SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

TRISPORIN

Cefdinir

1.1. Strength

125 mg/5ml

1.2. Pharmaceutical form

Powder for oral suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 Qualitative declaration

Cefdinir

For the complete list of the excipients, see section 6.1.

2.2 Quantitative declaration

Each 5 ml of Trisporin suspension contains 125 mg Cefdinir.

Excipients with known effect

Sodium benzoate 5 mg/5ml
Sucrose: 1,5 g/5ml

3. PHARMACEUTICAL FORM

Powder for oral suspension

Cream-yellow coloured, strawberry and cream flavoured, homogeneous granule powder.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Trisporin suspension is designed for treatment of pediatric infections.

- **Acute otitis media** caused by *Haemophilus influenzae* (including beta lactamase producing strains), *Streptococcus pneumoniae* (penicillin-sensitive strains only) and *Moraxella catarrhalis* (including beta-lactamase producing strains).
- **Acute maxillary sinusitis** caused by *Haemophilus influenzae* (including beta lactamese producing strains), *Streptococcus pneumoniae* (penicillin-sensitive strains only) and *Moraxella catarrhalis* (including beta-lactamase producing strains).
- **Angina and tonsillitis** caused by *Streptococcus pyogenes.*
- **Uncomplicated skin infections** caused by *Staphylococcus aureus* (including beta-lactamase producing strains) and *Streptococcus pyogenes.*

4.2. Posology and method of administration

4.2.1 Posology

Children between 6 months and 12 years

Type of infection	Posologie	Duration
• Acute Otitis Media • Acute Maxillary Sinusitis • Pharyngitis/Tonsillitis	7 mg/kg each 12 hours or 14 mg/kg in one single dose per day	5 to 10 days 10 days
• Uncomplicated Skin Infections	7 mg/kg each 12 hours	10 days

Body weight	Quantity of Trisporin Suspension 125 mg/5 ml to be administered
9 kg	2,5 ml each 12 hours or 5 ml in one single dose per day
18 kg	5 ml each 12 hours or 10 ml in one single dose per day
27 kg	7,5 ml each 12 hours or 15 ml in one single dose per day
36 kg	10 ml each 12 hours or 20 ml in one single dose per day
≥ 43 kg	12 ml each 12 hours or 24 ml in one single dose per day

- Children with a body weight of 43 kg or more have to receive the maximal daily dose of 600 mg.
- The daily dose should not exceed 600 mg.
- Once daily dosing for 10 days is as effective as BID dosing.
- Once-daily dosing have not been studied in skin infections; therefore, Trisporin suspension should be administrated twice daily in this infection.

4.2.2 Special populations

Usage in patients with renal insufficiency

- For paediatric patients with creatinine clearance <30ml/min/1.73m², the dose should be 7 mg/kg (up to 300 mg) given once daily.
- Haemodialysis removes cefdinir from the body. The recommended initial dosage is 300 mg (or 7 mg/kg) every other day. At the conclusion of each haemodialysis session, 300 mg (or 7 mg/kg) dose should be administrated. Subsequent doses should be 300 mg (or 7 mg/kg) every other day.

4.2.3 Pediatric population

- Safety and efficacy in neonates and infants under 6 months of age have not been established.
- From the age of 13 years on, Trisporin tablets are to be preferred in children.

4.2.4 Method of administration

- Oral use following reconstitution of the powder to suspension; administration via a measuring device.

  Trisporin may be administrated without regard to meals.

  Directions for the reconstitution and use of the oral suspension

  - Put clean and fresh water up to the half level of the sign on the bottle than shake well, wait for 5 minutes to get a homogeneous dispersal.
  - Add water up to the sign level and then shake again.
  - Shake the suspension well before and close the bottle tightly after each use.
  - After reconstitution, the suspension is stored at controlled room temperature; it may be used for 10 days after which any unused portion should be discarded.

4.3. Contraindications

Trisporin suspension is contraindicated

- in patients with known hypersensitivity to the cephalosporin class of antibiotics.
- In patients presenting hypersensitivity to one of the exepients listed in section 6.1.

4.4. Special warnings and precautions for use

4.4.1 General information

Cross-hypersensitivity

Before starting therapy with cefdinir, inquiry should be made to determine whether the patient has shown previous hypersensitivity reactions to cefdinir, other cephalosporins, penicillins or other drugs. If cefdinir is to be given to penicillin-sensitive patients, caution should be exercised because cross-hypersensitivity among beta-lactam antibiotics has been clearly documented and may occur in up to 10% of patients with a history of penicillin allergy. If an allergic reaction to cefdinir occurs, the drug should be discontinued. Serious

acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures including intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines and airway management with oxygen.

Pseudomembranous colitis

Cases of pseudomembranous colitis have been reported with nearly all antibacterial agents including cefdinir. Therefore, it is important to be careful in patients reporting diarrhea subsequent to the administration of antibacterial agents. Treatment with antibacterial agents alters the normal flora of the colon. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of antibiotic-associated colitis. After diagnosis of pseudomembranous colitis has been established, appropriate therapy should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation and treatment with an antibacterial drug clinically effective against *Clostridium difficile*.

Superinfection

As with other broad-spectrum antibiotics, prolonged treatment may result in overgrowth of resistant organisms. Careful observation of the patient is essential. If superinfection occurs, appropriate alternative therapy should be administrated.

Sucrose

Trisporin contains 1.5 g sucrose per 5 ml suspension. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

4.4.2 Pediatric polulation

Sodium benzoate

Trisporin contains 5 mg sodium benzoate per 5 ml suspension: may increase bilirubinaemia following its displacement from albumin it may increase neonatal jaundice which may develop in kernicterus.

4.5. Interactions with other medicinal products and food

- Cefdinir should be taken at least 2 hours before or after intake of an antiacid medicine.
- As with other drugs, probenecid inhibits the renal excretion of cefdinir.
- In the case of concomitant administration of cefdinir with iron containing drugs, cefdinir should be taken at least 2 hours before or after this drug.
- Alcohol may interfere with the actions of cefdinir.

4.6. Pregnancy, lactation and fertility

Pregnancy

There are no adequate and well-controlled studies in pregnant women, therefore it should be used during pregnancy only if clearly needed.

Lactation

After administration of single 600 mg doses, it was not detected in breast milk.

Fertility

No data available

4.7. Effects on ability to drive and use machines

Adverse effects on the ability to drive or to operate machinery have not been observed.

4.8. Undesirable effects

Undesirable effects after the use of cefdinir are mild and self-limiting.

The most common reported side effects are:

- Diarrhea (8-15%),

- Vaginal moniliasis (<4%),
- Nausea (3%),
- Rash (3%),
- Headache (2%),
- Increased urine leukocytes (2%),
- Increased urine protein (1-2%),
- Decreased lymphocytes (1%),
- Increased alkaline phosphatase (1%),
- Increased eosinophils (1%),
- Increased platelets (1%).
- Glycosuria (1%),

4.9. Overdosage

Information on cefdinir overdosage in humans is not available. Toxic signs and symptoms following overdosage with other beta-lactam antibiotics are nausea, vomiting, epigastric distress, diarrhea and convulsions. Hemodialysis removes cefdinir from the body.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Other beta-lactam antibacterials, third-generation cephalosporins
ATC code: J01DD15.

Cefdinir is a broadspectrum semisynthetic cephalosporin. Cefdinir is a third generation cephalosporin having a bactericidal effect by disrupting the synthesis of bacterial cell walls. Some micro-organisms resistant to penicillins and certain cephalosporins are still sensitive to cefdinir. Cefdinir has more affinity to penicillin binding protein (PBP) 3,2,1 of *S.aureus* and

penicillin binding protein (PBP) 2 and 3 of *E.faecalis* than the other cephalosporins. Cefdinir inhibits the myeloperoxidase excretion of neutrophils at the time of neutrophil stimulation by the mediators.

Microbiology

Cefdinir is effective on the following micro-organisms:

Aerobic Gram-Positive:

- *Staphylococcus aureus* (including beta-lactamase producing strains, excluding methicillin-resistant strains);
- *Streptococcus pneumoniae* (penicillin- sensitive strains only);
- *Streptococcus pyogenes; Staphylococcus epidermidis* (methicillin- sensitive strains only);
- *Streptococcus agalactiae*;
- *Streptococcus viridans species*;

Aerobic Gram-Negative:

- *Haemophilus influenzae* (including beta-lactamase producing strains);
- *Haemophilus parainfluenzae* (including beta-lactamase producing strains);
- *Moraxella catarrhalis* (including beta-lactamase producing strains);
- *Citrobacter diversus;*
- *Escherichia coli;*
- *Klebsiella pneumoniae;*
- *Proteus mirabilis*.

5.2. Pharmacokinetic properties

Absorption

Maximal plasma concentrations occur 2 to 4 hours postdose following oral administration. Cefdinir concentration in plasma increases with dosage, however not proportionally with the range of dosage increases. Bioavailability of cefdinir is determined 21% after using 300 mg and 16% after intake of a 600 mg cefdinir tablet.

After high-fat diet absorption of cefdinir (C_{max}) and amount (AUC) decreases respectively 16% and 10%, but this is clinical irrelevant. Cefdinir can be taken independently of meals.

Parameters following administration of one tablet of cefdinir.

	Single dose of 300 mg	Single dose of 600 mg
Cmax (µg/ml)	1,60	2,87
tmax (heures)	2,9	3,0
AUC (µg/hours/ml)	7,05	11,1

Cefdinir does not accumulate in plasma following once or twice daily administration to patients with normal renal functions.

Distribution

The mean volume of distribution is 0.67 l/kg (±0.29).
Cefdinir is 60% to 70% bound to plasma proteins in both adults and children. The protein binding is independent of concentration.

Metabolism and excretion

Cefdinir is not substantially metabolised and is eliminated mainly unchanged via renal excretion with a mean plasma elimination half-life ($t_{½}$) of 1.7 hours. Renal clearance is

2.0(±1.0) ml/min/kg after taking 300 mg and 600 mg cefdinir tablet by patients with normal renal functions. The amount excreted unchanged in urine is respectively 18.4% (±6.4) and 11.6% (±4.6). Cefdinir clearance is reduced in patients with renal dysfunction. Because renal excretion is the predominant pathway of elimination, dosage should be adjusted in patients with renal function disorder or who are undergoing hemodialysis.

5.3 Preclinical safety data

No data available

6. PHARMACEUTICAL PROPERTIES

6.1. List of excipients

- Citric Acid,
- Sodium Citrate,
- Sodium Benzoate,
- Xanthan Gum,
- Guar Gum
- Colloidal silica,
- Magnesium Stearate,
- Strawberry Flavour,
- Cream Flavour,
- Sucrose.

6.2 Incompatabilities

Not applicable

6.3 Shelf life

36 months.

6.4. Special precautions for storage

Store below 30^{o}C , in its original package.

After reconstitution, the suspension is stored at controlled room temperature; it may be used for 10 days after which any unused portion should be discarded.

6.5 Nature and contents of container

Trisporin Suspension is 65 g of a cream-yellow powder, packaged in a 100 ml graduated brown glass bottle, closed with plastic screw-cap. The box contains a measuring spoon.

6.6 Special precautions for disposal and other handlings

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7- MARKETING AUTHORISATION HOLDER AND MANUFACURING SITE ADDRESS

7.1 Marketing Authorisation Holder

Dafra Pharma GmbH Mühlenberg 7, 4052 Basel, Switzerland.

7.2 Manufacturer

PharmaVision Sanayi ve Ticaret A. Ş., Davutpaşa Cad. No: 145, 34010 Topkapı / Istanbul, Turkey.

8- MARKETING AUHORISATION NUMBER

See list of MAs per country

9- DATE OF FIRST REGISTRATION

See list of MAs per country

10- DATE OF REVISION OF TEXT

April 2019.