the first weeks of therapy and mostly resolved on continued treatment. These include decreased weight, anorexia, insomnia, nausea, headache, GI upset.

Contraindications

Moderate to severe hepatic impairment (Child-Pugh B or C),

Precaution

Roflumilast is not a bronchodilator and therefore is not indicated for the relief of acute symptoms.

It should not be given in latent infections and psychiatric disorders especially in patients with history of psychiatric symptoms or taking other medications associated with psychiatric reactions. Patients are advised to report any changes in behavior or mood.

Special populations

Use in Pregnancy and lactation: Not recommended during pregnancy and lactation. FDA pregnancy category is C.

Use in Pediatrics: Less than 18 years, not recommended.

Drug interaction

Cimetidine and other inhibitors of CYP3A4 (e.g. erythromycin, ketoconazole) or CYP1A2 (e.g. fluvoxamine), strong P450 inducers (e.g. rifampicin, carbamazepine, phenobarbital, phenytoin),

Overdose and treatment

No case of overdose has been reported in clinical studies with Roflumilast. But In case of overdose, patients should seek immediate medical help. Appropriate supportive medical care should be provided. Since Roflumilast is highly protein bound, hemodialysis is not likely to be an efficient method of drug removal. It is not known whether Roflumilast is dialyzable by peritoneal dialysis.

PHARMACEUTICAL INFORMATION

Storage Condition

Store in a cool and dry place, away from light. Keep out of the reach of children.

Presentation and packaging

Each commercial box contains 30 tablets in Alu-PVC blister pack.

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BEACON®
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