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1.4.1 Prescribing information (Summary of Product Characteristics)

1. Name of the medicinal product

Cefi-Q Oral Solution 100mg/5ml

2. Qualitative and quantitative composition

Each 5mL contains
Cefixime……100mg
(As Cefixime Trihydrate)

Excipients with known effect:

Each ml contains 472 mg of Sucrose (Sugar).

3. Pharmaceutical form

Oral suspension.

4. Clinical particulars

4.1 Therapeutic indications

Cefixime is indicated for oral treatment of the following bacterial infections when caused by susceptible organisms.

- Acute exacerbations of chronic bronchitis
- Community – acquired pneumonia
- ENT infections (e.g. otitis media, sinusitis, tonsillitis, pharyngitis, laryngitis)
- Uncomplicated lower urinary tract infections including gonococcal urethritis
- Uncomplicated pyelonephritis

4.2 Posology and method of administration

Adults

The usual daily dose is 200-400 mg in single or twice daily dosage regimen. The recommended dose of cefixime is 400 mg daily. For the treatment of uncomplicated cervical/urethral gonococcal infections, a single oral dose of 400 mg is recommended. The capsule may be administered without regard to food.

In the treatment of infections due to Streptococcus pyogenes, a therapeutic dosage of cefixime should be administered for at least 10 days.

Pediatric Patients (6 months or older)

The recommended dose is 8 mg/kg/day of the suspension. This may be administered as a single daily dose or may be given in two divided doses, as 4 mg/kg every 12 hours.

PEDIATRIC DOSAGE CHART			
		100 mg/5 mL	200 mg/5 mL
Patient Weight (kg)	**Dose/Day (mg)**	**Dose/Day (mL)**	**Dose/Day (mL)**
5 to 6.2	50	2.5	1.25
6.3 to 12.5	100	5	2.5
6.3 to 12.5	150	7.5	3.75
18.9 to 25	200	10	5
25.1 to 31.3	250	12.5	6.25
31.4 to 37.5	300	15	7.5
37.6 to 43.8	350	17.5	8.75
43.9 to 50	400	20	10

Children weighing more than 50 kg or older than 12 years should be treated with the recommended adult dose.
Otitis media should be treated with the suspension. Clinical trials of otitis media were conducted with the suspension, and the suspension results in higher peak blood levels than the tablet when administered at the same dose.
In the treatment of infections due to Streptococcus pyogenes, a therapeutic dosage of cefixime should be administered for at least 10 days

Renal Impairment

Cefixime may be administered in the presence of impaired renal function. Normal dose and schedule may be employed in patients with creatinine clearances of 60 mL/min or greater. Patients whose clearance is between 21 and 60 mL/min or patients who are on renal hemodialysis may be given 6.5 ml of Cefixime for Oral Suspension (200 mg/5 mL) daily or 13 ml of Cefixime for Oral Suspension (100 mg/5 mL) daily. Patients whose clearance is 20 mL/min or less, or patients who are on continuous ambulatory peritoneal dialysis may be given 200 mg daily (i.e. half of the 400 mg tablet). Neither hemodialysis nor peritoneal dialysis removes significant amounts of drug from the body.
After reconstitution, the suspension may be kept for 14 days either at room temperature, or under refrigeration, without significant loss of potency. Keep tightly closed. Shake well before using.
Discard unused portion after 14 days.

4.3 Contraindications

Cefixime is contraindicated in cases of hypersensitivity to Cefixime, to any other cephalosporin antibiotics, or a known immediate and severe hypersensitivity reaction to penicillin or any beta-lactam antibiotic or to one of the excipients of the medicinal product.
For cross allergy Cefixime is contraindicated in preterm and term newborn infants (0-27 days).

4.4 Special warnings and precautions for use

Hypersensitivity Reactions

Anaphylactic/anaphylactoid reactions (including shock and fatalities) have been reported with the use of cefixime.
Before therapy with Cefixime is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins, or other drugs. If this product 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 Cefixime occurs, discontinue the drug.

Clostridium difficile-Associated Diarrhea

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Cefixime, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.
C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing isolates of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

Dose Adjustment in Renal Impairment
The dose of cefixime should be adjusted in patients with renal impairment as well as those undergoing continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis (HD). Patients on dialysis should be monitored carefully.

Coagulation Effects
Cephalosporins, including cefixime, may be associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.

Development of Drug-Resistant Bacteria
Prescribing cefixime in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

4.6 Fertility, pregnancy and lactation
Pregnancy:
There is insufficient evidence of safety for use during human pregnancy. Animal studies do not reveal a teratogenic effect Cefixime passes through the placenta. The risk/benefit of administration of Cefixime should be highly critically considered, in particular during the first 3 months of pregnancy.
Lactation:
No Cefixime concentrations could be determined in breast milk. Nevertheless, until further clinical experience is available, Cefixime should not be given to nursing mothers or they should use a breast pump for the duration of therapy and dispose of the milk.
Fertility:
Reproduction studies performed in mice and rats have revealed no evidence of impaired fertility.

4.7 Effects on ability to drive and use machines
Cefixime has **no known influence** on the ability to drive and use machines. However, side effects (for example vertigo) may occur, which may influence the ability to drive and use machines.

4.8 Undesirable effects

Very common (≥ 1/10)
Common (≥ 1/100 to < 1/10)
Uncommon Rare (≥ 1/1,000 to <1/100)
Rare (≥ 1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)

System Organ Class	Common ≥1/100 to <1/10	Uncommon ≥1/1,000 to <1/100	Rare ≥1/10,000 to <1/1,000	Very rare <1/10,000	Not known (cannot be estimated from the available data)
Infections and infestations			Prolonged or repeated use may lead to secondary superinfections caused by insusceptible bacteria or fungi.		
Blood and lymphatic system disorders			Eosinophilia	Alteration in blood picture like for example leukopenia, agranulocytosis, pancytopenia or thrombocytopenia. Blood clotting impairment, hemolytic anemia.	Granulocytopenia
Immune system disorders1			Hypersensitivity reactions in all degrees, – such as flush, palpitations, dyspnea, drop in blood pressure, bronchospasm, angioneurotic oedema. Severe acute hypersensitivity reactions may manifest as: Facial oedema, swollen tongue, swelling of the inner larynx with restriction of airway, racing heart, shortness of breath (respiratory distress), and decrease of blood pressure leading to life threatening shock. Any of these occurrences requires immediate medical treatment.	Anaphylactic shock, Reactions similar to serum disease such as arthralgia, arthritis, joint swelling, myalgia, urticaria	

Nervous system disorders2		Headache	Dizziness	Transient hyperactivity	Convulsions
Gastrointestinal disorders	Soft stools and diarrhea	Disorders in the form of stomach ache, digestive impairment, nausea, vomiting	Lack of appetite, flatulence	Cases of pseudomembranous colitis	
Hepatobiliary disorders		A reversible increase in liver enzymes (transaminase, alkaline phosphatase) in serum		Hepatitis and cholestatic jaundice	Increase of bilirubin
Skin and subcutaneous tissue disorders		Skin rashes (erythema, exanthema)	Pruritus and inflammation of the mucous membranes	Erythema exsudativum multiforme, Lyell syndrome and Stevens-Johnson syndrom3	DRESS syndrome
Renal and urinary disorders			Transient increase in urea concentrations in serum have been	Increase in creatinine concentrations in serum, interstitial nephritis	Acute renal failure including tubulointestinal nephritis
General disorders and administration site conditions			Mucosal inflammation, pyrexia Drug fever		

1 Severe acute hypersensitivity reactions may manifest as:
Facial oedema, swollen tongue, swelling of the inner larynx with restriction of airway, racing heart, shortness of breath (respiratory distress), decrease of blood pressure leading to life-threatening shock. Any of these occurrences requires immediate medical treatment.
2 As with other cephalosporins, a raised tendency to convulsive attacks cannot be ruled out.
3 Lyell syndrome and Stevens-Johnson syndrome may result in life-threatening conditions.

4.9 Overdose

Symptoms of intoxication

Intoxication in its strictest sense is unknown.

Treatment of intoxication

Treatment is done by symptomatic measures. No relevant amounts of substance are eliminated by haemodialysis or peritoneal dialysis. There is no specific antidote known.

5. Pharmacological properties
5.1 Pharmacodynamic properties
Mechanism of Action
Bactericidal action of cefixime results from inhibition of cell-wall synthesis. Cefixime has been shown to be active against most isolates of the following bacteria both in vitro and in clinical infections

Gram-positive bacteria
Streptococcus pneumoniae
Streptococcus pyogenes
Gram-negative bacteria
Haemophilus influenzae
Moraxella catarrhalis
Escherichia coli
Proteus mirabilis
Neisseria gonorrhoeae

The following in vitro data are available, but their clinical significance is unknown. Cefixime exhibits in vitro MICs of 1 mcg/mL or less against most (≥ 90%) isolates of the following bacteria; however, the safety and effectiveness of Cefixime in treating clinical infections due to these bacteria have not been established in adequate and well-controlled clinical trials.

Gram-positive bacteria
Streptococcus agalactiae
Gram-negative bacteria
Haemophilus parainfluenzae
Proteus vulgaris
Klebsiella pneumoniae
Klebsiella oxytoca
Pasteurella multocida
Providencia species
Salmonella species
Shigella species
Citrobacter amalonaticus
Citrobacter diversus
Serratia marcescens

Susceptibility Tests Methods
When available, the clinical microbiology laboratory should provide the results of in vitro susceptibility test results for antimicrobial drugs used in resident hospitals to the physician as periodic reports that describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting an antibacterial drug product for treatment.

Dilution Techniques:
Quantitative methods are used to determine the minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using standardized test methods (broth, and/or agar). The MIC values should be interpreted according to the criteria in Table 1.

Diffusion Techniques:
Quantitative methods that require measurement of zone diameters can also
provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The zone size provides an estimate of the susceptibility of bacteria to antimicrobial compounds. The zone size should be determined using standardized method.2,3 This procedure uses paper disks impregnated with 5 mcg of cefixime to test the susceptibility of bacteria to cefixime. The disk diffusion interpretive criteria are provided in Table 1.

Table 1: Susceptibility interpretive criteria for cefixime

Pathogen	**Minimum Inhibitory Concentrations (mcg/ml)**			**Disk Diffusion Zone Diameter (mm)**		
	S	I	R	S	I	R
Neisseria gonorrhoeae	≤ 0.25	- a	-	≥ 31	-	-
H. influenzae	≤1	-	-	≥21	-	-
E. coli and P. mirabilis	≤1	2	≥4	≥19	16 - 18	≤15

A report of "Susceptible" indicates that the antimicrobial is likely to inhibit growth of the pathogen if the antimicrobial compound reaches the concentration at the infection site necessary to inhibit growth of the pathogen. A report of "Intermediate" indicates that the result should be considered equivocal, and if the microorganism is not fully susceptible to alternative clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated. This category also provides a buffer zone that prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of "Resistant" indicates that the antimicrobial is not likely to inhibit growth of the pathogen if the antimicrobial compound reaches the concentrations usually achievable at the infection site; other therapy should be selected.

Quality Control
Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of supplies and reagents used in the assay, and the techniques of the individuals performing the test. The standard cefixime powder should provide the following range of MIC values provided in Table 2. For the diffusion technique using the 5-mcg cefixime disk the criteria provided in Table 2 should be achieved.

Table 2: Acceptable Quality Control Ranges for Susceptibility Testing

Quality Control Organisms	**Minimum Inhibitory Concentrations (mcg/ml)**	**Disk Diffusion (zone diameters in mm)**
E. coli ATCC 25922	0.25 - 1	23 - 27
S. aureus ATCC 29213	8 - 32	-
H. influenzae ATCC 49247	0.12-1	25-33
N. gonorrhoeae ATCC 49226 0	0.004 - 0.03	37 - 45

Pharmacokinetic properties
Cefixime tablets and suspension, given orally, are about 40% to 50% absorbed whether administered with or without food; however, time to maximal absorption is increased approximately 0.8 hours when administered with food. A single 200 mg tablet of cefixime produces an average peak serum concentration of approximately 2 mcg/mL (range 1 to 4 mcg/mL); a single 400 mg tablet produces an average peak concentration of approximately 3.7 mcg/mL (range 1.3 to 7.7 mcg/mL). The oral suspension produces average peak concentrations approximately 25% to 50% higher than the tablets, when tested in normal adult volunteers. Two hundred and 400 mg doses of oral suspension produce average peak concentrations of 3 mcg/mL (range 1 to 4.5 mcg/mL) and 4.6 mcg/mL (range 1.9 to7.7 mcg/mL), respectively, when tested in normal adult volunteers. The area under the time versus concentration curve (AUC) is greater by approximately 10% to 25% with the oral suspension than with the tablet after doses of 100 to 400 mg, when tested in normal adult volunteers. This increased absorption should be taken into consideration if the oral suspension is to be substituted for the tablet. Because of the lack of bioequivalence, tablets should not be substituted for oral suspension in

the treatment of otitis media. Crossover studies of tablet versus suspension have not been performed in children.

The 400 mg capsule is bioequivalent to the 400 mg tablet under fasting conditions. However, food reduces the absorption following administration of the capsule by approximately 15% based on AUC and 25% based on Cmax.

Peak serum concentrations occur between 2 and 6 hours following oral administration of a single 200 mg tablet, a single 400 mg tablet or 400 mg of cefixime suspension. Peak serum concentrations occur between 2 and 5 hours following a single administration of 200 mg of suspension.

Distribution
Serum protein binding is concentration independent with a bound fraction of approximately 65%. In a multiple dose study conducted with a research formulation which is less bioavailable than the tablet or suspension, there was little accumulation of drug in serum or urine after dosing for 14 days. Adequate data on CSF levels of cefixime are not available.

Metabolism and Excretion
There is no evidence of metabolism of cefixime in vivo. Approximately 50% of the absorbed dose is excreted unchanged in the urine in 24 hours. In animal studies, it was noted that cefixime is also excreted in the bile in excess of 10% of the administered dose. The serum half-life of cefixime in healthy subjects is independent of dosage form and averages 3 to 4 hours but may range up to 9 hours in some normal volunteers.

Special Populations
Geriatrics: Average AUCs at steady state in elderly patients are approximately 40% higher than average AUCs in other healthy adults. Differences in the pharmacokinetic parameters between 12 young and 12 elderly subjects who received 400 mg of cefixime once daily for 5 days are summarized as follows:

Pharmacokinetic Parameters (mean ± SD) for Cefixime in Both Young & Elderly Subjects		
Pharmacokinetic parameter	**Young**	**Elderly**
Cmax (mg/L)	4.74 ± 1.43	5.68 ± 1.83
Tmax (h)*	3.9 ± 0.3	4.3 ± 0.6
AUC (mg.h/L)*	34.9 ± 12.2	49.5 ± 19.1
T½ (h)*	3.5 ± 0.6	4.2 ± 0.4
Cave (mg/L)*	1.42 ±0.50	1.99 ± 0.75
*Difference between age groups was significant. ($p<0.05$)		

5.3 Preclinical safety data
Lifetime studies in animals to evaluate carcinogenic potential have not been conducted. Cefixime did not cause point mutations in bacteria or mammalian cells, DNA damage, or chromosome damage in vitro and did not exhibit clastogenic potential in vivo in the mouse micronucleus test. In rats, fertility and reproductive performance were not affected by cefixime at doses up to 25 times the adult therapeutic dose.

6. Pharmaceutical particulars

6.1 List of excipients

Sucrose (Sugar)
Sodium Benzoate
Xanthan Gum
Colloidal Silicon
Dioxide (Aerosil 200)
Strawberry Durarome
Flavour
Purified Talc
Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 30ºC, protected from moisture and light.
Keep out of the reach and sight of children.

6.5 Nature and contents of container

60ml Amber glass bottle with powder enclosed with P.P Aluminum cap along with 20ml Purified water filled in plastic bottle enclosed with plastic nozzle, 5ml Plastic Spoon and Package Insert

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.