SUMMARY OF PRODUCT CHARACTERIZATION (SMPC) FOR

FAL-ASMANIL TABLET

1. Name of the medicinal product

Fal Asmanil Tablet

2. Qualitative and quantitative composition

Each tablet contains Ephedrine HCL 16mg Theophylline

60mg

chlorphenamine maleate 2mg

Excipients with known effect

Each tablet contains methyl parahydroxybenzoate (E218), 0.054mg 0.026mg and propyl parahydroxybenzoate (E216),

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Modified release tablet

A white round, biconvex uncoated tablets inscribed with "Fal" on one side and plain on the other side. 4. Clinical particulars

4.1 Therapeutic indications

For the treatment and prophylaxis of bronchospasm associated with asthma, chronic obstructive pulmonary disease and chronic bronchitis. Also indicated for treatment of left ventricular and congestive cardiac failure.

4.2 Posology and method of administration

Posology

Adults, elderly and children over 12 years of age

One or two tablets daily. One tablet should be taken in the morning on rising and a further tablet may be taken at night if required.

Paediatric population

Not recommended in children under 12 years of age.

Method of administration Oral

administration.

4.3 Contraindications

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

Use in patients with coronary thrombosis, hypertension, thyrotoxicosis and those on treatment with monoamine oxidase inhibitors.

4.4 Special warnings and precautions for use

Fal-Asmanil Tablets should be swallowed whole and not sucked or chewed. Do not exceed the stated dose. Asthmatics should consult their doctor before using this product. May cause drowsiness, if affected do not drive or operate machinery. Avoid alcoholic drink.

Due to potential decreased theophylline clearance, dose reduction and monitoring of serum theophylline concentrations may be required in elderly patients and patients with:

- ✦ cardiac disease
- ✦ hepatic disease
- ✦ exacerbations of lung disease
- ✦ hypothyroidism
- ✦ fever
- ✦ viral infections.

Due to potential increased theophylline clearance, dose increase and monitoring of serum theophylline concentrations may be required in patients with hyperthyroidism (and when starting acute hyperthyroidism treatment) and cystic fibrosis.

Theophylline may:

- act as a gastrointestinal tract irritant and increase gastric secretion, therefore caution should be exercised in patients with peptic ulcers;
- exacerbate cardiac arrhythmias and therefore caution should be exercised in patients with cardiac disorders;
- exacerbate frequency and duration of seizures and therefore caution should be exercised in patients with history of seizures and alternative treatment considered.

Use with caution in patients with severe hypertension, or chronic alcoholism. Caution should be exercised in elderly males with pre-existing partial urinary tract obstruction, such as prostatic enlargement, due to risk of urinary retention. Particular care is advised in patients suffering from severe asthma who require acute theophylline administration. It is recommended that serum theophylline concentrations are monitored in such situations.

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

Excipients

This medicine contains hydrogenated castor oil which may cause stomach upset and diarrhea.

This medicine contains methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216), which may cause allergic reactions (possibly delayed).

4.5 Interaction with other medicinal products and other forms of interaction The following increase clearance of theophylline and it may therefore be necessary to increase dosage to ensure a therapeutic effect: aminoglutethimide, carbamazepine, isoprenaline, phenytoin, rifampicin, ritonavir, sulphinpyrazone, barbiturates and hypericum perforatum (St John's Wort).

Smoking and alcohol consumption can also increase clearance of theophylline. The following reduce clearance and a reduced dosage may therefore be necessary to avoid side-effects: aciclovir, allopurinol, carbimazole, cimetidine,

clarithromycin, diltiazem, disulfiram, erythromycin, fluconazole, interferon, isoniazid, methotrexate, mexiletine, nizatidine, pentoxifylline, propafenone, propranolol, thiabendazole, verapamil and oral contraceptives (see section 4.9). Theophylline has been shown to interact with some quinolone antibiotics including ciprofloxacin and enoxacin which may result in elevated plasma theophylline levels.

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

Factors such as viral infections, liver disease and heart failure also reduce theophylline clearance (see section 4.9). There are conflicting reports concerning the potentiation of theophylline by influenza vaccine and physicians should be aware that interaction may occur resulting in increased serum theophylline levels. A reduction of dosage may also be necessary in elderly patients. Thyroid disease or associated treatment may alter theophylline plasma levels.

Concurrent administration of theophylline may:

- ✦ inhibit the effect of adenosine receptor agonists (adenosine, regadenoson, dipyridamol) and may reduce their toxicity when used for cardiac perfusion scanning;
- ✦ oppose the sedatory effect of benzodiazepines;
- ✦ result in the occurrence of arrhythmias with halothane;
- ✦ result in thrombocytopenia with lomustine; ✦ increase urinary lithium clearance.

Therefore, these drugs should be used with caution.

Theophylline may decrease steady state phenytoin levels.

Hypokalaemia resulting from beta2 agonist therapy, steroids, diuretics and hypoxia may be potentiated by xanthines. Particular care is advised in patients suffering from severe asthma who require hospitalisation. It is recommended that serum potassium concentrations are monitored in such situations. Care should be taken in its concomitant use with β-adrenergic agonists, glucagon and other

xanthine drugs, as these will potentiate the effects of theophylline. Co-administration with ketamine may cause reduced convulsive threshold; with doxapram may cause increased CNS stimulation.

The incidence of toxic effects may be enhanced by the concomitant use of ephedrine.

4.6 Fertility, pregnancy and lactation

Fal-Asmanil Tablets are contra-indicated during pregnancy and during breastfeeding.

4.7 Effects on ability to drive and use machines

Fal-Asmanil Tablets have a moderate influence on the ability to drive and use machines.

4.8 Undesirable effects

Although the combination of ephedrine with the anti-histamine chlorphenamine is intended to reduce side-effects, slight drowsiness may occur. Side effects of ephedrine are rare at the low dose employed in this preparation, however in particularly susceptible patients, effects such as giddiness, palpitations and muscular weakness may be experienced transiently.

4.9 Overdose

Management

Treatment should include gastric lavage. In the event of convulsions sedate with intramuscular paraldehyde. Respiratory depression may necessitate mechanical ventilation. Symptomatic treatment of cardiovascular dysfunction should be given with careful patient monitoring. The physician should be aware that tablets in the intestine will continue to release the active ingredients for a period of hours.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihistamines for systemic use, substituted alkylamides, ATC code: R03D A04

Mechanism of action

Chlorphenamine is a potent H1-blocking drug. It antagonises the pharmacological actions of histamine released by antigen-antibody reaction in allergic diseases, thus providing symptomatic relief. Chlorphenamine alone is less effective when pollen counts are high, allergen exposure is prolonged and nasal congestion has become prominent.

Ephedrine has mild CNS stimulant properties which counteract any drowsiness produced by chlorphenamine. In addition, it produces a decongestant action on nasal mucosal surfaces relieving mucosal congestion in conditions such as hay fever and allergic rhinitis.

Theophylline is a bronchodilator. In addition it affects the function of a number of cells involved in the inflammatory processes associated with asthma and chronic obstructive airways disease. Of most importance may be enhanced suppressor T-lymphocyte activity and reduction of eosinophil and neutrophil function. These actions may contribute to an anti-inflammatory prophylactic activity in asthma and chronic obstructive airways disease.

Theophylline stimulates the myocardium and produces a diminution of venous pressure in congestive heart failure leading to marked increase in cardiac output

5.2 Pharmacokinetic properties

Chlorphenamine is readily absorbed after oral administration and may undergo enterohepatic re-circulation in man. It is eliminated with a t½ of 12-15 hours. Ephedrine is completely absorbed following oral administration and is eliminated with a t½ of 3-6 hours.

Theophylline

Absorption

Following oral administration, theophylline is efficiently absorbed and is associated with an absolute bioavailability approximating 100%. Following oral administration of Fal Asmanil tablets, the delivery of theophylline is controlled

and, at steady state, peak concentrations are typically seen after approximately 5 hours.

An effective plasma concentration is considered to be 5-12 micrograms/ml, although plasma concentrations up to 20 micrograms/ml may be necessary to achieve efficacy in some cases. Do not exceed 20 micrograms/ml.

Distribution and protein binding

Theophylline is distributed through all body compartments; approximately 60% is bound to plasma proteins.

An effective plasma concentration is considered to be 5-12 micrograms/ml, although plasma concentrations up to 20 micrograms/ml may be necessary to achieve efficacy in some cases. Do not exceed 20 micrograms/ml.

Biotransformation

Theophylline is metabolised in the liver to 1, 3-dimethyl uric acid and 3-methylxanthine.

Elimination

Theophylline and its metabolites are excreted mainly in the urine. Approximately 10% is excreted unchanged. The mean elimination half life associated with Fal Asmanil tablets is approximately 7 hours.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SmPC.

6. Pharmaceutical particulars

6.1 List of excipients

Magnesium stearate

Methyl parahydroxybenzoate (E218)

Propyl parahydroxybenzoate (E216)

Purified talc

Lactose

Corn Starch

PVP K 30

6.2 Incompatibilities Not known.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage condition.

6.5 Nature and contents of container Alu/Alu

blisters.

Pack size of 30 tablets.

6.6 Special precautions for disposal and other handling No

special requirements.

7. Marketing authorization holder

Distributed by

Daily Sun Pharmaceutical Company Limited

Plot 3 & 4, Tomori Industrial Estate, Off Idi-Iroko Road, Ota, Ogun State, Nigeria.

Manufactured by

Daily Sun Pharmaceutical Company Limited

Plot 3 & 4, Tomori Industrial Estate, Off Idi-Iroko Road, Ota, Ogun State, Nigeria.