1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

1.1 Name of the Medicinal Product

BIVA PLUS [Cyproheptadine with Multivitamin Tablets]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:

Cyproheptadine Hydrochloride (Anhydrous) BP	4.0 mg
Vitamin A (as Acetate) BP	2500 IU
Vitamin D3 BP	200 IU
Vitamin B1 BP	2 mg
Riboflavin BP	2 mg
Cyanocobalamin BP	1 mcg
Nicotinamide BP	25 mg
Calcium Pantothenate	5 mg
Calcium Lactate BP	100 mg
Excipients	q.s.

3. PHARMACEUTICAL FORM

Film coated Tablet for oral use.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Cyproheptadine HCl in Biva Plus is indicated for the Anorexia (lack of appetite). Anorexia Nervosa is a psychological condition where patient does not want to take food. This condition is predominantly seen in young girls who tend to avoid taking foods in fear of becoming bulky.

Biva Plus is indicated for loss of appetite, weight loos, anorexia nervosa and as adjunct to anti-tubercular and anti-retroviral regimens for weight gain.

In children, Biva Plus is indicated in underweight children who have inadequate dietary intake or loss of appetite and children in deficiency of Vitamins.

Vitamin A: Helps eye health play an essential role in metabolic functioning of the retina.

VitaminD3: Maintain blood levels of calcium.

Vitamin B1: Needed to process carbohydrates fats, help convert carbohydrates into the fuel.

Nicotinamide: Process of releasing energy from carbohydrates.

Calcium Pantothenate: is a nutritional supplement and usually used in conjunction with other B group vitamins.

Calcium lactate: is used in calcium deficiency state resulting from dietary deficiency of ageing.

Cyanocobalamin: Maintaining normal vitamin B12 blood levels and also used to treat or prevent low blood levels of vitamin B12 that may be caused by other conditions.

4.2. Posology and method of administration

Route of administration: Oral.

The usual recommended dose of Biva Plus tablet in adult is one tablet twice in a day or as directed by the physician.

4.3. Contra-indications

Newborn or Premature Infants

This drug should **not** be used in newborn or premature infants.

Nursing Mothers

Because of the higher risk of antihistamines for infants generally and for newborns and premature in particular, antihistamine therapy is contraindicated in nursing mothers.

Other Conditions

Hypersensitivity to Cyproheptadine and other drugs of similar chemical structure

Monoamine oxidase inhibitor therapy

Angle-closure glaucoma

Stenosing peptic ulcer

Symptomatic prostatic hypertrophy

Bladder neck obstruction

Pyloroduodenal obstruction

Elderly, debilitated patients

4.4. Special warnings and special precautions for use

Pediatric Patients

Overdosage of antihistamines, particularly in infants and young children, may produce hallucinations, central nervous system depression, convulsions, respiratory and cardiac arrest, and death. Antihistamines may diminish mental alertness; conversely, particularly, in the young child, they may occasionally produce excitation.

CNS Depressants

Antihistamines may have additive effects with alcohol and other CNS depressants, e.g., hypnotics, sedatives, tranquilizers, antianxiety agents.

Activities Requiring Mental Alertness

Patients should be warned about engaging in activities requiring mental alertness and motor coordination, such as driving a car or operating machinery.

Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients.

PRECAUTIONS

General

Cyproheptadine has an atropine-like action and, therefore, should be used with caution in patients with:

History of bronchial asthma

Increased intraocular pressure

Hyperthyroidism

Cardiovascular disease

Hypertension

4.5. Interactions with other Drug products and other forms of interaction

Drug Interactions

MAO inhibitors prolong and intensify the anticholinergic effects of antihistamines.

Antihistamines may have additive effects with alcohol and other CNS depressants, e.g., hypnotics, sedatives, tranquilizers, antianxiety agents.

4.6. Pregnancy and lactation

Fertility

Cyproheptadine had no effect on fertility in a two-litter study in rats or a two generation study in mice at about 10 times the human dose.

Cyproheptadine did not produce chromosome damage in human lymphocytes or fibroblasts *in vitro*; high doses (10-4M) were cytotoxic. Cyproheptadine did not have any mutagenic effect in the Ames microbial mutagen test; concentrations of above 500 mcg/plate inhibited bacterial growth.

Pregnancy

Pregnancy Category B

Reproduction studies have been performed in rabbits, mice, and rats at oral or subcutaneous doses up to 32 times the maximum recommended human oral dose and have revealed no evidence of impaired fertility or harm to the fetus due to Cyproheptadine. Cyproheptadine has been shown to be fetotoxic in rats when given by intraperitoneal injection in doses four times the maximum recommended human oral dose. Two studies in pregnant women, however, have not shown that Cyproheptadine increases the risk of abnormalities when administered during the first, second and third trimesters of pregnancy. No teratogenic effects were observed in any of the newborns. Nevertheless, because the studies in humans cannot rule out the possibility of harm, Cyproheptadine should be used during pregnancy only if clearly needed.

Lactation

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from Cyproheptadine, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7. Effects on ability to drive and use machines

This product may cause drowsiness and somnolence. Patients receiving it should not drive or operate machinery unless it has been shown that their physical and mental capacity remains unaffected.

4.8. Undesirable effects

There is no undesirable effect observed.

4.9 Overdose

Adverse events experienced in higher than recommended doses were similar to those seen at normal doses. In the event of overdosage, general symptomatic and supportive measures are indicated as required.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Cyproheptadine is a piperidine antihistamine. Unlike other antihistamines, this drug also antagonizes serotonin receptors. This action makes Cyproheptadine useful in conditions such as vascular headache and anorexia. Cyproheptadine does not prevent the release of histamine

but rather competes with free histamine for binding at HA-receptor sites. Cyproheptadine competitively antagonizes the effects of histamine on HA-receptors in the GI tract, uterus, large blood vessels, and bronchial smooth muscle. Most antihistamines possess significant anticholinergic properties, but Cyproheptadine exerts only weak anticholinergic actions. Blockade of central muscarinic receptors appears to account for Cyproheptadine's antiemetic effects, although the exact mechanism is unknown.

Cyproheptadine also competes with serotonin at receptor sites in smooth muscle in the intestines and other locations. Antagonism of serotonin on the appetite center of the hypothalamus may account for Cyproheptadine's ability to stimulate appetite. Cyproheptadine also has been used to counter vascular headaches, which many believe are caused by changes in serotonin activity; however it is unclear how Cyproheptadine exerts a beneficial effect on this condition.

5.2 Pharmacokinetic Properties

Absorption

Well absorbed after oral administration.

Metabolism

Hepatic (cytochrome P-450 system) and some renal.

Elimination

After a single 4 mg oral dose of14C-labelled Cyproheptadine HCl in normal subjects, given as tablets 2% to 20% of the radioactivity was excreted in the stools. At least 40% of the administered radioactivity was excreted in the urine.

5.3. Preclinical safety data

Not Applicable

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sodium Benzoate, Butyl Hydroxy toluene, Aerosil, P.V.P.K-30, Microcrystalline Cellulose, Lactose, Croscarmellose Sodium, Purified Talc, Magnesium Stearate, Sodium Starch Glycolate, Erythrosine & Tartrazine.

6.2. Incompatibilities

Not applicable

6.3. Shelf life

24 Months

6.4 Special precautions for storage

Storage below 30ºC, Protected from the sunlight.

Keep out of reach and sight of children.

6.5. Nature and contents of container

3 x 10 Tablets in Blister Pack

6.6. Instruction for use and handling

No special requirements.

7. PPLICANT/SUPPLIER

BLISTERS LTD.

Post Office 89, Ashaiman, 23321 Tema, Ghana

8. FDA APPLICATION NUMBER

Not Applicable

9. DATE OF REGISTRATION / RENEWAL OF REGISTRATION

Not Applicable

10. DATE OF REVISION OF THE TEXT

Not Applicable