The magnitude of these age and gender-related variations in the pharmacokinetics of cefprozil was approximately 35-60% higher than that of healthy young adults and comparable to age and gender variations observed in normal adult subjects. The AUC of cefprozil to pediatric patients after 7.5, 15 and 30 mg/kg doses is similar to that observed in normal adult subjects approximately 1.5 hours. The plasma elimination half-life is 5.9 hours. The half-life is shortened during hemodialysis to 2.1 hours. Excretion pathways in patients with markedly impaired renal function have been determined. The plasma half-life prolongation is related to the degree of the renal dysfunction and may be prolonged up to 5.2 hours. In patients with complete absence of renal function, the plasma half-life of cefprozil averaged 18.3 hours. Plasma protein binding is approximately 36% and is independent of concentration in the range of 2 mcg/mL to 20 mcg/mL. There is no evidence of accumulation of cefprozil in the plasma in individuals with normal renal function following multiple oral doses of up to 1 g every 8 hours for 10 days.

### Pharmacokinetics

Cefprozil is well absorbed following oral administration in both fasting and non-fasting subjects. The oral bioavailability of cefprozil is about 90%. The pharmacokinetics of cefprozil are not altered when administered with meals, or when coadministered with antacid. Average plasma concentrations after administration of cefprozil to fasting subjects are shown in the following table. Urinary recovery accounts for 60% of the administered dose.

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Mean Plasma Cefprozil* Concentrations (mcg/mL)</th>
<th>8-hour Urinary Excretion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Peak-1.5 hr</td>
<td>4 hr</td>
</tr>
<tr>
<td>250 mg</td>
<td>6.1</td>
<td>1.7</td>
</tr>
<tr>
<td>500 mg</td>
<td>10.5</td>
<td>3.2</td>
</tr>
<tr>
<td>1 g</td>
<td>18.3</td>
<td>8.4</td>
</tr>
</tbody>
</table>

*Data represent mean values from 12 healthy, young male volunteers.

During the first four-hour period after drug administration, the average urine concentrations following the 250 mg, 500 mg, and 1 g doses were approximately 170 mcg/mL, 450 mcg/mL and 600 mcg/mL, respectively. The average plasma half-life in normal subjects is 1.3 hours. Plasma protein binding is approximately 36% and is independent of concentration in the range of 2 mcg/mL to 20 mcg/mL. There is no evidence of accumulation of cefprozil in the plasma in individuals with normal renal function following multiple oral doses of up to 1 g every 8 hours for 10 days.

### Special Populations and Conditions

**In patients with renal insufficiency:** In patients with reduced renal function, the plasma half-life prolongation is related to the degree of the renal dysfunction and may be prolonged up to 5.2 hours. In patients with complete absence of renal function, the plasma half-life of cefprozil averaged 5.9 hours. The half-life is shortened during hemodialysis to 2.1 hours. Excretion pathways in patients with markedly impaired renal function have not been determined. (See PRECAUTIONS and DOSAGE AND ADMINISTRATION.)

**In patients with hepatic insufficiency:** In patients with impaired hepatic function, no differences in pharmacokinetic parameters were observed, when compared to normal control subjects.

**In elderly subjects:** Following administration of a single 1 g dose of cefprozil, the average AUC observed in healthy elderly subjects (≥65 years of age) was approximately 35-60% higher than that of healthy young adults and the average AUC in females was approximately 15-20% higher than in males. The magnitude of these age and gender-related variations in the pharmacokinetics of cefprozil are not sufficient to necessitate dosage adjustments.

**In pediatric subjects:** Comparable pharmacokinetic parameters of cefprozil are observed between pediatric patients (6 months-12 years) and adults following oral administration. The maximum plasma concentrations are achieved at 1-2 hours after dosing. The plasma elimination half-life is approximately 1.5 hours. The AUC of cefprozil to pediatric patients after 7.5, 15 and 30 mg/kg doses is similar to that observed in normal adult subjects after 250, 500 and 1000 mg doses, respectively.

### INDICATIONS AND CLINICAL USE

Cefprozil (cefpodoxime) is indicated for the treatment of the following infections caused by susceptible strains of the designated microorganisms:

**Upper Respiratory Tract**

Pharyngitis/tonsillitis caused by group A β-hemolytic (GABHS) Streptococcus pyogenes.

Substantial data establishing the efficacy of cefprozil in the subsequent prevention of rheumatic fever are not available at present, although no case was reported during its evaluation in over 978 pediatric and 831 adult patients in controlled clinical trials.

Otitis media caused by Streptococcus pneumoniae, Haemophilus influenzae and Moraxella (Branhamella) catarrhalis.

Acute sinusitis caused by Streptococcus pneumoniae, Haemophilus influenzae, (beta-lactamase positive and negative strains), and Moraxella (Branhamella) catarrhalis.

**Skin and Skin Structure**

Uncomplicated skin and skin-structure infections caused by Staphylococcus aureus (including penicillinase-producing strains) and Streptococcus pyogenes.

**Urinary Tract**

Uncomplicated urinary tract infections (including acute cystitis) caused by Escherichia coli, Klebsiella pneumoniae and Proteus mirabilis.

Cultures and susceptibility studies should be performed when appropriate.

### CONTRAINDICATIONS

Sandoz Cefprozil is contraindicated in patients with known allergy to the cephalosporin class of antibiotics or to any component of the cefprozil preparations (see AVAILABILITY OF DOSAGE FORMS, Composition).

### WARNINGS

**Hypersensitivity**

BEFORE THERAPY WITH SANDOZ CEPFROZIL IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPFROZIL, CEPHALOSPORINS, PENICILLINS OR OTHER DRUGS. IF THIS PRODUCT IS TO BE GIVEN TO PENICILLIN-SENSITIVE PATIENTS, CAUTION SHOULD BE EXERCISED BECAUSE CROSS-SENSITIVITY 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 Sandoz Cefprozil occurs, discontinue the drug. Serious acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures, including oxygen, intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines, and airway management, as clinically indicated.

**Gastrointestinal**

Clostridium difficile-associated disease

Clostridium difficile-associated disease (CDAD) has been reported with use of many antibacterial agents, including cefprozil. CDAD may range in severity from mild diarrhea to fatal colitis. It is important to consider this diagnosis in patients who present with diarrhea, or symptoms of colitis, pseudomembranous colitis, toxic megacolon, or perforation of colon subsequent to the administration of any antibacterial agent. CDAD has been reported to occur over 2 months after the administration of antibacterial agents.

Treatment with antibacterial agents may alter the normal flora of the colon and may permit overgrowth of Clostridium difficile. C. difficile produces toxins A and B, which contribute to the development of CDAD. CDAD may cause significant morbidity and mortality. CDAD can be refractory to antimicrobial therapy.
If the diagnosis of COAD is suspected or confirmed, appropriate therapeutic measures should be initiated. Mild cases of COAD usually respond to discontinuation of antibacterial agents not directed against *Clostridium difficile*. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial agent clinically effective against *Clostridium difficile*. Surgical evaluation should be instituted as clinically indicated, as surgical intervention may be required in certain severe cases (see ADVERSE REACTIONS).

**Hemolytic Anemia**

**SANDOZ CEFPROZIL SHOULD NOT BE USED IN PATIENTS WITH A HISTORY OF CEPHALOSPORIN-ASSOCIATED HEMOLYTIC ANEMIA SINCE THE RECURRENCE OF HEMOLYSIS IS MUCH MORE SEVERE.**

An immune mediated hemolytic anemia has been observed in patients receiving cephalosporin class antibacterials. Severe cases of hemolytic anemia, including fatalities, have been reported in both adults and children. If a patient develops anemia anytime during, or within 2-3 weeks subsequent to the administration of cefprozil, the diagnosis of a cephalosporin-associated anemia should be considered and the drug discontinued until the etiology is determined.

Patients may benefit from periodic monitoring for signs and symptoms of hemolytic anemia, including measurement of hematological parameters or drug-induced antibody testing, where appropriate (see ADVERSE REACTIONS).

**Phenyketonurics**

Sandoz Cefprozil (ceprozil powder for oral suspension) contains aspartame, a source of phenylalanine (28 mg of phenylalanine per 5 mL).

**PRECAUTIONS**

**General**

Evaluation of renal status before and during therapy is recommended, especially in seriously ill patients. In patients with known or suspected renal impairment (see DOSAGE AND ADMINISTRATION), careful clinical observation and appropriate laboratory studies should be done prior to and during therapy. The total daily dose of cefprozil should be reduced in patients with creatinine clearance values <30 mL/min because high and/or prolonged plasma antibiotic concentrations can occur from usual doses in such individuals. Cephalosporins, including cefprozil, should be given with caution to patients receiving concurrent treatment with potent diuretics since these agents are suspected of adversely affecting renal function.

Prolonged use of cefprozil 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.

Positive direct Coombs tests have been reported during treatment with cephalosporin antibiotics.

Sandoz Cefprozil should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

**Drug Interactions**

Nephrotoxicity has been reported following concomitant administration of aminoglycoside antibiotics and cephalosporin antibiotics. Concomitant administration of probenecid doubled the area under the curve for cefprozil.

If an aminoglycoside is used concurrently with cefprozil, especially if high dosages of the former are used or if therapy is prolonged, renal function should be monitored because of the potential nephrotoxicity and ototoxicity of aminoglycoside antibiotics.

**Drug/laboratory test interactions:** Cephalosporin antibiotics may produce a false-positive reaction for glucose in the urine with copper reduction tests (Benedict’s or Feiling’s solution or with Clinitest tablets), but not with enzyme-based tests (glucose oxidase) for glycemia. A false-negative reaction may occur in the ferricyanide test for blood glucose. The presence of cefprozil in the blood does not interfere with the assay of plasma or urine creatinine by the alkaline picrate method.

**Use in pregnancy:** Reproduction studies have been performed in mice, rats and rabbits at doses 14, 7 and 0.7 times the maximum human daily dose (1000 mg) based upon mg/m², and have revealed no evidence of harm to the fetus due to cefprozil. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk.

**Nursing mothers:** Less than 1.0% of a maternal dose is excreted in human milk. Caution should be exercised when Sandoz Cefprozil is administered to a nursing mother. Consideration should be given to temporary discontinuation of nursing and use of formula feeding.

**Pediatric use:** The use of cefprozil in the treatment of acute sinusitis in these age groups is supported by evidence from adequate and well-controlled studies of cefprozil in adults and from pediatric pharmacokinetic studies.

Safety and effectiveness in children below the age of 6 months have not been established. Accumulation of other cephalosporin antibiotics in newborn infants (resulting from prolonged drug half-life in this age group) has been reported.

**Geriatric use:** Cefprozil has not been studied in the chronically ill or institutionalized elderly subjects. In these subjects, drug clearance by the kidney may be reduced even with normal serum creatinine clearance. Reduction of dose or of frequency of administration may be indicated.

**ADVERSE REACTIONS**

The adverse reactions to cefprozil are similar to those observed with other orally administered cephalosporins. Cefprozil was usually well tolerated in controlled clinical trials. Approximately 2% of patients discontinued cefprozil therapy due to adverse events.

The most common adverse events (of probable or unknown relationship to study drug) observed in 4227 patients treated with cefprozil in clinical efficacy trials are:

**Gastrointestinal:** Diarrhea (2.7%), nausea (2.3%), vomiting (1.4%) and abdominal pain (0.9%).

**Hepatobiliary:** As with some penicillins and some other cephalosporin antibiotics, cholestatic jaundice has been reported rarely.

**Hypersensitivity:** Rash (1.2%), erythema (0.1%), pruritus (0.3%) and urticaria (0.07%). 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.

**CNS:** Dizziness, hyperactivity, headache, nervousness, insomnia, confusion and drowsiness have been reported rarely (<1%) and causal relationship is uncertain. All were reversible.

**Other:** Genital pruritus (0.8%) and vaginitis (0.7%).

**Laboratory abnormalities**

Transient abnormalities in clinical laboratory test results of uncertain etiology have been reported during clinical trials as follows:

**Hepatobiliary:** Elevations of AST, ALT, alkaline phosphatase, and bilirubin.

**Hematopoietic:** Transiently decreased leukocyte count and eosinophilia.

**Renal:** Slight elevations in BUN and serum creatinine.

Adverse reactions reported from post-marketing experience and which were not seen in the clinical trials include anaphylaxis (see WARNINGS), angioedema, serum sickness, colitis including pseudomembranous colitis (see WARNINGS), erythema multiforme, fever, Stevens-Johnson syndrome, thrombocytopenia and exfoliative dermatitis. Tooth discoloration has been reported during post-marketing surveillance. The association between these events and cefprozil administration is unknown.

Hepatotoxicity, including hepatitis, has been reported during post-marketing surveillance, including cases in which a causal role of cefprozil could not be excluded.

In addition to the adverse reactions listed above which have been observed in patients treated with cefprozil, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics. Toxic epidermal necrolysis, renal dysfunction, toxic nephropathy, aplastic anemia, hemolytic anemia (see WARNINGS), hemorrhage, prolonged prothrombin time, positive Coombs’s tests, elevated LDH, pancytopenia, neutropenia, agranulocytosis.

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment, when the dosage was not reduced...
REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
  - Postal Locator 0701E
  - Ottawa, (Ontario) K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre immediately.

Since no case of overdose has been reported to date, no specific information on symptoms or treatment of overdose is available. In animal toxicology studies, single doses as high as 5000 mg/kg were without serious or lethal consequences.

Cefprozil is eliminated primarily by the kidneys. In case of severe overdosage, especially in patients with compromised renal function, hemodialysis will aid in the removal of cefprozil from the body.

DOSE AND ADMINISTRATION

Recommended Dose and Dosage Adjustment

Sandoz Cefprozil (cefprozil) is administered orally (with or without food), in the treatment of infections due to susceptible bacteria in the following doses:

Adults (13 years and older)
- Upper respiratory tract (pharyngitis/tonsillitis) 500 mg q24h
- Acute sinusitis 250 mg or 500 mg q12h
- Skin & skin structure 250 mg q12h or 500 mg q24h
- Uncomplicated urinary tract 500 mg q24h

Children (2 years-12 years)
- Skin & skin structure 20 mg/kg q24h

* Ages given are a useful guide only. Correct dosage should be determined by weight.

Infants and children (6 months-12 years)

<table>
<thead>
<tr>
<th>Age * (years)</th>
<th>Weight (kg)</th>
<th>Multidose Bottle</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>125 mg/5 mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>tsp/dose mL/dose</td>
</tr>
<tr>
<td>0–6</td>
<td>1.5–9</td>
<td>2.0</td>
</tr>
<tr>
<td>7–9</td>
<td>11–15</td>
<td>3.0</td>
</tr>
<tr>
<td>10–11</td>
<td>22–30</td>
<td>4.0</td>
</tr>
</tbody>
</table>

* Ages given are a useful guide only. Correct dosage should be determined by weight.

Per weight dosing for infants and children:

**Sandoz Cefprozil for oral suspension 125 mg/5 mL and 250 mg/5 mL are available in bottles of 75 mL and 100 mL.**

Dosage forms

Sandoz Cefprozil for oral suspension contains cefprozil, in an orange-flavoured mixture, equivalent to 125 mg or 250 mg cefprozil per 5 mL of constituted solution.

Composition

In addition to the active ingredient cefprozil, Sandoz Cefprozil for oral suspension also contains: aspartame, citric acid, colloidial silicone dioxide, colours (natural and artificial), FD&C Yellow no. 6, microcrystalline cellulose, sodium benzoate, sodium carboxymethylcellulose, sodium chloride, simethicone, sucrose, polysorbate 80 and glucose.

Packaging

Sandoz Cefprozil for oral suspension 125 mg/5 mL and 250 mg/5 mL are available in bottles of 75 mL and 100 mL.
STORAGE AND STABILITY

Sandoz Cefprozil powder for oral suspension must be stored between 15 and 30°C and protected from light and excessive humidity.

RECONSTITUTION

Prior to dispensing, the pharmacist must constitute the dry powder with water as follows:

<table>
<thead>
<tr>
<th>Sandoz Cefprozil for oral suspension</th>
<th>Bottle size (mL)</th>
<th>Diluent (water) added to bottle (mL)</th>
<th>Approximate available volume (mL)</th>
<th>Final concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>125 mg/5 mL</td>
<td>75</td>
<td>54</td>
<td>75</td>
<td>125 mg/5 mL</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>72</td>
<td>100</td>
<td>125 mg/5 mL</td>
</tr>
<tr>
<td>250 mg/5 mL</td>
<td>75</td>
<td>54</td>
<td>75</td>
<td>250 mg/5 mL</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>72</td>
<td>100</td>
<td>250 mg/5 mL</td>
</tr>
</tbody>
</table>

For ease in preparation, the water can be added in two portions. Shake well after each addition and prior to use.

STORAGE OF RECONSTITUTED SUSPENSION

The constituted Sandoz Cefprozil oral suspension must be refrigerated between 2 and 8°C for up to 14 days. Keep container tightly closed. Discard unused portion after 14 days.

This leaflet was prepared by Sandoz Canada Inc.