SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ENCEF 300 mg Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Cefdinir 300 mg

Excipient(s):
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule
Whitish-yellow dry granules in No:0 hard gelatin capsule with opaque ivory yellow body, opaque dark green cap.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

ENCEF is indicated for the treatment of the following infections caused by susceptible microorganisms.

Adults and adolescents:
- **Community-acquired pneumonia** caused by *Haemophilus influenzae* (including beta-lactamase producing strains), *Haemophilus parainfluenzae* (including beta-lactamase producing strains), *Streptococcus pneumoniae* (penicillin-sensitive strains only) and *Moraxella catarrhalis* (including beta-lactamase producing strains).
- **Acute exacerbation of chronic bronchitis** caused by *Haemophilus influenzae* (including beta-lactamase producing strains), *Haemophilus parainfluenzae* (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-lactamase producing strains), *Streptococcus pneumoniae* (penicillin-sensitive strains only) and *Moraxella catarrhalis* (including beta-lactamase producing strains).
- **Pharyngitis/tonsillitis** caused by *Streptococcus pyogenes*.
- **Uncomplicated skin and soft tissue infections** caused by *Staphylococcus aureus* (including beta-lactamase producing strains) and *Streptococcus pyogenes.*

Pediatric patients:
- **Acute bacterial 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).
- **Pharyngitis/tonsillitis** caused by *Streptococcus pyogenes.*
- **Uncomplicated skin and soft tissue infections** caused by *Staphylococcus aureus* (including beta-lactamase producing strains) and *Streptococcus pyogenes.*

4.2. Posology and method of administration

Posology/Frequency and duration of administration:
The recommended dose and duration of treatment for adults and adolescents aged 13 years and over are listed in the table below. The total daily dose for all infections is 600 mg. Once-daily dosing for 10 days is equivalent to twice-daily administration. Since single dose administration has not been studied in skin infections or pneumonia, ENCEF should be administered twice daily in these infections.

Adults and Adolescents 13 Years and Over

Type of infection	Dosage	Duration of treatment
Community-acquired pneumonia	300 mg per 12 hour period	10 days
Exacerbation of chronic bronchitis	300 mg per 12 hour period or 600 mg single daily dose	5 to 10 days 10 days
Acute maxillary sinusitis	300 mg per 12 hour period or 600 mg single daily dose	10 days 10 days
Pharyngitis/Tonsillitis	300 mg per 12 hour period or 600 mg single daily dose	5 to 10 days 10 days
Uncomplicated skin and soft tissue infections	300 mg per 12 hour period	10 days

Method of administration
ENCEF can be used regardless of meals.

Additional information on special populations:
Renal impairment
For adult patients with creatinine clearance < 30mL/min, the dose should be 300 mg given once daily. Hemodialysis removes cefdinir from the body.
The recommended initial dosage in chronic hemodialysis patients is 300 mg or 7 mg/kg every other day. At the conclusion of each hemodialysis session, 300 mg or 7 mg/kg dose should be administered.
Subsequent doses should be 300 mg or 7 mg/kg every other day.

Hepatic impairment
There is no information on the use of this drug in patients with hepatic insufficiency.

Pediatric population
Efficacy and safety in neonates and infants younger than 6 months have not been established.

Geriatric population
Dose adjustment in elderly patients is not necessary unless renal function is impaired.

4.3. Contraindications

ENCEF is contraindicated in patients with hypersensitivity to the cephalosporin class of antibiotics.

4.4. Special warnings and precautions for use

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 may occur in 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, intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines and airway management with oxygen.

Pseudomembranous colitis has been reported with nearly all antibacterial agents including cefdinir. Therefore, caution should be exercised in cases of diarrhea that develops after treatment with antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the gut and leads to the growth of bacteria such as *Clostridium*. 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. Moderate cases of pseudomembranous colitis usually respond to drug discontinuation alone. In severe colitis cases, management with fluid and electrolytes, protein supplementation and treatment with an antibacterial drug clinically effective against *Clostridium difficile* are required.

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 administered.

Cefdinir, as with other broad-spectrum antibiotics, should be administrated carefully to the patients with a history of colitis.

In patients with renal insufficiency (creatinine clearance <30 mL/min), the dose of cefdinir should be adjusted.

4.5. Interaction with other medicinal products and other forms of interaction

Antacids containing aluminum or magnesium
If antacids are required during cefdinir treatment, cefdinir should be taken at least 2 hours before or after taking antacids.

Probenecid
As with other beta-lactam antibiotics, probenecid inhibits the renal excretion of cefdinir.

Iron supplements and iron-fortified foods
If iron supplements are required during cefdinir treatment, cefdinir should be taken at least 2 hours before or after taking iron supplements.

Additional information on special populations
There are no known interactions.

Pediatric population:
There are no known interactions.

4.6. Fertility, pregnancy and lactation

General recommendation
Pregnancy category is B.

Women of childbearing potential / Birth control (Contraception)
There are no data on the use of cefdinir in women of childbearing potential.

Pregnancy
No clinical data on pregnancies are available for cefdinir.
Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy/embryonal/ fetal development/parturition or postnatal development.
Caution should be exercised when administered to pregnant women.

Breastfeeding
Cefdinir was not detected in breast milk following a single 600 mg dose.

Reproductive ability / Fertility
It has no known effect on reproductive ability

4.7. Effects on ability to drive and use machines

No effects on the ability to drive and use machines have been reported.

4.8. Undesirable effects

Most of the side effects seen in adult and adolescent patients treated with the recommended dose of cefdinir capsule (600 mg/day) in clinical trials were mild and individual. No deaths or permanent disabilities were observed. Discontinuation of drug therapy was mainly due to gastrointestinal disturbances, particularly diarrhea or nausea. Some of the patients also discontinued the treatment due to the rash.

The distribution of side effects according to their frequency is as follows:

Side effects with a frequency of 1% or more: Diarrhea, vaginal moniliasis, nausea, headache, abdominal pain, vaginitis.

Side effects with a frequency of > 0.1% to < 1%: Rash, dyspepsia, flatulence, vomiting, defecation disorder, anorexia, constipation, drowsiness, dry mouth, asthenia, insomnia, leukorrhea, moniliasis, pruritus and somnolence.

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 the national reporting system.

4.9. Overdose

Information on cefdinir overdosage in humans is not available. Symptoms following overdose of other beta-lactam antibiotics are nausea, vomiting, epigastric pain, diarrhea and convulsions. Cefdinir is removed from the body by hemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Systemic antibacterials, third-generation cephalosporins
ATC code: J01DD15

As with other cephalosporins, the bactericidal activity of cefdinir is mediated by inhibition of cell wall synthesis. Cefdinir is stable in the presence of certain beta-lactamase enzymes. As a result, many organisms resistant to penicillins and some cephalosporins are susceptible to cefdinir.

Cefdinir has been shown to be effective on many strains of the following microorganisms:

Aerobic Gram-Positive Microorganisms:
Staphylococcus aureus (including beta-lactamase producing strains)
Note: Cefdinir is inactive against methicillin-resistant staphylococci.
Streptococcus pneumoniae (penicillin-sensitive strains only)
Streptococcus pyogenes
Staphylococcus epidermidis (penicillin-sensitive strains only)
Streptococcus agalactiae
Viridans group streptococci
Cefdinir is inactive against *Enterococcus* and methicillin-resistant *Staphylococcus* species.

Aerobic Gram-Negative Microorganisms:
Haemophilus influenzae (including beta-lactamase producing strains)
Haemophilus parainfluenzae (including beta-lactamase producing strains)
Morcocella catarrhalis (including beta-lactamase producing strains)
Citrobacter diversus
Escherichia coli
Klebsiella pneumoniae
Proteus mirabilis
Note: Cefdinir is inactive against *Pseudomonas* and *Enterobacter* species.

5.2. Pharmacokinetic properties

General properties
Absorption
Maximal plasma concentrations are reached 2-4 hours after oral administration of cefdinir. The estimated bioavailability of cefdinir capsules is 21% following administration of a 300 mg capsule and 16% following administration of a 600 mg capsule.
Cefdinir can be taken regardless of meals.
Following administration of 300 mg dose of cefdinir capsules to adults, C_{max} (µg/mL), t_{max} (hour) and AUC (µg/hour/mL) values have been determined as 1.60, 2.9, 7.05 and following intake of a single dose 600 mg; 2.87, 3.0, 11.1 respectively.

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

Distribution
The mean volume of distribution of cefdinir is 0.35 L/kg (±0.29) in adults and 0.67 L/kg (±0.38) in children (6 months to 12 years). Cefdinir is 60% to 70% bound to plasma proteins in both adults and children; binding is independent of concentration.

Biotransformation
Cefdinir is not significantly metabolized.

Elimination
It is eliminated via renal excretion with a mean plasma elimination half-life ($t_{1/2}$) of 1.7 (±0.6) hours. 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.

Linearity/Nonlinearity:
Plasma cefdinir concentrations increase with dose, but the increases are less dose proportional in the range of 300 mg (7 mg/kg) to 600 mg (14 mg/kg).

Additional information on special populations
Patients with renal impairment
Dose adjustment is recommended in patients with marked renal impairment (creatinine clearance < 30 mL/min).

Hemodialysis patients:
Dose adjustment is recommended in this patient group.

Patients with hepatic impairment
Since cefdinir is primarily renally excreted and is not significantly metabolized, no dose adjustment is required in this patient group.

Elderly patients:
No dosage adjustment is required in elderly patients without renal dysfunction.

Gender and race:
Race or gender had no apparent effect on cefdinir pharmacokinetics.

5.3. Preclinical safety data

The carcinogenic potential of cefdinir has not been evaluated. No mutagenic effects were seen in the bacterial reverse mutation assay (Ames) or point mutation assay at the hypoxanthine-guanine phosphoribosyltransferase locus (HGPRT) in V79 Chinese hamster lung cells. No clastogenic effects were observed in vitro in the structural chromosome aberration assay in V79 Chinese hamster lung cells or *in vivo* in the micronucleus assay in mouse bone marrow. In rats, fertility and reproductive performance were not affected by cefdinir at oral doses up to 1000 mg/kg/day (70 times the human dose based on mg/kg/day, 11 times based on mg/m^2/day).

Cefdinir was not teratogenic in rats at oral doses up to 1000 mg/kg/day (70 times the human dose based on mg/kg/day, 11 times based on mg/m^2/day) or in rabbits at oral doses up to 10 mg/kg/day (0.7 times the human dose based on mg/kg/day, 0.23 times based on mg/m^2/day). Maternal toxicity (decreased body weight gain) was observed in rabbits at the maximum tolerated dose of 10 mg/kg/day without adverse effects on offspring. Decreased body weight occurred in rat fetuses at ≥ 100 mg/kg/day, and in rat offspring at ≥ 32 mg/kg/day. No effects were observed on maternal reproductive parameters or offspring survival, development, behavior, or reproductive function.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Carboxymethyl cellulose
Polyoxyl 40 stearate
Croscarmellose sodium
Colloidal silicon dioxide
Magnesium stearate

Excipients in the capsule structure:
Titanium dioxide
Indigotine FD&C Blue #2
Yellow iron oxide
Gelatine

6.2. Incompatibilities

There is no known incompatibility.

6.3. Shelf life

36 months

6.4. Special precautions for storage

Store at room temperature below 25°C.

6.5. Nature and contents of container

Primary packaging material is opaque PVC-Aclar/Aluminium blister.
Available in packs of 10 and 20 capsules.

6.6. Special precautions for disposal and other handling

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

7. MARKETING AUTHORIZATION HOLDER

DEVA Holding A.Ş.
Halkalı Merkez Mah. Basın Ekspres Cad. No:1
34303 Küçükçekmece - İSTANBUL/TÜRKİYE

8. MARKETING AUTHORIZATION NUMBER

239/93

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization : 01.02.2012
Date of last renewal :

10. DATE OF REVISION OF THE TEXT

14.06.2017