Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Suprax 100mg/5ml Powder for Paediatric Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml dose of reconstituted suspension and each single dose sachet contains 100 mg cefixime.

Excipients - contains sucrose 2.525g

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Powder for oral suspension
When reconstituted with water gives a strawberry flavoured suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For use in the treatment of infections due to micro-organisms sensitive to the antibiotic including pathogens such as *Streptococci pneumoniae and pyogenes*, *E.coli*, Proteus, *H. influenza* and *B. catarrhalis* (both beta lactamase positive and negative), Klebsiella and Enterobacter species.

Most Enterococci, Staphylococci, Pseudomonas, Clostridia, *Bacteroides fragili*s and *Listeria monoyctogenes* are resistant to Cefixime.

4.2 Posology and method of administration

Route of administration is oral.

Adults and children of 12 years and over (or more than 50kg body weight):
The usual daily dose is 200-400mg in single or twice daily dosage regimen.
In uncomplicated upper respiratory tract infections or urinary tract infections a daily dose of 200 mg may be sufficient.

Children aged 9 to 12 years:
The usual total daily dose is 300mg (15ml of oral suspension) in single or twice daily regimen.

Children aged 5 to 8 years:
The usual total daily dose is 200 mg (10ml of oral suspension) in single or twice daily dosage regimen.

Children aged 2 to 4 years:
The usual total daily dose is 100 mg (5ml of oral suspension) in single or twice daily dosage regimen.

Children aged 6 months to 2 years:
The usual total daily dose in 8 mg/kg in single or twice daily regimen.

The safety and efficacy of use in infants less than 6 months of age has not been established.

Elderly:
The usual dosage is as for adults with appropriate modifications on the basis of renal impairment.

Patients with Renal Impairment
Dosage does not require modification in patients with a creatinine clearance of 20 ml/minute or greater.

In patients with a creatinine clearance less than 20 ml/minute a dose of 200 mg once daily should not be exceeded. The same dosage regimen is applied to those patients maintained on chronic ambulatory peritoneal dialysis or haemodialysis.

4.3 Contraindications

Cefixime is contraindicated in patients with known hypersensitivity to the cephalosporin group of antbiotics or any of the other components of the product.

4.4 Special warnings and precautions for use

- Prolonged use of an anti-infective may result in overgrowth of non-susceptible organisms. With an oral medication the normal colonic flora may be altered allowing the overgrowth by Clostridia with consequent pseudomembranous colitis.

- Severe cutaneous adverse reactions such as toxic epidermal necrolysis, Stevens-Johnson syndrome and drug rash with eosinophilia and systemic symptoms (DRESS) have been reported in some patients on cefixime. When severe cutaneous adverse reactions occur, cefixime should be discontinued and appropriate therapy and/or measures should be taken.

- Emergence of resistance to cefixime has not to date been shown to be clinically significant. Nevertheless it is recommended that newer antibiotics such as cefixime should usually be reserved for infections which are recurrent or resistant to other agents.

- Particular care should be exercised in patients with severe gastrointestinal disturbances involving vomiting and diarrhoea. The product should be discontinued if severe diarrhoea develops.

- As with other cephalosporins, cefixime may cause acute renal failure including tubulointerstitial nephritis as an underlying pathological condition. When acute renal failure occurs, cefixime should be discontinued and appropriate therapy and/or measures should be taken.

- The product should be used with caution in patients with renal functional impairment. Renal function should be monitored with particular care when combining cefixime with aminoglycoside antibiotic, polymyxin B, colistin or high-dosed loop diuretics (e.g. furosemide). This is applied especially to patients with pre-existing renal impairment.

- Cross allergenicity may exist between cephalosporins and penicillins. Use of the product should be cautious in patients allergic to penicillins.

- Particular care should be exercised in patients with poor oral nutrition, patients receiving parenteral nutrition, elderly patients or patients in a debilitated state.

- Particular care should be exercised in patients with a personal or familial predisposition to allergic reaction such as bronchial asthma, rash or urticaria.

- Adverse reactions to drugs are liable to occur more frequently in the elderly patients since they usually have physiological hypofunction. Bleeding tendency due to Vitamin K deficiency may occur in the elderly.

- The safety of cefixime in premature or newborn infant has not been established.

- Drug-induced haemolytic anaemia, including severe cases with a fatal outcome, has been described for cephalosporins (as a class). The recurrence of haemolytic anaemia after re-administration of cephalosporins in a

patient with a history of cephalosporin (including cefixime) –associated haemolytic anaemia has also been reported.

- Beta-lactams, including cefixime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment.

4.5 Interaction with other medicinal products and other forms of interaction

Cefixime should be administered with caution to patients receiving coumarin-type anticoagulants, e.g. warfarin potassium. Since cefixime may enhance effects of the anticoagulants, prolonged prothrombin time with or without bleeding may occur.

A false positive direct Coomb's test may occur with cefixime.

The administration of cefixime may result in false-positive results for glucose in the urine using Benedict's solution, Fehling's solution, or Clinitest. It is recommended that glucose tests based on enzymatic glucose oxidase reactions (e.g. Tes-Tape) be used.

4.6 Fertility, pregnancy and lactation

Pregnancy:
Safety of cefixime in pregnant women has not been established.

Lactation:
It is not known whether cefixime is excreted in human milk.

4.7 Effects on ability to drive and use machines

In the case of side effects such as encephalopathy (which may include convulsions, confusion, impairment of consciousness, movement disorders), the patient should not operate machines or drive a vehicle.

4.8 Undesirable effects

The following adverse reactions will be considered listed:

System Organ Class	Preferred Term
Blood and lymphatic system class:	Eosinophilia Granulocytopenia Haemolytic anaemia Thromocytopenia Prolonged PT/Coagulation
Gastrointestinal disorders:	Abdominal pain Diarrhoea Dyspepsia Nausea Vomiting Anorexia Flatulence
General disorders and administration site conditions:	Pyrexia Face oedema
Hepatobiliary disorders:	Jaundice Hepatitis
Infections and infestations:	Pseudomembranous colitis Vaginitis

Immune System Disorders:	Anaphlactic reaction Serum sickness-like reaction
Investigations:	Aspartate aminotransferase increased Alanine aminotransferase increased Blood alkaline phosphatase increased Blood bilirubin increased Blood urea increased Blood creatinine increased
Nervous System Disorders:	Dizziness Headache *Frequency not known:* Cases of convulsions have been reported with cephalosporins including cefixime Beta-lactams, including cefixime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment.
Respiratory, thoracic and mediastinal disorders:	Dyspnoea
Renal and urinary disorders	Renal failure acute including tubulointerstitial nephritis as an underlying pathological condition
Skin and subcutaneous tissue disorders:	Drug Rash with eosinophilia and systemic symptoms (DRESS) Erythema multiforme Pruritus Rash Stevens-Johnson syndrome Toxic epidermal necrolysis Urticaria Genital pruritus

The above mentioned listed adverse reactions have been observed during clinical studies and/or during marketed use.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

4.9 Overdose

Signs and Symptoms
There is a risk of encephalopathy in cases of administration of beta-lactam antibiotics, including cefixime, particularly in case of overdose or renal impairment.

No specific antidote exists. General supportive measures are recommended.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Cefixime inhibits the cell wall synthesis of various bacteria. Cefixime has high affinity for penicillin binding proteins (PBP) 1 (1a, 1b and 1c) and 3 and prevents cross-linking reaction. Cefixime has broad spectrum activity against Gram-positive and Gram-negative bacteria. Sensitivity will vary according to area, and local prescribing guidelines should always be consulted. Where possible microbiological sensitivity tests should guide treatment as resistance can emerge. Its mechanism of action is bactericidal.

5.2 Pharmacokinetic properties

Absorption:
Following oral administration of cefixime to healthy volunteers, peak serum concentrations are generally attained in 3 to 4 hours. After a single oral dose of 50, 100 and 200mg mean peak serum concentrations were 1.02, 1.46 and 2.63 mg/L respectively in 12 healthy volunteers of Western origin and 0.69, 1.13 and 1.95 mg/L respectively in 12 healthy Japanese volunteers.

Paediatric Populations:
Following a single oral dose of 1.5, 3.0 and 6.0 mg/kg of cefixime in Japanese paediatric patients, maximum serum concentrations at around 3 to 4 hours were 1.14, 2.01 and 3.97 mg/L, respectively.

Distribution:
In human plasma, cefixime is approximately 70% protein bound, a value not concentration dependent in the range 0.5 to 30mg/L. Cefixime is distributed to target organs/tissues such as tonsils, maxillary sinus mucosal tissue, lung tissue and gallbladder tissue.

Metabolism & Excretion:
No biologically active metabolites of cefixime were identified in plasma or urine following oral administration to healthy volunteers. Around 20% of a 200mg dose of cefixime is recovered unchanged over 24 hours in the urine of healthy volunteers. The elimination half-life is 2-4 hours.

Renal Impairment:
Studies in patients with various degrees of renal dysfunction administered single 400mg oral doses of cefixime indicated that elimination half-life, oral clearance (CL/F), renal clearance and AUC were altered in patients with severe renal dysfunction (creatinine clearance < 20 mL/min) and in those on hemodialysis or continuous ambulatory peritoneal dialysis (CAPD), as compared with healthy subjects. Please also see section 4.4

Table Pharmacokinetic properties (mean values) of cefixime in healthy volunteers and patients with various degrees of renal dysfunction

Study Group	CLCr (mL/min/1.73m^2)	Cmax (mg/L)	Tmax (h)	$T1/2_\beta$ (h)	AUC (mg.h/L)	CL/F (mL/kg/h)	Renal Clearance (mL/kg/h)
Healthy Volunteers	111	4.9	4.9	3.2	40	141	22
Renal dysfunction							
Very mild	71	5.8	4.0	4.7	57	127	22
Mild	51	7.6	4.5	7.0	90	70	10
Moderate	28	7.5	3.5	7.2	100	80	3.7
Severe	9.8	9.6	6.0	11.5#	188#	41#	2.1#
Hemodialysis	1.3	6.2	4.8	8.2	94	73	0.4#
CAPD	3.0	10.2	5.0	14.9#	220#	42#	0.5#

Difference statistically significant compared with healthy volunteers
Abbreviations: CLCr = creatinine clearance, $T1/2_\beta$= elimination half life, Cl/F = oral clearance, CAPD = continuous ambulatory peritoneal dialysis
#p <0.05 compared with healthy volunteers

5.3 Preclinical safety data

No relevant data.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Xanthium gum
Sodium benzoate
Strawberry flavour

Containing:
Maltodextrin
Acacia gum
Propylene glycol
Glyceryl triacetate
Maltol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

(a) The shelf life expiry date for this product shall not exceed 2 years.
(b) After reconstitution the suspension can be stored for up to two weeks at room temperature.
(c) Any unused suspension should be discarded and not stored for subsequent use.

6.4 Special precautions for storage

Do not store above 25ºC. Do not freeze.

Do not keep suspension after 14 days of first opening.

6.5 Nature and contents of container

Bottles: Type III amber screw necked bottle with child resistant push/turn closure with white polyethylene cap with polyethylene film seal on expanded low density polyethylene.

The bottles are supplied with a single ended transparent polypropylene (plastic) measuring spoon.

Pack sizes: 5ml (sample pack), 37.5ml, 50ml, 75ml, 100ml.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

To reconstitute: shake to loosen powder. Add 4ml of water (5ml bottle), 25ml of water (37.5ml bottle), 33ml of water (50ml bottle), 50ml of water (75ml bottle) or 66ml of water (100ml bottle) in two portions shaking after each addition.

After reconstitution, the suspension may be stored at room temperature (below 25) for 14 days without significant loss of potency.

Do not freeze. Discard any unused portion after 14 days. Keep bottles tightly closed and shake well before use.

Dilution of the suspension is not recommended.

7 MARKETING AUTHORISATION HOLDER

Sanofi-Aventis Ireland Ltd. T/A SANOFI
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0540/016/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 05 January 1989

Date of last renewal: 05 January 2009

10 DATE OF REVISION OF THE TEXT

March 2018