130 (L) x 55(B) 32(H) mm Prepared On : 27March2017

10 x 10 Tablets

Pelinol

(Salbutamol and Theophylline Tablets)

NAFDAC REG. NO.: A4-2840

Mancare

COMPOSITION :

Each uncoated tablet contains :

Salbutamol (as salbutamol Sulphate)	B.P.	2 mg.
Theophylline (Anhydrous)	B.P.	120 mg.
Excipients		q.s.

Dosage: As directed by the physician.

WARNING: FOR PRESCRIPTION USE ONLY.

Keep all medicines out of reach of children.

Store in a cool, dry & dark place below 30°C.

18906062954178

Mfg. Lic. No. : KD-493

Batch No. :

Mfg Date :

Exp Date :

Manufactured By :

Mancare

PHARMACEUTICALS PVT. LTD.

Plot No. 59, 60, 85, 86, V.M.I.E, Dowali Village,
Vasai (W), Dist. Thane, Maharashtra, India.
E-mail: mancerp@yahoo.co.in

Sole Agent:

MC FORIS PHARMACEUTICALS LTD
7 APOSTOLIC CHURCH STREET,
AJAO ESTATE, LAGOS STATE.

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MANCARE PHARMACEUTICAL PVT.LTD	
BRAND NAME:	**SALBUTAMOL AND THEOPHYLLINE TABLETS (PELINOL)**
GENERIC NAME:	**SALBUTAMOL AND THEOPHYLLINE TABLETS**

Module 1 Application Information

1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

1. Name of drug product

SALBUTAMOL AND THEOPHYLLINE TABLETS

1.1 (Trade) name of product

SALBUTAMOL AND THEOPHYLLINE TABLETS (PELINOL)

1.2 Strength

Each uncoated tablet contains:

Salbutamol sulphate B.P.

Equivalent to salbutamol……. 2 mg

Theophylline (Anhydrous) BP…….120 mg

1.3 Pharmaceutical Dosage Form

Tablets for oral administration

MANCARE PHARMACEUTICAL PVT.LTD	
BRAND NAME:	**SALBUTAMOL AND THEOPHYLLINE TABLETS (PELINOL)**
GENERIC NAME:	**SALBUTAMOL AND THEOPHYLLINE TABLETS**

Module 1 Application Information

2. QUALITATIVE & QUANTITATIVE COMPOSITION

2.1 Qualitative Declaration

SALBUTAMOL AND THEOPHYLLINE TABLETS (PELINOL)

Each uncoated tablet contains:

Salbutamol sulphate B.P. Equivalent to salbutamol……. 2 mg

Theophylline (Anhydrous) BP…….120 mg

2.2 Quantitative Declaration

Batch Formula:

Batch Size: 100,000 Tablets

Sr. No	Ingredients	Grade	Rationale	Label Claim	Over ages (%)	Quantity per Unit (mg)	Quantity per Batch (Actual-Kg)
	Mixing						
1.	Salbutamol Sulphate B.P. Eq to Salbutamol	BP	Active	2.00	4.2%	2.50	0.250
2.	Theophylline (Anhy)	BP	Active	120.0	-----	120.0	12.0
3.	Maize Starch	BP	Diluent	-----	-----	79.60	7.96
4.	Microcrystalline cellulose	BP	Disintegrant	-----	-----	10.0	1.0
5.	Maize Starch (Paste)	BP	Binder	-----	-----	4.91	0.491
6.	Gelatine	BP	Binder	-----	-----	1.4	0.14
7.	Sodium Methyl Paraben	BP	Preservative	-----	-----	0.260	0.0260
8.	Sodium Propyl Paraben	BP	Preservative	-----	-----	0.026	0.0026
9.	Purified Water	BP	Vehicle	-----	-----	90.0	9.00
	Lubrication						
10.	Talcum	BP	Glidant	-----	-----	4.400	0.440
11.	Sodium Lauryl Sulphate	BP	solubilising agent	-----	-----	0.250	0.025
12.	Sodium Starch Glycolate	BP	Disintigrant	-----	-----	2.00	0.200
13.	Magnesium Stearate	BP	Lubricant	-----	-----	1.50	0.150

MANCARE PHARMACEUTICAL PVT.LTD	
BRAND NAME:	**SALBUTAMOL AND THEOPHYLLINE TABLETS (PELINOL)**
GENERIC NAME:	**SALBUTAMOL AND THEOPHYLLINE TABLETS**

Module 1 Application Information

3. PHARMACEUTICAL DOSAGE FORM

Tablet for oral administration

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Salbutamol:

1. For the relief of bronchospasm in bronchial asthmas of all types.

2. Chronic bronchitis.

3. Emphysema.

Theophylline:

PELINOL are indicated for the prophylaxis and treatment of reversible bronchospasm associated with asthma and chronic obstructive pulmonary disease.

Because effective plasma levels are maintained for up to twelve hours from a single dose, less frequent dosing is required than with conventional theophylline preparations.

Theophylline should not be used as first drug of choice in the treatment of asthma in children.

4.2 Posology and Method of Administration

Salbutamol:

Route of administration Oral.

Adults:

The usual effective dose is 4mg three or four times per day. If adequate bronchodilation is not obtained each single dose may be gradually increased to as much as 8mg. However, it has been established that some patients obtain adequate relief with 2mg three or four times daily. In elderly patients or in those known to be unusually sensitive to beta-adrenergic stimulant drugs, it is advisable to initiate treatment with 2 mg three or four times per day.

Children:

The following doses should be administered three or four times daily.

2-6 years: 1-2mg

6-12 years: 2mg

Over 12 years: 2-4mg

The product is not recommended for children under 2 years of age. The drug is well tolerated by children so that, if necessary, these doses may be cautiously increased.

Posology

One tablet twice daily, preferably after food, increasing to two tablets twice daily, if necessary.

Paediatric population

Below 6 months: Theophylline should not be used in children below 6 months of age.

Below 6 years: Theophylline should not be used in children below 6 years of age. Other dosage forms are available that are more suitable for children aged less than 6 years.

6 to 12 years: One tablet twice daily, preferably after food.

Elderly

Elderly patients may require lower doses due to reduced theophylline clearance.

Method of administration

PELINOL tablets are scored and may be halved but should not be crushed or chewed.

The dosage should be titrated for each individual and adjusted with caution. Serum theophylline levels should be monitored to ensure that they remain within the therapeutic range.

4.3 Contraindications

1. Salbutamol should not be used for threatened abortion during the first or second trimester of pregnancy.

2. Salbutamol and beta-blocking drugs such as propranolol should not usually be prescribed together.

3. Salbutamol tablets are contraindicated in patients with a history of hypersensitivity to any of their components.

Porphyria Hypersensitivity to any constituent or to xanthines. Concomitant use with ephedrine in children.

Children under 6 months of age.

Hypersensitivity to the active ingredient or to any of the excipients listed in section 6.1.

4.4 Special Warnings and Precautions for Use

Patients with rare hereditary problems of galactose intolerance, the lapp lactase deficiency or glucose

– galactose malabsorption should not take this medicine.

Bronchodilators should not be the only or main treatment in patients with severe or unstable asthma. Increasing use of bronchodilators in particular short-acting inhaled beta$_2$-agonists to relieve symptoms indicates deterioration of asthma control. If patients find that short acting relief bronchodilator treatment becomes less effective or they need more inhalations than usual, medical attention must be sought.

Salbutamol causes peripheral vasodilation which may result in reflex tachycardia and increased cardiac output

Hyperthyroidism

Salbutamol should only be administered cautiously to patients suffering from thyrotoxicosis after careful evaluation of the benefits and risks of treatment.

Constant monitoring of potassium levels in patients with severe asthma is essential, potentially serious hypokalaemia may result from beta-2 agonist therapy.

Diabetes

Administration of beta agonists is associated with a rise of blood glucose. Therefore blood glucose and lactate levels should be monitored in diabetics and diabetic treatment adjusted accordingly to meet the needs of the diabetic during tocolysis (see section 4.5). Diabetic patients may be unable to compensate for the increase in blood glucose and the development of ketoacidosis has been reported.

Concurrent administration of corticosteroids can exaggerate this effect.

Cardiovascular effects may be seen with sympathomimetic drugs, including salbutamol. There is some evidence from post-marketing data and published literature of myocardial ischaemia associated with beta agonists.

Respiratory indications

Patients with underlying severe heart disease (e.g. ischaemic heart disease, arrhythmia or severe heart failure) who are receiving salbutamol should be warned to seek medical advice if they experience chest pain or other symptoms of worsening heart disease. Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be of either respiratory or cardiac origin.

The patients response to therapy should be carefully monitored. Worsening of asthma symptoms requires urgent medical attention.

In case of insufficient effect of the recommended dose and in case of adverse events, theophylline plasma concentration should be monitored.

Use with caution in patients with cardiac arrhythmias, peptic ulcer, hyperthyroidism, severe hypertension, acute porphyria, hepatic dysfunction, chronic alcoholism, and chronic lung disease.

Use with caution in patients with acute febrile illness, as fever decreases the clearance of theophylline. It may be necessary to decrease the dose to avoid intoxication.

Smoking and alcohol consumption may increase theophylline clearance and increased doses of theophylline are therefore required. In patients with cardiac failure, hepatic dysfunction/disease and fever the reverse is true and these patients may require a reduced dosage.

Alternative bronchodilator therapy should be used in patients with a history of seizures.

It is not recommended that the product be used concurrently with other preparations containing xanthine derivatives.

WARNINGS: Xanthines can potentiate hypokalaemia resulting from beta-2-agonist therapy steroids, diuretics and hypoxia. Particular caution is advised in severe asthma. It is recommended that serum potassium levels are monitored in such situations.

PRECAUTIONS: In the case of an acute asthmatic attack in a patient receiving a sustained action theophylline preparation, great caution should be taken when administering intravenous aminophylline. Half the recommended loading dose of aminophylline (generally 6 mg/kg) should be given, i.e. 3 mg/kg, cautiously.

4.5 Interaction with Other Drugs, Other Forms of Interactions

The effects of salbutamol may be altered by guanethidine, reserpine, methyldopa, tricyclic antidepressants and monoamine oxidase inhibitors.

There is an increased risk of hypokalaemia if high doses of theophylline or high doses of corticosteroids are given with higher doses of salbutamol.

Halogenated anaesthetics

Owing to the additional antihypertensive effect, there is increased uterine inertia with risk of haemorrhage; in addition, serious ventricular rhythm disorders due to increased cardiac reactivity, have been reported on interaction with halogenated anaesthetics. Treatment should be discontinued, whenever possible, at least 6 hours before any scheduled anaesthesia with halogenated anaesthetics.

Anti-diabetics

The administration of beta-agonists is associated with a rise of blood glucose, which can be interpreted as an attenuation of anti-diabetic therapy; therefore individual anti-diabetic therapy may need to be adjusted (see section 4.4).

Potassium depleting agents

Owing to the hypokalaemic effect of beta-agonists, concurrent administration of serum potassium depleting agents known to exacerbate the risk of hypokalaemia, such as diuretics, digoxin, methyl xanthines and corticosteroids, should be administered cautiously after careful evaluation of the benefits and risks with special regard to the increased risk of cardiac arrhythmias arising as a result of hypokalaemia (see section 4.4).

Cimetidine, allopurinol, corticosteroids, frusemide, isoprenaline, oral contraceptives, thiobendazole, PELINOL, erythromycin or other macrolide antibiotics and the calcium channel blockers, diltiazem

and verapamil, nizatidine, norfloxacin, isoniazid, fluconazole, carbimazole, mexiletine, propafenone, oxpentifylline, disulfiram, viloxazine, interferon alfa, and influenza vaccine increase plasma theophylline concentrations. A reduction of the theophylline dosage is recommended.

Phenytoin, carbamazepine, barbiturates, rifampicin, sulphinpyrazone, ritonavir, primidone and aminoglutethimide may reduce plasma theophylline concentrations and therefore the theophylline dosage may need to be increased.

Theophylline can increase lithium excretion.

The concomitant use of theophylline and fluvoxamine should usually be avoided. Where this is not possible, patients should have their theophylline dose halved and plasma theophylline should be monitored closely.

Warnings about the concurrent use of xanthines and xanthine derivatives are shown in Section 4, Special Warnings.

Plasma concentrations of theophylline can be reduced by concomitant use of the herbal remedy St John's wort (Hypericum perforatum).

Other interactions: β-Blockers: antagonism of bronchodilation. Ketamine: reduced convulsive threshold. Doxapram: increased CNS stimulation.

Also see Warnings.

4.6 Fertility, pregnancy and lactation

Salbutamol should only be used during pregnancy if it is considered essential by the physician.

As salbutamol is probably secreted in breast milk its use in nursing mothers requires careful consideration. It is not known whether salbutamol has a harmful effect on the neonate, and so its use should be restricted to situations where it is felt that the expected benefit to the mother is likely to outweigh any potential risk to the neonate.

Pregnancy

Administration of theophylline drugs during pregnancy should only be considered if there is no safe alternative and the benefits of treatment outweigh the risks.

Breast-feeding

Theophylline is excreted in breast milk and should not therefore be routinely administered to nursing mothers.

4.7 Effects on ability to drive and operate machine

None known.

4.8 Undesirable effects

The only side effect of significance is a fine tremor of skeletal muscle, which occurs in some patients, usually the hands and the effects are dose related. A few patients feel tense; this is also due to the effects on skeletal muscle and not to direct CNS stimulation. With doses of salbutamol higher than those recommended or in patients who are unusually sensitive to beta-adrenergic stimulants, peripheral vasodilation and a compensatory increase in heart rate may occur.

Occasionally headaches have been reported. Lactic acidosis, myoclonus, pulmonary oedema, hypokalaemia, cardiac arrhythmias may also occur and very rarely hypersensitivity reactions including angioedema, urticaria, bronchospasm, hypotension and collapse.

There have been spontaneously reports of myocardial ischemia in post-marketing experience (frequency unknown, see section 4.4).

The side-effects commonly associated with xanthine derivatives such as nausea, gastric irritation, palpitations, tachycardia, arrhythmias, convulsions, headache, CNS stimulation and insomnia are much diminished when a sustained action preparation such as PELINOL is used. These side-effects are mild and infrequent when the plasma concentration is maintained at less than 20 microgrammes/ml.

4.9 Overdose

The preferred antidote for overdosage with salbutamol is a cardioselective beta blocking agent, but beta blocking drugs should be used with caution in patients with a history of bronchospasm.

Hypokalaemia may occur following overdose with salbutamol. Serum potassium levels should be monitored.

Over 3 g could be serious in an adult (40 mg/kg in a child). The fatal dose may be as little as 4.5 g in an adult (60 mg/kg in a child), but is generally higher.

Symptoms

Warning: Serious features may develop as long as 12 hours after overdosage with sustained release formulations.

Alimentary features:

Nausea, vomiting (which is often severe). epigastric pain and haematernesis. Consider pancreatitis if abdominal pain persists.

Neurological features:

Restlessness, hypertonia. exaggerated limb reflexes and convulsions. Coma may develop in very severe cases.

Cardiovascular features:

Sinus tachycardia is common. Ectopic beats and supraventricular and ventricular tachycardia may follow.

Metabolic features:

Hypokalaemia due to shift of potassium from plasma into cells is common, can develop rapidly and may be severe. Hyperglycaemia. hypomagnesaemia and metabolic acidosis may also occur. Rhabdomyolysis may also occur.

Management

Activated charcoal or gastric lavage should be considered if a significant overdose has been ingested within 1-2 hours. Repeated doses of activated charcoal given by mouth can enhance theophylline elimination. Measure the plasma potassium concentration urgently, repeat frequently and correct

hypokalaemia. BEWARE! If large amounts of potassium have been given, serious hyperkalaemia may develop during recovery. If plasma potassium is low then the plasma magnesium concentration should be measured as soon as possible.

In the treatment of ventricular arrhythmias, proconvulsant antiarrhythmic agents such as lignocaine (lidocaine) should be avoided because of the risk of causing or exacerbating seizures.

Measure the plasma theophylline concentration regularly when severe poisoning is suspected, until concentrations are falling. Vomiting should be treated with an antiemetic such as metoclopramide or ondansetron.

Tachycardia with an adequate cardiac output is best left untreated. Beta-blockers may be given in extreme cases but not if the patient is asthmatic.

Control isolated convulsions with intravenous diazepam. Exclude hypokalaemia as a cause.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Salbutamol is a selective Beta-2-adrenergic agonist administered for the symptomatic relief of bronchospasm associated with chronic or acute asthma, bronchitis or other obstructive pulmonary diseases. Because of its relative specificity for β_2 receptors, salbutamol relaxes smooth muscle of the bronchi, uterus and vascular supply to the skeletal muscle, but generally has much less stimulant action on the heart than does isoproterenol which has powerful action on all beta receptors.

Pharmacotherapeutic group: drugs for obstructive airway disease, ATC code: R03DA04

Theophylline directly relaxes smooth muscle thus acting mainly as a bronchodilator and vasodilator. The drug also possesses other action typical of the xanthines derivatives - coronary vasodilator, diuretic, cardiac stimulant, cerebral stimulant and skeletal muscle stimulant.

5.2 Pharmacokinetic properties

Salbutamol is readily absorbed from the gastrointestinal tract. Its effects occur within 15 minutes and last for about 14 hours. The drug is excreted in urine in about 24 hours, 50% of the drug being excreted within 4 hours. The peak plasma concentration of salbutamol and its metabolites is 5.1-

11.7µg% at 2.5-3 hours after an oral dose of 4mg. Salbutamol does not cross the blood brain barrier to a significant extent, but it crosses the placental barrier.

It has been established that the xanthines, which include theophylline, are readily absorbed after oral, rectal or parenteral administration and this is well documented in published literature.

Effective plasma concentrations: 5-12 µg/ml (do not exceed 20 µg/ml). Theophylline is mainly excreted by the kidneys.

Theophylline is excreted in the urine as metabolites, mainly 1,3-dimethyluric acid and 3-methylxanthine, and about 10% is excreted unchanged.

Plasma half-lives ranging from3 to 9 hours and therapeutic plasma concentrations from about 5 to 20 µg per ml have been reported.

5.3 Pre-clinical safety data

Not applicable.

6. Pharmaceutical particulars

6.1 List of excipients

Sodium Starch Glycolate BP

Maize Starch BP

Microcrystalline Cellulose BP

Maize Starch (Paste) BP

Sodium Methyl Paraben BP

Sodium Propyl Paraben BP

Gelatine BP

Talcum BP

Sodium Lauryl Sulphate BP

Magnesium stearate BP

6.2 Incompatibilities

Not Applicable

6.3 Shelf-Life

36 months from the date of manufacture.

6.3 Special Precautions for Storage

Do not store above 30°C. Blister: Store in the original package in order to protect from moisture.

6.4 Nature and Contents of Container

Alu-Alu Strip with 10 Tablets of SALBUTAMOL AND THEOPHYLLINE TABLETS.

7. Marketing authorisation holder

MANCARE PHARMACEUTICAL PVT.LTD

MANCARE PHARMCEUTICALS PVT. LTD

PLOT NO.60, DHOWALI VILLAGE, VASAI MUNICIPAL IND.ESTATE, VASAI (W), DIST-THANE

8. Marketing authorisation number(s)

9. Date of first authorisation/renewal of the authorisation

10. Date of revision of the text