AUSTRALIAN PRODUCT INFORMATION
APO-CEFACLOR (CEFACLOR MONOHYDRATE)
SUSPENSION

1  NAME OF THE MEDICINE
Cefaclor monohydrate.

2  QUALITATIVE AND QUANTITATIVE COMPOSITION
Each bottle contains either 125 mg or 250 mg cefaclor per 5mL when reconstituted.

Excipients with known effect
Sodium benzoate, sucrose.
For the full list of excipients see section 6.1 List of Excipients.

3  PHARMACEUTICAL FORM
125 mg/5 mL
White to off-white granular powder which forms a red strawberry flavoured suspension upon reconstitution with 70 mL water.

250 mg/5 mL
White to off-white granular powder which forms a red strawberry flavoured suspension upon reconstitution with 53 mL water.

4  CLINICAL PARTICULARS
4.1  THERAPEUTIC INDICATIONS
Cefaclor is indicated for the treatment of the following types of infections caused by or likely to be caused by susceptible organisms:

- **Lower respiratory infections**, including pneumonia, bronchitis and exacerbations of chronic bronchitis.
- **Upper respiratory tract infections**, including pharyngitis, tonsillitis and otitis media.
- **Skin and skin structure infections**.
- **Urinary tract infections**, including pyelonephritis and cystitis.

Note:
1. Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. Cefaclor appears to be as effective as phenoxybenzylpenicillin in the eradication of streptococci from the nasopharynx; however, substantial data establishing the efficacy of cefaclor in the subsequent prevention of rheumatic fever are not available at present.

2. Appropriate culture and susceptibility studies should be performed to determine susceptibility of the causative organism to cefaclor.
4.2 DOSE AND METHOD OF ADMINISTRATION

APO-Cefaclor Oral Suspension is intended for oral administration.

Reconstitution of Oral Suspension

For 125 mg/5 mL bottles add 70 mL water, in two portions, to the granular powder. Shake well after each addition.

For 250 mg/5 mL bottles add 53 mL water, in two portions, to the granular powder. Shake well after each addition.

The reconstituted suspension should be stored under refrigeration at 2-8°C. The suspension may be kept for 14 days without significant loss of potency.

Adults

The usual adult dosage is 250 mg every eight to twelve hours. For bronchitis and pneumonia, the dosage is 250 mg three times daily. For more severe infections or those caused by less susceptible organisms, doses may be doubled (500 mg every eight hours).

Doses of 2 g daily should not be exceeded.

For skin and skin structure infections, the dosage is 250 mg two to three times daily.

Children

The usual recommended daily dosage for children with mild to moderate infections is 20 mg/kg/day in divided doses every 8 hours. The maximum dose is 1 g daily.

For streptococcal pharyngitis or tonsillitis and impetigo, administration every twelve hours appears equally effective.

In more serious infections, otitis media and infections caused by less susceptible organisms, the recommended dosage is 40 mg/kg/day in divided doses every eight to twelve hours (maximum 2 g/day). For otitis media, administration every twelve hours appears equally effective.

Renal Impairment

Cefaclor may be administered in the presence of impaired renal function. Under such a condition, the dosage is usually unchanged (see section 4.4 – Special warnings and precautions for use).

β-haemolytic Streptococcal Infections

In the treatment of β-haemolytic streptococcal infections, a therapeutic dosage of cefaclor should be administered for at least ten days.

4.3 CONTRAINDICATIONS

Known allergy to cephalosporins or previous experience of a major allergy to penicillin (see section 4.4 – Special warnings and precautions for use) or any of the excipients listed (see section 6.1 List of excipients).

Infants under the age of 1 month; safety and efficacy of this product have not been established in premature infants and infants under 1 month of age.
4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Except under special circumstances, this medication should not be used when the following medical problem exists:

Penicillin Sensitive Patients, or those with Hypersensitivity to other Allergens

Cephalosporin antibiotics should be administered cautiously in this patient group. There is clinical and laboratory evidence of partial cross allergenicity of the penicillins and the cephalosporins and there are instances in which patients have had reactions, including anaphylaxis, to both drug classes. Serious and occasionally fatal hypersensitivity (anaphylactic/anaphylactoid) reactions have been reported in patients on penicillin/cephalosporin therapy. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins/cephalosporins. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin/cephalosporin hypersensitivity who have experienced severe reactions when treated with a penicillin/cephalosporin.

Severe Allergic Reaction to Penicillin or Cephalosporin Class of Drugs, or other Allergens

Past history of a severe allergic reaction to drug from the penicillin or cephalosporin group of drugs is a contraindication to the use of cefaclor. Before initiating therapy with any cephalosporin careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. If an allergic reaction occurs, cefaclor should be discontinued and the appropriate therapy instituted. Serious anaphylactoid reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids and airway management, including intubation, should also be administered as indicated.

History of Colitis or Gastrointestinal Disease

Broad spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, especially ulcerative colitis, regional enteritis, or antibiotic-associated colitis.

Risk-Benefit Should be Considered when the following medical problems exist:

Pseudomembranous Colitis

Antibiotic associated pseudomembranous colitis has been reported with many antibiotics including cefaclor. A toxin produced with Clostridium difficile appears to be the primary cause. The severity of the colitis may range from mild to life threatening. It is important to consider this diagnosis in patients who develop diarrhoea or colitis in association with antibiotic use (this may occur up to several weeks after cessation of antibiotic therapy). Mild cases usually respond to drug discontinuation alone. However, in moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against Clostridium difficile should be considered. Fluids, electrolytes and protein replacement should be provided when indicated.

Drugs which delay peristalsis, e.g. opiates and diphenoxylate with atropine (Lomotil), may prolong and/or worsen the condition and should not be used.

History of Bleeding Disorders

All cephalosporins may cause hypoprothrombinaemia and, potentially, bleeding.

Adequate Treatment Period
As with antibiotic therapy in general, administration of cefaclor should be continued for a minimum of 48 to 72 hours after the patient becomes asymptomatic or after evidence of bacterial eradication has been obtained. A minimum of 10 days of treatment is recommended in infections caused by group A β-haemolytic Streptococci in order to guard against the risk of rheumatic fever or glomerulonephritis.

**Prolonged Use of Cefaclor**

This may result in the overgrowth of non-susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

**Use in Hepatic Impairment**

Cefaclor should be used with caution in patients with hepatic disease, as documented clinical experience in this group of patients is lacking.

**Use in Renal Impairment**

Many cephalosporins are excreted renally. Cefaclor should be administered with caution in the presence of markedly impaired renal function. Since the half-life of cefaclor in anuria is 2.3 to 2.8 hours, dosage adjustments for patients with moderate or severe renal impairment are usually not required. Clinical experience with cefaclor under such conditions is limited; therefore, careful clinical observation and laboratory studies should be made.

**Use in the Elderly**

Cephalosporins have been used in the geriatric population, and no geriatrics-specific problems have been documented to date. However, elderly patients are more likely to have an age-related decrease in renal function, which may require and adjustment in dosage and/or dosing interval in patients receiving cephalosporins.

**Paediatric Use**

Safety and effectiveness of this product for use in infants less than 1 month of age have not been established. Serum sickness-like reactions including arthritis and arthralgia have been reported more frequently in children than in adults.

**Effects on Laboratory Tests**

**Glucose, Urine**

Administration of cefaclor may result in a false positive reaction for glucose in the urine. This phenomenon has been seen in patients taking cephalosporin antibiotics when the test is performed using Benedict’s and Fehling’s solutions and also with Clinitest tablets but not with Tes-Tape (Glucose Enzymatic Test Strip USP).

**Coombs’ (antiglobulin) Tests**

Positive direct Coombs’ tests have been reported during treatment with cefaclor. In haematological studies or in transfusion cross matching procedures when antiglobulin tests are performed on the minor side or in Coombs’ testing of newborn infants whose mothers have received cephalosporin antibiotics before parturition, it should be recognised that a positive Coombs’ test may be due to the drug.

**Dental**

Long-term therapy with cephalosporins may allow for the overgrowth of *Candida albicans*, resulting in oral candidiasis.
4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Anti-coagulants, Coumarin- or Indandione-derivative, or Heparin or Thrombolytic Agents
Because all cephalosporins can inhibit vitamin K synthesis by suppressing gut flora, prophylactic vitamin K therapy is recommended when any of these medications is used for prolonged periods in malnourished or seriously ill patients.

Platelet Aggregation Inhibitors
Hypoprothrombinaemia induced by large doses of salicylates and/or cephalosporins, and the gastrointestinal ulcerative or hemorrhagic potential of non-steroidal anti-inflammatory drugs (NSAIDs), salicylates, or sulfinpyrazone may increase the risk of haemorrhage.

Antacids
The extent of absorption of cefaclor is diminished if magnesium or aluminium hydroxide containing antacids are taken within one hour of administration.

Probenecid
As with other ß-lactam antibiotics, the renal excretion of cefaclor is inhibited by probenecid.

Probenecid decreases renal tubular secretion of those cephalosporins excreted by this mechanism, resulting in increased and prolonged cephalosporin serum concentrations, prolonged elimination half-life, and increased risk of toxicity.

Prothrombin Time (PT)
May be prolonged.

Creatinine (serum)
Concentrations may be increased.

Carnitine or Haematocrit
Values may decrease during therapy.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility
Adequate and well-controlled studies in humans have not been done. Reproduction studies have revealed no evidence of impaired fertility.

Use in Pregnancy
Category B1

The oral administration of high dose cefaclor (500 mg/kg) in pregnant rats and mice has resulted in a slight increase of minor skeletal malformation. Safety of this product for use during pregnancy has not been established. Cefaclor should not be used in women of childbearing potential unless, in the judgment of the treating physician, its use is considered essential to the welfare of the patient and the expected benefits outweigh potential risks.

Use in Lactation
Small amounts of cefaclor have been detected in breast milk following administration of single 500 mg doses of cefaclor. Average levels were 0.18, 0.20, 0.21 and 0.16 µg/mL at 2, 3, 4 and 5 hours respectively. Trace amounts were detected at 1 hour. The effect on breastfed infants is not known. Caution should be exercised when cefaclor is administered to a breastfeeding woman.
Labour and Delivery
Cefaclor has not been studied for use during labour and delivery. Treatment should be given only if clearly needed.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
The effects of this medicine on a person’s ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Gastrointestinal
The most frequent side effect has been diarrhoea. Nausea and vomiting have been reported rarely. Colitis, including rare instances of pseudomembranous colitis, has been reported in conjunction with therapy with cefaclor (see section 4.4 – Special warnings and precautions for use). Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.

Hepatic
Transient hepatitis and cholestatic jaundice have been reported rarely.

Immune System Disorders
Hypersensitivity - Allergic reactions, such as urticaria and morbilliform eruptions, have been observed, as have pruritus and positive Coombs’ tests. These reactions usually subsided upon discontinuation of the drug. Angioedema and fever have been reported rarely.

Cases of serum sickness-like reactions have been reported with the use of cefaclor. These have been reported more frequently in children than in adults, with an overall occurrence ranging from 0.5% (1 in 200) in one trial, to 0.024% (2 in 8,346) in overall clinical trials (with an incidence in children in clinical trials of 0.055%). The worldwide reporting rate for serum sickness-like reactions in adults is very rare (<0.01%). Serum sickness-like reactions are characterised by findings of erythema multiforme, rashes and other skin manifestations accompanied by arthritis/arthralgia, with or without fever, and differ from classic serum sickness in that there is infrequently associated lymphadenopathy and proteinuria, no circulating immune complexes and no evidence to date of sequelae of the reaction. While further investigation is ongoing, serum sickness-like reactions appear to be due to hypersensitivity and more often occur during or following a second (or subsequent) course of therapy with cefaclor. Such reactions have been reported more frequently in children than in adults. Signs and symptoms usually occur a few days after initiation of therapy and subside within a few days after cessation of therapy; occasionally these reactions have resulted in hospitalisation, usually of short duration (median hospitalisation: 2 to 3 days, based on postmarketing surveillance studies). In those requiring hospitalisation, the symptoms have ranged from mild to severe at the time of admission with more of the severe reactions occurring in children. Antihistamines and glucocorticoids appear to enhance resolution of the signs and symptoms. No serious sequelae have been reported. More severe hypersensitivity reactions, including Stevens-Johnson syndrome, toxic epidermal necrolysis and anaphylaxis, have been reported rarely. Anaphylaxis may be more common in patients with a history of penicillin allergy. The worldwide reporting rate for anaphylaxis in the total population is very rare (<0.01%).

Anaphylactoid events may present as solitary symptoms, including angioedema, asthenia, oedema (including face and limbs), dyspnoea, paraesthesias, syncope, or vasodilatation.

Rarely, hypersensitivity symptoms may persist for several months.
The following reactions have been reported rarely in patients treated with cefaclor:

**Hepatobiliary Disorders**

Hepatic dysfunction, including transient hepatitis and cholestatic jaundice have been reported rarely.

**Blood and Lymphatic System Disorders**

Eosinophilia, transient lymphocytosis leucopenia and, rarely, thrombocytopenia, thrombocytosis, haemolytic anaemia, aplastic anaemia, agranulocytosis and reversible neutropenia of possible clinical significance. There have been rare reports of increased prothrombin time with or without clinical bleeding in patients receiving cefaclor and warfarin concomitantly.

There have also been reports of transient fluctuations in leucocyte count, predominantly lymphocytosis in infants and young children.

**Renal and Urinary Disorders**

Slight elevation in serum urea or serum creatinine or abnormalities of urinalysis (haematuria; pyuria), reversible interstitial nephritis.

**Superinfection**

Genital pruritus, moniliasis or vaginitis.

**Nervous System Disorders**

Rarely, reversible hyperactivity, nervousness, insomnia, confusion, hypertonia, dizziness, hallucinations, headache or somnolence have been reported.

**Other**

Transitory abnormalities in clinical laboratory test results have been reported, but their clinical significance is uncertain. These include slight elevations in AST, ALT or alkaline phosphatase values; transient fluctuations in leukocyte count, predominantly lymphocytosis in infants and young children; and slight elevations in serum urea or serum creatinine or abnormalities of urinalysis (haematuria, pyuria).

The following adverse reactions have been reported in patients treated with other beta-lactam antibiotics:

Renal dysfunction, and toxic nephropathy.

Several beta-lactam antibiotics have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy should occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

**Reporting Suspected Adverse Effects**

Reporting suspected adverse reactions after registration 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 at http://www.tga.gov.au/reporting-problems and contact Apotex Medical Information enquiries/Adverse Drug Reaction Reporting on 1800 195 055.
4.9 OVERDOSE

Symptoms

The toxic symptoms following an overdose of cefaclor may include nausea, vomiting, epigastric distress and diarrhoea. The severity of the epigastric distress and the diarrhoea are dose related. If other symptoms are present, it is probable that they are secondary to an underlying disease state, an allergic reaction, or the effects of other intoxication.

Treatment

In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in the patient.

Protect the patient’s airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient’s vital signs, blood gases, serum electrolytes, etc. Absorption of drugs from the gastrointestinal tract may be decreased by giving activated charcoal, which in many cases is more effective than emesis or lavage; consider charcoal instead of or in addition to gastric emptying. Repeated doses of charcoal over time may hasten elimination of some drugs that have been absorbed. Safeguard the patient’s airway when employing gastric emptying or charcoal.

Forced diuresis, peritoneal dialysis, haemodialysis or charcoal haemoperfusion have not been established as beneficial for an overdose of cefaclor.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Cefaclor is a semisynthetic, broad spectrum cephalosporin antibiotic for oral administration.

Mechanism of Action

Microbiology

*In vitro* tests demonstrate that the bactericidal action of the cephalosporins results from inhibition of cell wall synthesis. Cefaclor is stable in the presence of bacterial β-lactamases; consequently, β-lactamase producing organisms resistant to penicillins and some cephalosporins may be susceptible to cefaclor. Cefaclor has been shown to be active against most strains of the following organisms both *in vitro* and in clinical infections:

Staphylococci, including coagulase positive and penicillinase producing strains (but not methicillin resistant strains of *Staphylococcus aureus*);

*Streptococcus pyogenes* (group A β-haemolytic Streptococci), *Streptococcus (Diplococcus) pneumoniae*;

*Escherichia coli*;

*Proteus mirabilis*;

*Klebsiella sp*;

*Haemophilus influenzae*;
Neisseria gonorrhoeae (penicillinase and non-penicillinase producing strains);

Moraxella (Branhamella) catarrhalis.

Note: Pseudomonas sp., Acinetobacter calcoaceticus, Enterococci, Enterobacter sp., indole-positive Proteus, and Serratia sp. are resistant to cefaclor. Methicillin resistant strains are also resistant to cefaclor.

Susceptibility Testing

**Dilution or diffusion techniques** – either quantitative (MIC) or breakpoint, should be used following a regularly updated, recognised and standardised method (e.g. NCCLS). Standardised susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures.

A report of “Susceptible” indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable.

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 or in situations where high dosage of drug can be used. This category also provides a buffer zone, which prevents small uncontrolled technical factors from causing major discrepancies in interpretation.

A report of “Resistant” indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.

Note: The prevalence of resistance may vary geographically for selected species and local information on resistance is desirable, particularly when treating severe infections.

Clinical Trials

No data available.

5.2 **PHARMACOKINETIC PROPERTIES**

Absorption

Cefaclor is well absorbed after oral administration, whether taken with food or while fasting. However, when it is taken with food, the peak concentration achieved is 50 to 75% of that observed when the drug is administered to fasting subjects and generally appears from 45 to 60 minutes later. The presence of food in the gastrointestinal tract does not alter the total amount of cefaclor absorbed.

Following administration of 250 mg, 500 mg and 1 g doses to fasting subjects, average peak plasma levels of antibacterial activity (expressed as µg/mL of cefaclor) of 7, 13 and 23 µg/mL, respectively, were obtained at 30 to 60 minutes. The reduced peak serum levels resulting from the administration of cefaclor with food should be considered with reference to the sensitivity of the infecting organism, severity of illness, the dose being administered and the variability in the peak plasma levels which occur with cefaclor.

The plasma half-life in healthy subjects is independent of dosage form and averages 40 to 60 minutes. In elderly subjects (>65 years) with normal serum creatinine values, a higher peak plasma concentration and area under the curve are effects resulting from mildly diminished renal function and are not expected to have clinical significance. Therefore dosage change is not necessary in elderly subjects with normal renal function.
Metabolism
There is no evidence of metabolism of cefaclor in humans.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity
No data available.

Carcinogenicity
No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

- Xanthan gum
- Sodium benzoate
- Sucrose
- Colloidal anhydrous silica
- Allura red AC
- Strawberry flavouring (PI)
- Sodium citrate dihydrate
- Citric acid
- Simethicone emulsion (PI).

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Powder

Store below 25°C. Protect from light and moisture.

After Mixing

Store in a refrigerator (2 - 8°C. Refrigerate. Do not freeze). Discard unused suspension after 14 days.

6.5 NATURE AND CONTENTS OF CONTAINER

125 mg/5 mL
HDPE bottles of 100 mL when reconstituted (AUST R 226396).

250 mg/5 mL
HDPE bottles of 75 mL when reconstituted (AUST R 226397).
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Cefaclor monohydrate is a white to off-white crystalline powder, slightly soluble in water, but is insoluble in alcohol and chloroform.

**Chemical structure**

![Chemical structure of Cefaclor monohydrate]

Chemical name: 3-chloro-7-D-(2-phenylglycinamido)-3-cephem-4-carboxylic acid monohydrate.

**CAS number**

70356-03-5.

**Molecular Formula:** \( \text{C}_{15}\text{H}_{14}\text{ClN}_{3}\text{O}_{4}\text{S.H}_{2}\text{O.} \)

**Molecular Weight:** 385.8.

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 – Prescription Only Medicine.

8 SPONSOR

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9 DATE OF FIRST APPROVAL

26 February 2010.

10 DATE OF REVISION

22 September 2018.
## Summary table of changes

<table>
<thead>
<tr>
<th>Section Changed</th>
<th>Summary of new information</th>
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<td>All sections</td>
<td>Reformatted product information</td>
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| 6.1             | Update ingredient name to comply with the new Australian Approved Name (AAN) as per current TGA approved terminology for medicines in the TGA eBusiness Services code tables.  
|                 | Sodium citrate changed to sodium citrate dihydrate.  
|                 | Anhydrous citric acid changed to citric acid. |