SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

A-ferin Plus Pediatric Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 mL contains;

Paracetamol

Chlorpheniramine maleat

Pseudoephedrin HCl

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Syrup

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

A-ferin Plus, is indicated for temporary relief of fever and pain accompanying flu and common cold.

4.2 Posology and method of administration

3 months-1 years of age :	¼ spoon measure (1,25 mL) every 4-6 hours
1-2 years of age :	½ spoon measure (2,5 mL) every 4-6 hours
2-6 years of age :	1 spoon measure (5 mL) every 4-6 hours
6-12 years of age :	2 spoon measure (10 mL) every 4-6 hours

Unless the physician dictates otherwise, A-ferin Pediatric Syrup should not be used more than 4 times daily. It should be used with medical consultancy in children less than 6 years of age.

4.3 Contraindications

A-ferin should not be used in patients with known hypersensitivity to any ingredient of the product. It is also contraindicated in patients with liver failure.

Pseudoephedrin is contraindicated in patients with hypertension and coronary artery disease. A-ferin Plus, should not be used in patients using MAO inhibitors or patients used MAO inhibitors with in 2 weeks. Furazolidone and A-ferin Plus should not be used concomitantly, as an antibacterial agent furazolidon inhibits MAO.

4.4 Special warnings and precautions for use

A-ferin Plus should not be used for pain lasting longer than 5 days or in children less than 6 years of age unless it is recommended by the physician.

Prolonged treatment or administration in high doses may cause severe renal damage and changes in the blood counts.

Liver necrosis may develop. Liver necrosis is the complication of overdosage of paracetamol. Liver enzymes may elevate in 12-48 hours. Prothrombin time may prolong. However, clinical symptoms may not become overt until 1-6 days after the ingestion of the overdosage. If the patient ingested more than 10 g, toxicity risk increases significantly.

Concomitant administration of A-ferin Plus with some ototoxic antibacterial agents prevents the appearance of the signs of ototoxicity and it may not be diagnosed until it become irreversible.

A-ferin Plus should be used with caution in patients receiving anticoagulant therapy. Protrombin time should be carefully followed as parcetamol can increase the effect of anticoagulants.

As A-ferin Plus contains pseudoephedrine, should be used cautiously to the patients with arrhythmia and renal insufficiency.

A-ferin Plus should be used with caution in patients elder than 60 years old and patients with hypertension, hyperthyroidism, diabetes mellitus, cardiovascular disease, ischemic heart disease, glaucoma or prostate hypertrophy. Long term administration should be avoided. It should not be used longer than 5 days.

Geriatric patients can be more sensitive to the CNS effects of pseudoephedrine.

Long QT Syndrom causes Torsades de Pointes. Therefore it solud not be used in patients with suspected or examined QT syndrome or Torsades de Pointes. It should not be used in children under 2 years of age.

4.5 Interaction with other medicinal products and other forms of interaction

Chronic alcohol consumption can increase the heaptotoxicity of paracetamol.

Anticonvulsans such as phenytoin, barbiturate and karbamazepin induces hepatic microsomal enzymes and increases hepatotoxicity by increasing the transformation of the paracetamol to the hepatotoxic metabolites.

Concomitant use of paracetamol with isoniasid can increase the risk of hepatotoxicity, but the mechanism of interaction has not known yet.
Prolonged treatment or administration in high doses of paracetamol may increase the effect of anticoagulants.

It should be observed that hypothermia can be caused when used with Phenotiazine because of antipyretic effect.

Central depressive effects of antihistaminics can be enhanced with the concomitant use of barbiturates, tranquilizantes and alcohol.

Should not be used concomitantly with MAO inhibitors, alcohol, tranquilizer agents and central nervous depressant agent Since it may increase its anticholinergic effect.

Pseudoephedrine, must be used cautiously since it might increase the toxicity and efficiency when used with other sympathomimethic drugs.

β-adrenergic blockers like propranolole, may increase the effect of pseudoefedrine.
Pseudoefedrine may decrease the effect of antihypertensives like reserpine or methyldopa.

If anticonvulsants and steroidal contraceptives are used for a long time, they may induce the liver enzymes and increase the clearance and paracetamol metabolism.

If paracetamol and rifampin are used concomitant for a long time, hepatotoxicity risk is maximized.

4.6 Fertility, pregnancy and lactation

Pregnancy category: C

There are no adequate, well controlled studies of paracetamol and pseudoephedrine in pregnant women. For this reason, it can be used considering risk/benefit ratio.

Lactation:

It is known as paracetamol is safe in breast feeding. Pseudoephedrine is excreted with milk but there are no adequate data concerning the effects on the baby. Lactating women should use the drug if a physician recommends.

4.7 Effects on ability to drive and use machines

Avoid operating machinery or driving a motor vehicle.

4.8 Undesirable effects

Allergic reactions, skin rashes, rarely blood count disorders (leukopenia, neutropenia, pancytopenia), nausea, vomiting, constipation, lethargy, dry mouth, confusion, sleepiness, sweating, dizziness, flushing may be seen.

IN CASE OF AN UNEXPECTED SIDE EFFECT, CONSULT YOUR PHYSICIAN.

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. Healthcare professionals are asked to report any suspected adverse reactions via EFDA yellow Card Scheme, online at https://primaryreporting.who-umc.org/ET or toll free call 8482 to Ethiopian food and drug authority (EFDA).

4.9 Overdose

The overdosage of paracetamol causes hepatotoxicity. In adults and adolescents (younger than 12) in 8 hours or less 7.5 g – 10 g or even more paracetamol dosage administration may cause hepatoxicity.Death is not often seen. (3-4 % of the cases without medication) Death is rarely reported for the doses under 15 g. Hepatoxicity is is not observed under the doses of 150 mg/kg in children (under the age of 12). Potentially , after the overdosage use that may cause hepatoxicity , womiting, diaphoresis and general weakness are observed.

Clinical an laboratory symptoms related with hepatoxicity may not be observed in 48 -72 hours after the overdosage use. In adults and children , in the cases ;which the level of paracetamol used is not known or the time of use is suspected, the paracetamol level must be defined and these patients should be medicated by using N – acetylcysteine. Before starting N- acetylcysteine medication the consequences of paracetamol level in the plasma should not be waited.

Paracetamol level in the plasma should be identified as soon as possible. However examimation should be done at least 4 hours after the overdosage use. In the case of overdosage, stomach should be emptied by gastric lavage or medical aid.

The overdosage of chlorpheniramine maleate is usually treated as the overdosage of antihistamines, anticholinergic agents.

The overdosage of Pseudoephedrine HCl causes slight anxiety, hypertension, tachycardia. Symptoms are observed 4-8 hour after the overdose administration and is temporary and medication is not needed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A-ferin Plus is an antipyretic, analgesic, anti-allergic and decongestant drug.

Paracetamol has shown its analgesic and antipyretic properties in a way similar to salicylic acid. Paracetamol decreases increased body temperature hence rarely
decreases normal body temperature. Paracetamol has minimal effects on cardiovascular and respiratory system at therapeutic levels.

Chlorpheniramine maleate is an alkylamine derivative antihistamine. It competitively blocks histamine at H1 receptors and reversibly relieves the allergic signs and symptoms of allergic diseases of the upper respiratory tract such as nasal discharge, sneezing and watery eyes.

Pseudoephedrine directly effects α- and has less effect on β-adrenergic receptors. Pseudoephedrine causes vasoconstriction by directly effecting α- adrenergic receptors of respiratory tract mucosa and eases breathing by decreasing hyperemia, odema and nasal congestion. Increases drainage of sinusal secretions and relieves the obstruction of Eustachian.

5.2 Pharmacokinetic properties

Following oral administration of paracetamol, it is rapidly and almost completely absorbed. Its effect begins in 30 minutes and usually lasts for 4 hours. Paracetamol diffuses readily into most of the body fluids. Paracetamol binds to %10-30 of plasma proteins. It is metabolized in liver and excreted as glucoronide and sulfate conjugates via the kidneys. The capacity of glucoronide conjugation is low in new borns.

Chlorpheniramine maleate is well absorbed from the gastrointestinal tract. However, it goes first pass metabolism in liver and its bioavailability is decreased. Following oral administration, it achieves peak plasma concentration in 2-6 hours. Paracetamol binds to %69-72 of plasma proteins. Its elimination half-life is 12-43 hours in adult with normal renal and hepatic functions and 9,6-13,1 hours in children. It diffuses readily into body fluids including central nervous system. Chlorpheniramine is widely metabolized and excreted primarily via kidneys.

Pseudoephedrine is well absorbed from the gastrointestinal tract. It does not metabolize with the first pass. It reaches peak plasma concentrations of 180-300 ng/mL after 1.3-2 hours of administration. In pediatric patients 24 hours after the administration it reaches plasma peak concentration of 492 ng/mL. Food can delay the absorption. Nasal decongestant effect begins with in 15-30 minutes and lasts for 3-4 hours. Volume of distribution in pediatric patients is 2.4 L/kg. It is minimally metabolized in liver (less than %1) and excreted via kidneys.

5.3 Preclinical safety data

There is no animal study carried out with A-FERİN PLUS pediatric syrup.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propyl Paraben (Propyl parahydroxybenzoate (E216))
Methyl Paraben (Methyl parahydroxybenzoate (E218))
Trisodium citrate dihydrate
Sodium saccharin dihydrate
Citric acid anhydrous
Sodium chloride
Sodium CMC (200 -600 cps)

Caramel (EEH-2 SFC)

Essence Nectarin 502.881/A

Sorbitol 70% (Crystalline)

Glycerol

Polyethylene glycol 1500

Purified water

Glycerine

6.2 Incompatibilities

None

6.3 Shelf life

48 months

6.4 Special precautions for storage

Store in a dry place below 30°C.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

It is presented in 100 mL Type III amber glass bottles capped with white LDPE screwed cap with seal together with 5 mL plastic measuring spoon and patient information leaflet in cardboard box.

6.6 Special precautions for disposal <and other handling>

Any unused medicinal product or waste material should be disposed of in accordance with "Regulation on Control of Medical Waste" and "Regulation on Control of Packaging and Packaging Wastes".

7. MARKETING AUTHORISATION HOLDER

Name and address: HÜSNÜ ARSAN İLAÇLARI A. Ş. Kaptanpaşa Mah. Zincirlikuyu Cad. No: 184 34440 Beyoğlu-ISTANBUL-TURKEY

Tel: +90 (212) 365 15 00

Fax: +90 (212) 276 29 19

8. MARKETING AUTHORISATION NUMBER(S)

Certificate No: 05805/07782/REN/2021

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Mar 23, 2021

10. DATE OF REVISION OF THE TEXT

September 2023