1. NAME OF THE MEDICINAL PRODUCT
Avro Apetit Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 5ml contains

Cyproheptadine Hydrochloride	2mg
Vitamin B1 (Thiamine)	1mg
Vitamin B_2 (Riboflavin)	0.5mg
Vitamin B_6 (Pyridoxine Hydrochloride)	0.5mg
Vitamin B_{12} (Cyanocobalamin)	2mcg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM
Oral Liquid.
Yellowish syrup with taste of orange flavour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
Avro-Apetit syrup is indicated for:
- Loss of appetite
- Weight loss
- Physical fatigue or weakness
- Recovery form illness
- Nutritional supplement in cases of insufficient dietary intake.
- Symptomatic relief of allergic conditions

4.2 Posology and method of administration

Method of administration: Oral

Dosage and Administration
Children:
1 - 5 years: 2.5ml two times daily.
6 - 12 years: 5ml two times daily.
Above 12 years: 10ml two times daily

Shake the bottle before use.

4.3 Contraindications
- Cases of known hypersensitivity to any of the ingredients.
- Stomach ulcers or other intestinal diseases.
- Patients with history of impairment of vitamin absorption.
- Debilitated elderly patients
- Newborn or premature infants and young children
- Pregnant or breastfeeding mothers except if clearly needed
- Patients with angle- closure glaucoma, urinary retention, bladder neck obstruction, prostatic hyperplasia or pyloroduodenal obstruction, acute asthma, stenosing peptic ulcer and patients with history of epilepsy.
- Monoamine Oxidase Inhibitor (MAOI) therapy
- Use of CNS depressants like alcohol, hypnotics, sedatives, tranquilizers and anti-anxiety agents.

4.4 Special warnings and precautions for use
- Use with caution in patients with renal impairment

4.5 Interaction with other medicinal products and other forms of interaction

CYPROHEPTADINE

Cyproheptadine may enhance the sedative effects of CNS depressants including alcohol, barbiturates, hypnotics, opiod analgesics, anxiolytic sedatives and antipsychotics.

Cyproheptadine has an additive antimuscarinic action with other antimuscarinic drugs such as atropine and some antidepressants (both tricyclic and MAOIs).

It has been suggested that some sedating antihistamines could mask the warning signs of damage caused by ototoxic drugs such as aminoglycoside antibacterials.

Antihistamines may suppress the cutaneuos response to allergen extracts and should be stopped several days before skin testing

VITAMIN B_6 (PYRIDOXINE)

- Pyridoxine antagonizes the therapeutic action of levodopa by facilitating the transformation of levodopa into dopamine before levodopa can cross the blood-brain-barrier and enter the CNS.
- Pyridoxine reduces the activity of altretamine.
- Also, many drugs can increase the requirement for pyridoxine, such drugs include hydralazine, Isoniazid, penicillamine and oral contraceptives.

4.6 Pregnancy and Lactation

Several large studies have failed to find any strong associations between foetal abnormalities and antihistamines taken during pregnancy.
However for reasons of safety to the foetus, it is advised that cyproheptadine not be used in pregnancy and by breast feeding mothers because neonates and young children are more susceptible to the antimuscarinic effects of antihistamines.

4.7 Effects on ability to drive and use machines

Avro Apetit may cause drowsiness in some individuals. If affected, do not drive or operate machinery or appliances requiring alertness.

4.8 Undesirable effects

Side effects are rare and usually well tolerated. Most common is drowsiness. Dizziness and incoordination may also occur. Sedative effects when they occur diminish after a few days of treatment.
Gastrointestinal effects which may occur occasionally include nausea, vomiting, diarrhoea or epigastric pain.
Increase in appetite with resultant weight gain has also been reported as well as paradoxical excitement in children.

4.9 Overdose

Overdosage with sedating antihistamines is associated with antimuscarinic, extrapyramidal and CNS effects. When CNS stimulation predominates over CNS depression, which is more likely in children or the elderly, it causes ataxia, excitement, tremors, psychoses, hallucinations and convulsions; hyperpyrexia may also occur. Deepening coma and cardiorespiratory collapse may follow. In adults, CNS depression is more common with drowsiness, coma and convulsions, progressing to respiratory failure and cardiovascular collapse.
Toxicity with the water soluble vitamins is rare because their solubility makes them readily excreted from the body before toxic levels are achieved.

In the case of over dosage, the presenting symptoms are treated symptomatically after gastric lavage or evacuation has been done.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Cyproheptadine Hydrochloride

Cyproheptadine Hydrochloride a piperidine derivative is a sedating antihistamine with antimuscarinic,

serotonin-antagonist and calcium-channel blocking actions.
It is used as the hydrochloride for the symptomatic relief of allergic conditions including urticaria and angioedema, rhinitis and conjunctivitis and in pruritic skin disorder.
Cyproheptadine has been widely used as an appetite stimulant including for anorexia nervosa and cachexia (weight loss). The appetite stimulating effect of cyproheptadine may be due to its antagonizing the stimulating effect of serotonin on the satiety centre. It has been shown to stimulate appetite and weight gain in children.

Thiamine Hydrochloride (Vit B1): A water soluble vitamin. It is a co-enzyme for carbohydrate metabolism.

Riboflavine (Vit B2): A water soluble vitamin converted in the body to flavine mononucleotide and flavine adenine dinucleotide and then involved as co-enzymes in oxidative and reductive metabolic processes.

Pyridoxine Hydrochloride (Vit B6): A water soluble vitamin. Involved in carbohydrate and fat metabolism, but also important in haemoglobin formation.

Vitamin B_{12} (Cyanocobalamin)
Vitamin B_{12}, water-soluble vitamins occur in the body mainly as methylcobalamin and as adenosylcobalamin and hydroxycobalamin. It act as coenzyme in nucleic acid synthesis.
Vitamin B_{12} preparations are used in the treatment and prevention of Vitamin B_{12} deficiency.

5.2 Pharmacokinetic properties

Cyproheptadine Hydrochloride
After absorption from the gastroinstestinal tract, cyproheptadine hydrochloride undergoes almost complete metabolism.metabolism are excreted principally in the urine as conjugates, and also in the faeces.

Thiamine Hydrochloride (Vit B1)
Thiamine is well absorbed from the gastro intestinal tract following oral administration, although the absorption of large doses is limited. It is also rapidly absorbed following intra muscular administration. It is widely distributed to most body tissues and appears in breast milk. Thiamine is not stored to any appreciable extent in the body and amounts in excess of the body's requirements are excreted in the urine as unchanged Thiamine or as metabolites.
Thiamine requirements are directly related to the carbohydrate intake and the metabolic rate. A daily dietary intake of 1 to 1.3mg of Thiamine is recommended for healthy men and 0.7 to 1mg for healthy women.

Riboflavine (Vit B2)
Riboflavine is readily absorbed from the gastro intestinal tract. Although Riboflavine is widely distributed to body tissues, little is stored in the body. Riboflavine is converted in the body to the coenzyme Flavine mononucleotide and then to another coenzyme Flavine adenine dinucleotide. About 60% of FMN and FAD are bound to plasma proteins. Riboflavine is excreted in urine, mainly as metabolites. As the dose increases, larger amounts are excreted unchanged. Riboflavine crosses the placenta and is distributed in breast milk.
The Riboflavine requirement is often related to the energy intake but it appears to be more closely related to the resting metabolic requirements. A daily dietary intake of about 1.3 to 1.8mg of Riboflavine is recommended.

Pyridoxine Hydrochloride (Vit B6)
Pyridoxine is readily absorbed from the gastro-intestinal tract following oral administration and is converted to the active forms pyridoxal phosphate and pyridoxamine phosphate. They are stored mainly in the liver where there is oxidation to 4-pyridoxic acid, which is excreted in the urine. Pyridoxine crosses the placenta and also appears in the breast milk.
For adults, the daily requirement of Pyridoxine is probably about 2mg and this amount is present in most normal diets. Meats, especially liver, cereals, eggs, fish and certain vegetables and fruits are good source of Pyridoxine.

Vitamin B_{12} (Cyanocobalamin)
Vitamin B_{12} substances bind to intrinsic factor and are then actively absorbed from the gastro intestinal tract. Absorption is impaired in patients with an absence of intrinsic factor, with a malabsorption syndrome or with disease or abnormality of the gut, or after gastrectomy.

Vitamin B_{12} is extensively bound to specific plasma proteins called Transcobalamins, Transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues. It is stored in the liver, excreted in the bile and undergoes enterohepatic recycling; part of a dose is excreted in the urine, most of it in the first 8 hours. Vitamin B_{12} diffuses across the placenta and also appears in breast milk.

5.3 Preclinical safety data
No formal preclinical studies have been conducted. However all the individual ingredients are well documented in the literature and the product has been available for many years with no adverse reports recorded.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Methyl Hydroxybenzoate
Sucrose
Glycerol
Sweet Orange Flavour
Xanthan Gum
Citric Acid
Deionised Water

6.2 Incompatibilities
None known

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Store below 30°C. Protect from light.

6.5 Nature and contents of container
200ml PET bottle with plastic screw cap.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Applicant/manufacturer
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