1.4 PRODUCT INFORMATION.
1.4.1 Prescribing information (Summary of Product Characteristics).
1. NAME OF THE MEDICINAL PRODUCT.
Minoline-100 Tablets.

1.1 Strength:
Aminophylline 100mg.

1.2 Pharmaceutical Form
Film Coated Tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each Film Coated tablet contains: Aminophylline BP 100mg.

3. PHARMACEUTICAL FORM
Film Coated Tablets.
Brown circular, biconvex film coated tablets plain on both sides. Packed in blisters of 10 x 10's, 100 x10's in a unit box and in 1000's in HDPE containers with literature insert.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications:
Aminophylline preparations may be used for the bronchodilatory action of aminophylline to alleviate bronchospasm in the management of reversible airways obstruction as occurs in asthma and in some patients with chronic obstructive pulmonary disease (COPD).

4.2 Dosage and Administration:
Method of Administration: Oral.
1. Management of acute bronchospasm:
Usual Adults dose 100mg to 300mg three to four times a daily after meals.
Children 6mg/kg body weight followed by maintenance doses every four to six hours to give average peak serum concentration of 12µg/mL.

2. Management of chronic bronchospasm:
Usual adult dose 300mg-1200mg daily in divided doses every 6-8 hours.
Children 6-12 years old: Half the recommended adult dosage.
Children 2- 6 years old: Quarter the recommended adult dosage.
Children below 2 years old: Not recommended.

Other observations related to dosage and administration:
1. When using tablets initiate treatment with lower doses and gradually adjust upwards if necessary.
2. Liquid oral aminophylline preparations are suggested in management of neonatal apnoea.
3. Maintain serum aminophylline therapeutic levels of 10-20 g/ml, monitoring is recommended.
4.Initial loading dose based on serum-theophylline concentrations should be determined in those patients already on theophylline, aminophylline or other xanthine-containing medication.

4.3 Method of administration:
Minoline-100 are administered orally.

4.4 Contraindications:
Patients with a history of hypersensitivity to aminophylline or theophylline should not be treated with Aminophylline. The drug should not be administered with other xanthine preparations. Aminophylline is also contraindicated in patients with peptic ulcer disease.

4.5 Special Warnings and Precautions for Use:
Warnings.
Caution should be exercised in patients with congestive heart failure and also renal and hepatic malfunction. Aminophylline should not be used in pregnancy or by breastfeeding mothers unless the potential benefits outweigh possible hazards.
Precautions.
Use with caution in patients with severe cardiac or hepatic failure, hypertension, hyperthyroidism or acute myocardial Injury. Aminophylline may also exacerbate peptic ulcer disease.

4.6 Paediatric Population:
Elimination of theophylline in children younger than 6 months of age, especially in neonates, appears to be reduced. Because of this variation in metabolism the use of Aminophylline in children under 6 months of age is not recommended.

4.7 Interaction with other medicinal products and other forms of interaction:
Elevated serum levels of theophylline may occur in patients receiving the antibiotics troleandomycin and erythromycin concurrently with theophylline. Toxic synergism may occur if aminophylline and ephedrine or other sympathomimetic drugs are given concurrently. Cigarette smoking on the other hand increases the rate of metabolism of theophylline which may increase the dosage requirements of aminophylline.

4.8 Additional information on special populations:
No information on this section has been provided.

4.9 Paediatric Population:
Elimination of theophylline in children younger than 6 months of age, especially in neonates, appears to be reduced. Because of this variation in metabolism the use of Aminophylline in children under 6 months of age is not recommended

4.10 Fertility, Pregnancy and Lactation:
Pregnancy: There are no adequate and well controlled studies in pregnant women. Additionally, there are no teratogenicity studies in non-rodents (e.g., rabbits). Theophylline was not shown to be teratogenic in CD-1 mice at oral doses up to 400 mg/kg, approximately 2.0 times the human dose on a mg/m2 basis or in CD-1 rats at oral doses up to 260 mg/kg, approximately 3.0 times the recommended human dose on a mg/m2 basis. At a dose of 220 mg/kg, embryo toxicity was observed in rats in the absence of maternal toxicity.
Nursing Mothers: Theophylline is excreted into breast milk and may cause irritability or other signs of mild toxicity in nursing human infants. The concentration of theophylline in breast milk is about equivalent to the maternal serum concentration. An infant ingesting a liter of breast milk containing 10-20 mcg/mL of theophylline is likely to receive 10-20 mg of theophylline per day. Serious adverse effects in the infant are unlikely unless the mother has toxic serum theophylline concentrations.

4.11 Effects on ability to drive and use machines:
Aminophylline tablets have no or negligible influence on the ability to drive and use machines.

4.12 Adverse actions:
The most frequently encountered adverse reactions observed with therapeutic levels of am1nophyllme are:
1. Gastrointestinal: Nausea, vomiting, anorexia and GIT distress.
2. Cardiovascular: palpitation, tachycardia, arrhythmias flushing and hypotension.
3. Central nervous system (CNS): Nervousness, agitation, headache, dizziness, vertigo, light headedness.
4. Respiratory: increase in respiratory rate.
5. Ermatological: urticaria, skin rash.

4.13 Overdose:
The following are the commonest reactions in overdosage with aminophylline.
1. Gastrointestinal: - Anorexia, nausea, vomiting and hematemesis.
2. CNS: -Nervousness, agitation headache, vertigo, hyperreflexia, fasciculations, stupor, coma and convulsions which may lead to death. This is common in children and infants.
3. Cardiovascular: -tachycardia or other arrhythmias, diaphoresis, hypotension and rarely vasomotor collapse.
4. Respiratory: Tachypnea, and hyperventilation. Respiratory failure may occur.
5. General systemic effects: syncope, collapse, fever, dehydration and hyperthermia.

Management of toxic symptoms.
1. Discontinue therapy at once.
2. There is no known specific antidote.
3. Treatment is supportive and symptomatic.
4. Avoid administration of sympathomimetic drugs.
5. Give I.V fluids, oxygen and other supportive measures to prevent hypotension; correct dehydration and acid base imbalance.
6. Keep the patient cool to prevent hyperthermia using a cooling blanket.
7. Control convulsions using barbiturates, benzodiazepines (short acting) or phenytoin.
8. Monitor theophylline serum levels until below 20g/mL.
9. Maintain patent airway.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties:

Pharmacotherapeutic group: Drugs for obstructive airways diseases, other systemic drugs for obstructive airway diseases, xanthines.

ATC code: R03DA05.

Aminophylline is a soluble complex containing approximately 65% anhydrous theophylline and 15% ethylenediamine. Theophylline belongs to a group of structurally related alkaloids called methylxanthines.

Aminophylline directly relaxes the smooth muscle of the bronchial airways and pulmonary blood vessels, thus acting mainly as a bronchodilator, pulmonary vasodilator and smooth muscle relaxant.

The drug also possesses other actions typical of the xanthine derivatives: coronary vasodilator, diuretic, cardiac stimulant and skeletal muscle stimulant.

5.2 Pharmacokinetic properties:

Aminophylline is readily absorbed after oral or parenteral administration. In absence of food peak serum levels are achieved within 2 hours. Distribution occurs in all body compartments. Methylxanthines cross the placenta and get sequestered in breast milk. Theophylline is bound to plasma proteins and the fraction bound decreases as concentration of Methylxanthines increases. Elimination is primarily by metabolism in the liver. Less than 20% is excreted in urine unchanged.

Note: There is marked inter-individual and intra-individual variation in elimination rate due to both genetic and environmental factors.

5.3 Preclinical safety data:

Genotoxicity and Carcinogenicity:

In vitro and in vivo assays, have shown both positive and negative genotoxic results for theophylline.

However, oral theophylline administered daily to rats and mice for 2 years did not show carcinogenicity. Therefore, it is unlikely that theophylline poses a carcinogenic risk in man.

Reproductive and Developmental Toxicity:

Theophylline has been shown to have effects upon the male reproductive system in rodents, but at doses considered in excess of the maximum human dose indicating little relevance to clinical use. Several embryo fetal development studies in rats, mice and rabbits have demonstrated. Developmental effects independent from maternal toxicity at high doses of theophylline. Therefore, theophylline should be considered to have the potential for developmental toxicity in man.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients.

- Microcrystalline Cellulose (MCC pH 102)
- Croscarmellose Sodium (Vivasol)
- Sodium Metabisulphite
- Sodium Starch Glycolate
- Sodium Lauryl Sulphate
- Aerosil 200 Pharma
- Purified Talc
- Magnesium Stearate
- Hydroxyl Propyl Methylcellulose (5 Cps)
- Ethyl Cellulose
- Titanium Dioxide
- Polyethylene Glycol 6000
- Iron Oxide Red
- Isopropyl Alcohol 99%
- Methylene Chloride

6.2 Incompatibilities:

None Known.

6.3 Shelf life:

30 Months.

6.4 Special precautions for storage:

Store in a dry place below 30ºC.

Protect from light.

Keep all medicines out of reach of children.

6.5 Nature and contents of container:
Brown circular, biconvex film coated tablets plain on both sides. Packed in blisters of 10 x 10's in a unit box and in 1000's in HDPE containers with literature insert.

6.6 Special precautions for disposal and other handling:
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESSES
Marketing Authorization Holder:
Company Name: Laboratory & Allied Limited.
Address: Plot No. 209/10349, Opposite Sameer Business Park, Next to Libra House, Mombasa Road, P.O. Box 42875 GPO 00100, Nairobi-Kenya.
Country: Kenya.
Telephone: +254 20 8040306.
Telefax: +254 20 8040309.
E-Mail: info@laballied.com.

Manufacturing Site Address:
Company Name: Laboratory & Allied Limited.
Address: Plot No. 209/10349, Opposite Sameer Business Park, Next to Libra House, Mombasa Road, P.O. Box 42875 GPO 00100, Nairobi-Kenya.
Country: Kenya.
Telephone: +254 20 8040306.
Telefax: +254 20 8040309.
E-Mail: info@laballied.com

8. MARKETING AUTHORIZATION NUMBER:
Kenya Reg No.: H82193.

9. DATE OF FIRST REGISTRATION/ RENEWAL OF THE REGISTRATION:
Registration Date: 12/11/1982.
Renewal Date: To be retained annually.

10. DATE OF REVISION OF THE TEXT:
March, 2024.

11. DOSIMETRY (IF APPLICABLE)
Not Applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)
Not Applicable.