SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) OF CENTONE SYRUP

1. NAME OF THE MEDICINAL PRODUCT: CENTONE SYRUP
(Cyproheptadine with Multivitamin Syrup)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 5 ml contains:
Cyproheptadine Hcl (Anhydrous) USP…..….2 mg
Thiamine Hcl (Vitamin B1) BP…….…….2 mg
Riboflavin (Vitamin B2) BP…..……..1 mg
(Riboflavin sodium Phosphate eq. to Riboflavin)
Pyridoxine Hcl (Vitamin B6) BP……1 mg
L-Lysine Hcl USP…….……..……..150 mg
Niacinamide (Vitamin B3) BP……..…..…7.5 mg
Zinc Sulphate BP……7 mg
Flavoured Syrup Base…….……q.s
Colour : Caramel
For a full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM : Syrup

4. Clinical Data:
4.1. Therapeutic Indications:
Combination of Cyproheptadine and multivitamins provides quick recovery from allergic disorders, treatment of inflammation of nasal mucosa such as rhinitis. Nutritional deficiencies, diet regulation in the course of treatment are corrected by the vitamins.
Cyproheptadine is indicated in the treatment of
* Perennial and seasonal allergic rhinitis
* Vasomotor rhinitis
* Allergic conjunctivitis due to inhalant allergens and foods
* Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.
* Amelioration of allergic reactions to blood or plasma
* Cold urticaria
* As therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.
Vitamin B1 is an essential coenzyme for carbohydrate metabolism. Treatment of deficiency disorders such as beri-beri, Wernicke- Korsakoff syndrome.
Riboflavin (Vitamin B2) is required for the utilization of energy from food, treatment of nutritional deficiency, glossitis, keratitis, seborrhoeic dermatitis.
Pyridoxine Hydrochloride (Vitamin B6) : As a supplement it is used to treat and prevent pyridoxine deficiency, sideroblastic anaemia, pyridoxine-dependent epilepsy, certain metabolic disorders, problems from isoniazid, and mushroom poisoning.
L-Lysine : Amino acid Supplementary.
Nicotinamide is used in the treatment and prevention of deficiency, in conjunction with lipid regulating agents in hyperlipidemia, in alcoholism.
Zinc Sulphate : Dietary Supplement for treating Zinc deficiency.

4.2 Posology & Method of administration
Children < 4 years old : 2.5 ml per day
Children > 4 years old : 5 ml per day or As directed by physician.

4.3. Contraindications:

'**CENTONE SYRUP'** is contraindicated in:

• Patients undergoing therapy for an acute asthmatic attack;

• Newborn or premature infants; use in infants has been associated with apnoea, cyanosis and respiratory difficulty;

• Breast-feeding mothers;

• Patients with known sensitivity to cyproheptadine hydrochloride or drugs with similar chemical structure;

• Concurrent use with monoamine oxidase inhibitors;

• Glaucoma;

• Patients with pyloroduodenal obstruction, stenosing peptic ulcer, symptomatic prostatic hypertrophy, predisposition to urinary retention or bladder neck obstruction;

• Elderly, debilitated patients.

Known hypersensitivity to any of the active constituents.

4.4. Warning & Special Precautions for administration:

Antihistamines should not be used to treat lower respiratory tract symptoms, including those of acute asthma.

The safety and efficacy of **CENTONE SYRUP** is not established in children under 2 years old.

Overdosage of antihistamines, particularly in infants and 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.

Patients should be warned against engaging in activities requiring motor co-ordination and mental alertness, such as driving a car or operating machinery (see section 4.7 'Effects on ability to drive and use machines').

Rarely, prolonged therapy with antihistamines may cause blood dyscrasias.

Because **CENTONE SYRUP** has an atropine-like action, it should be used cautiously in patients with a history of bronchial asthma, increased intra-ocular pressure, hyperthyroidism, cardiovascular disease, or hypertension.

Excipients

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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4.5. 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, tranquillisers and anti-anxiety agents.

Drugs with anti-serotonin activity, such as cyproheptadine, may interfere with serotonin-enhancing anti-depressants including selective serotonin re-uptake inhibitors (SSRI's). This may result in possible recurrence of depression and related symptoms.

Cyproheptadine may cause a false positive test result for tricyclic antidepressant drugs (TCA) when evaluating a drug screen (e.g. urine, serum). Because cyproheptadine and TCAs may produce similar overdose symptoms, physicians should carefully monitor patients for TCA toxicity in the event of combined overdose.

Pyridoxine may increase the peripheral metabolism of levodopa, reducing therapeutic efficacy of the latter drug. Therefore, patients with Parkinson's disease who are receiving treatment with plain levodopa should not take vitamin B_6 in doses which greatly exceed the daily requirement. This does not apply when levodopa is combined with a peripheral decarboxylase inhibitor.

4.6. Pregnancy & Breastfeeding:

The use of any drug in pregnancy or in women of child-bearing age requires that the potential benefit of the drug should be weighed against possible hazards to the embryo and fetus.
It is not known whether **CENTONE SYRUP** is excreted in human milk, and because of the potential for serious adverse reactions in breast-feeding infants from CENTONE SYRUP', a decision should be made whether to discontinue breast-feeding or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7. Side – Effects:

The side effects that appear frequently are drowsiness and somnolence. Many patients who initially complain of drowsiness may no longer do so after the first three to four days of continuous administration.
Side effects reported with antihistamines are:
Blood and lymphatic system disorders: Haemolytic anaemia, leucopenia, agranulocytosis, thrombocytopenia
Immune system disorders: Allergic manifestation of rash and oedema, anaphylactic shock
Metabolism and nutrition disorders: Anorexia, increased appetite
Psychiatric disorders: Confusion, restlessness, excitation, irritability, nervousness, insomnia, aggressive behaviour, hallucinations, hysteria and euphoria
Nervous system disorders: Sedation, sleepiness (often transient), dizziness, disturbed coordination, tremor, paraesthesiae, neuritis, convulsions, faintness, headache
Eye disorders: Blurred vision, diplopia
Ear and labyrinth disorders: Acute labyrinthitis, tinnitus, vertigo
Cardiac disorders: Palpitation, tachycardia, extrasystoles
Vascular disorders: Hypotension
Respiratory, thoracic and mediastinal disorders: Thickening of bronchial secretions, dryness of nose and throat, tightness of chest and wheezing, nasal stuffiness, epistaxis
Gastrointestinal disorder: Dryness of mouth, epigastric distress, nausea, vomiting, diarrhoea, constipation
Hepato-biliary disorders: Cholestasis, hepatic failure, hepatitis, hepatic function abnormality, jaundices
Skin and subcutaneous tissue disorders: Urticaria, photosensitivity, excessive perspiration
Renal and urinary disorders: Frequency and difficulty of micturition, urinary retention
Reproductive system and breast disorders: Early menses
General disorders and administration site conditions: Fatigue, rigors
Investigations: Weight gain

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. toxic effects are unlikely since any excess vitamin B is excreted.
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5. Pharmacological characteristics :

5.1. Pharmacodynamic characteristics :

Cyproheptadine hydrochloride is a serotonin and histamine antagonist with anticholinergic and sedative effects. Antiserotonin and antihistamine drugs appear to compete with serotonin and histamine, respectively, for receptor sites.

The inhibitory effect of cyproheptadine in histamine-induced gastric secretion is also unusual as specific anti-histamines do not influence this effect.

B-complex Vitamin

The vitamin B-complex comprises a group of water-soluble factors more or less closely associated in their natural occurrence. It is known that nearly every vitamin of the B-complex forms part of a co-enzyme essential for the metabolism of protein, carbohydrate or fatty acid.

5.2. Pharmacokinetics characteristics:

After a single 4 mg oral dose of ^{14}C-labelled cyproheptadine hydrochloride in normal subjects given as Syrup or syrup, 2 to 20% of the radioactivity was excreted in the stools. Only about 34% of the stool radioactivity was unchanged drug, corresponding to less than 5.7% of the dose. At lease 40% of the administered radioactivity was excreted in the urine.

No significant difference in the mean urinary excretion exists between the tablet and syrup formulations. No detectable amounts of unchanged drug were present in the urine of patients on chronic 12-20 mg daily doses of Periactin syrup. The principle metabolite found in human urine has been identified as a quaternary ammonium glucuronide conjugate of cyproheptadine. Elimination is diminished in renal insufficiency.

Nicotinamide is readily absorbed from the GI tract following oral administration and is widely distributed in the body tissues. Small amounts of nicotinamide are excreted unchanged in urine following therapeutic doses, however, the amount excreted unchanged is increased with larger doses.

Pyridoxine is absorbed from the GI tract and is converted to the active form pyridoxal phosphate. It is excreted in the urine as 4-pyridoxic acid.

Riboflavin is absorbed from the GI tract and in the circulation is bound to plasma proteins. Although widely distributed, little is stored in the body, and amounts in excess of requirements are excreted in the urine.

Thiamine is absorbed from the GI tract and is widely distributed to most body tissues. It is not stored to any appreciable extent in the body and amounts in excess of requirements are excreted in the urine as unchanged thiamine or metabolites.

5.3. Pre – Clinical Safety Data:

No relevant information.

6. Pharmaceutical Data:

6.1. List of excipients

Sr. No	Excipients	Specification
1	Arrow Super Gum	BP
2	Citric ACID (mono)	BP
3	Colour Caramel	INH
4	Disodium EDTA	BP
5	ENISWEET Powder	INH
6	Sodium Methyl paraben	BP

Sr. No	Excipients	Specification
7	Flavour - Vanilla coconut SKAF-M8879	INH
8	Sodium Propyl paraben	BP
9	Propylene glycol	BP
10	Sodium benzoate	BP
11	Sodium saccharine	BP
12	Sucrose	BP
13	Thio Urea	BP
14	Purified Water	BP

6.2. Incompatibilities: Not Applicable

6.3. Duration of Storage: 24 Months (2 years)

6.4. Special precautions for Storage:
Store in a cool, dry and dark place.
Keep out of reach of Children.

6.5. Nature and content of the external packaging:
200 ml amber coloured bottle packed in a carton along with insert.

6.6 Instructions for use and handling and disposal
No special requirements.

7. APPLICANT
HABMAY PHARMACY LIMITED
P.O.BOX AN 18113
ACCRA-NORTH
Telephone: 0302 260259
Fax: **0244483933**
E-mail: habmay1010@yahoo.com

8. MANUFACTURER

MERCURY LABORATORIES LIMITED
UNIT NO.2 VADODARA ROAD,
GUJARAT, INDIA

9. FDA APPLICATION NUMBER :

10. Number(s) in the national register of finished pharmaceutical products
Mfg. Lic. No. In India: KD-2447-A

11. Date of First Authorization/Renewal : 07 Jul. 2008 / 20 Jun. 2013

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