CEFOXITIN- cefoxitin injection, powder, for solution
SAMSON MEDICAL TECHNOLOGIES LLC

CEFOXITIN FOR INJECTION, USP

Rx only

PHARMACY BULK PACKAGE – NOT FOR DIRECT INFUSION

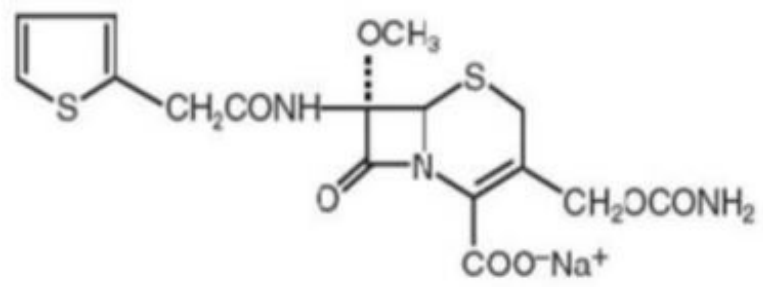
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cefoxitin for Injection, USP and other antibacterial drugs, Cefoxitin for Injection, USP should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

DESCRIPTION:

Cefoxitin for Injection, USP, Pharmacy Bulk Package bag SmartPak® should be used only in patients who require a 1 gram dose and not any fraction thereof. Cefoxitin for Injection USP, Pharmacy Bulk Package bag SmartPak® should not be used in patients who require less than the 1 gram dose of cefoxitin.

Cefoxitin for Injection, USP is a semi-synthetic, broad-spectrum cepha antibiotic for intravenous administration. It is derived from cephamycin C, which is produced by *Streptomyces lactamdurans*. Its chemical name is sodium (*6R,7S*)-3-(hydroxymethyl)-7-methoxy-8-oxo-7-[2-(2-thienyl)acetamido]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate carbamate (ester).

The empirical formula is $C_{16}H_{16}N_3NaO_7S_2$, and the structural formula is:



Cefoxitin for Injection contains approximately 53.8 mg (2.3 mEq) of sodium per gram of cefoxitin.

Solutions of Cefoxitin for Injection, USP range from colorless to light amber in color. The pH of freshly constituted solutions usually ranges from 4.2 to 7.0.

BEFORE ADMINISTRATION, THIS PHARMACY BULK PACKAGE REQUIRES RECONSTITUTION USING STERILE WATER FOR INJECTION, USP TO A CONCENTRATION OF 100 MG PER ML AND FURTHER DILUTION IN 50 ML OF A COMPATIBLE SOLUTION AND INFUSED INTRAVENOUSLY.

THIS PRODUCT IS NOT INTENDED TO BE USED IN PEDIATRIC AND RENALLY IMPAIRED PATIENTS WHO REQUIRE LESS THAN A 1 GRAM DOSE.

Each SmartPak® Pharmacy Bulk Package contains sterile Cefoxitin Sodium, USP equivalent to 100 grams of cefoxitin and is intended for intravenous infusion only. A Pharmacy Bulk Package is a container of a sterile preparation for parenteral use that contains many single doses. The contents are intended for use in a pharmacy admixture service and are restricted to the preparation of admixtures for intravenous infusion. FURTHER DILUTION IS REQUIRED BEFORE USE. **RECONSITITUTED BULK SOLUTION SHOULD NOT BE USED FOR DIRECT INFUSION.**

CEFOXITIN FOR INJECTION, USP SMARTPAK® PHARMACY BULK PACKAGE SHOULD NOT BE USED IN PATIENTS WHO REQUIRE LESS THAN A 1 GRAM DOSE OF CEFOXTIN.

CLINICAL PHARMACOLOGY:

Clinical Pharmacology

Following an intravenous dose of 1 gram of cefoxitin, serum concentrations were 110 mcg/mL at 5 minutes, declining to less than 1 mcg/mL at 4 hours. The half-life after an intravenous dose is 41 to 59 minutes. Approximately 85 percent of cefoxitin is excreted unchanged by the kidneys over a 6-hour period, resulting in high urinary concentrations. Probenecid slows tubular excretion and produces higher serum levels and increases the duration of measurable serum concentrations.

Cefoxitin passes into pleural and joint fluids and is detectable in antibacterial concentrations in bile.

In a published study of geriatric patients ranging in age from 64 to 88 years with normal renal function for their age (creatinine clearance ranging from 31.5 to 174 mL/min), the half-life for cefoxitin ranged from 51 to 90 minutes, resulting in higher plasma concentrations than in younger adults. These changes were attributed to decreased renal function associated with the aging process.

Microbiology

Mechanism of Action

Cefoxitin is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis. Cefoxitin has activity in the presence of some beta-lactamases, both penicillinases and cephalosporinases, of Gram-negative and Gram-positive bacteria.

Mechanism of Resistance

Resistance to cefoxitin is primarily through hydrolysis by beta-lactamase, alteration of penicillin-binding proteins (PBPs), and decreased permeability.

Cefoxitin has been shown to be active against most isolates of the following bacteria, both *in vitro* and in clinical infections as described in the **INDICATIONS AND USAGE** section.

Gram-positive bacteria
- *Staphylococcus aureus* (methicillin-susceptible isolates only)
- *Staphylococcus epidermidis* (methicillin-susceptible isolates only)
- *Streptococcus agalactiae*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*

Gram-negative bacteria
- *Escherichia coli*
- *Haemophilus influenzae*
- *Klebsiella* spp.
- *Morganella morganii*
- *Neisseria gonorrhoeae*
- *Proteus mirabilis*
- *Proteus vulgaris*
- *Providencia* spp.

Anaerobic bacteria
- *Clostridium* spp.
- *Peptococcus niger*
- *Peptostreptococcus* spp.

Bacteroides distasonis
Bacteroides fragilis
Bacteroides ovatus
Bacteroides thetaiotaomicron
Bacteroides spp.

The following *in vitro* data are available, **but their clinical significance is unknown**. At least 90 percent of the following microorganisms exhibit an *in vitro* minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for cefoxitin. However, the efficacy of cefoxitin in treating clinical infections due to these microorganisms has not been established in adequate and well-controlled studies.

Gram-negative bacteria
Eikenella corrodens [non-ß-lactamase producers]

Anaerobic bacteria
Clostridium perfringens
Prevotella bivia

Susceptibility Testing

For specific information regarding susceptibility test interprevtive criteria and associated test methods and quality control standards recognized by FDA for this drug, please see: https://www.fda.gov/STIC

INDICATIONS AND USAGE:

To reduce the development of drug-resistant bacteria and maintain the effectiveness of cefoxitin and other antibacterial drugs, Cefoxitin for Injection, USP should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Treatment

Cefoxitin for Injection, USP is indicated for the treatment of serious infections caused by susceptible strains of the designated microorganisms in the diseases listed below.

1. **Lower respiratory tract infections,** including pneumonia and lung abscess, caused by *Streptococcus pneumoniae,* other streptococci (excluding enterococci, e.g., *Enterococcus faecalis* [formerly *Streptococcus faecalis*]), *Staphylococcus aureus* (including penicillinase-producing strains), *Escherichia coli, Klebsiella* species, *Haemophilus influenzae,* and *Bacteroides* species.
2. **Urinary tract infections** caused by *Escherichia coli, Klebsiella* species, *Proteus mirabilis, Morganella morganii, Proteus vulgaris* and *Providencia* species (including *P. rettgeri*).
3. **Intra-abdominal infections,** including peritonitis and intra-abdominal abscess, caused by *Escherichia coli, Klebsiella* species, *Bacteroides* species including *Bacteroides fragilis*, and *Clostridium* species.
4. **Gynecological infections,** including endometritis, pelvic cellulitis, and pelvic inflammatory disease caused by *Escherichia coli, Neisseria gonorrhoeae* (including penicillinase-producing strains), *Bacteroides* species including *B. fragilis, Clostridium* species, *Peptococcus niger*, *Peptostreptococcus* species, and *Streptococcus agalactiae*. Cefoxitin for Injection, USP, like cephalosporins, has no activity against *Chlamydia trachomatis*. Therefore, when Cefoxitin for Injection, USP is used in the treatment of patients with pelvic inflammatory disease and *C. trachomatis* is one of the suspected pathogens, appropriate anti-chlamydial coverage should be added.
5. **Septicemia** caused by *Streptococcus pneumoniae*, *Staphylococcus aureus* (including penicillinase-producing strains), *Escherichia coli, Klebsiella* species, and *Bacteroides* species including *B. fragilis.*
6. **Bone and joint infections** caused by *Staphylococcus aureus* (including penicillinase-producing

strains).

7. **Skin and skin structure infections** caused by *Staphylococcus aureus* (including penicillinase-producing strains), *Staphylococcus epidermidis, Streptococcus pyogenes* and other streptococci (excluding enterococci e.g., *Enterococcus faecalis* [formerly *Streptococcus faecalis*]), *Escherichia coli, Proteus mirabilis, Klebsiella* species, *Bacteroides* species including *B. fragilis*, *Clostridium* species, *Peptococcus niger*, and *Peptostreptococcus* species.

Appropriate culture and susceptibility studies should be performed to determine the susceptibility of the causative organisms to cefoxitin. Therapy may be started while awaiting the results of these studies.

In randomized comparative studies, cefoxitin and cephalothin were comparably safe and effective in the management of infections caused by gram-positive cocci and gram-negative rods susceptible to the cephalosporins. Cefoxitin has a high degree of stability in the presence of bacterial beta-lactamases, both penicillinases and cephalosporinases.

Many infections caused by aerobic and anaerobic gram-negative bacteria resistant to some cephalosporins respond to cefoxitin. Similarly, many infections caused by aerobic and anaerobic bacteria resistant to some penicillin antibiotics (ampicillin, carbenicillin, penicillin G) respond to treatment with cefoxitin. Many infections caused by mixtures of susceptible aerobic and anaerobic bacteria respond to treatment with cefoxitin.

Prevention

Cefoxitin for Injection, USP is indicated for the prophylaxis of infection in patients undergoing uncontaminated gastrointestinal surgery, vaginal hysterectomy, abdominal hysterectomy, or cesarean section.

If there are signs of infection, specimens for culture should be obtained for identification of the causative organism so that appropriate treatment may be instituted.

CONTRAINDICATIONS:

Cefoxitin for Injection is contraindicated in patients who have shown hypersensitivity to cefoxitin and the cephalosporin group of antibiotics.

WARNINGS:

BEFORE THERAPY WITH CEFOXITIN IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEFOXITIN, CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN WITH CAUTION TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. IF AN ALLERGIC REACTION TO CEFOXITIN OCCURS, DISCONTINUE THE DRUG. SERIOUS HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including cefoxitin, 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 strains 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.

PRECAUTIONS:

General

This formulation of Cefoxitin for Injection USP – Pharmacy Bulk Package bags SmartPak® should not be used in renally impaired patients who require less than the 1 gram dose of cefoxitin. The total daily dose should be reduced when cefoxitin is administered to patients with transient or persistent reduction of urinary output due to renal insufficiency (see **DOSAGE AND ADMINISTRATION**), because high and prolonged serum antibiotic concentrations can occur in such individuals from usual doses.

Antibiotics (including cephalosporins) should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

As with other antibiotics, prolonged use of cefoxitin may result in overgrowth of nonsusceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Prescribing Cefoxitin for Injection in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Information for Patients

Patients should be counseled that antibacterial drugs including Cefoxitin for Injection should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When cefoxitin is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by cefoxitin or other antibacterial drugs in the future.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Laboratory Tests

As with any potent antibacterial agent, periodic assessment of organ system functions, including renal, hepatic, and hematopoietic, is advisable during prolonged therapy.

Drug Interactions

Increased nephrotoxicity has been reported following concomitant administration of cephalosporins and aminoglycoside antibiotics.

Drug/Laboratory Test Interactions

As with cephalothin, high concentrations of cefoxitin (>100 mcg/mL) may interfere with measurement of serum and urine creatinine levels by the Jaffé reaction, and produce false increases of modest degree in the levels of creatinine reported. Serum samples from patients treated with cefoxitin should not be analyzed for creatinine if withdrawn within 2 hours of drug administration.

High concentrations of cefoxitin in the urine may interfere with measurement of urinary 17-hydroxy-

corticosteroids by the Porter-Silber reaction, and produce false increases of modest degree in the levels reported.

A false-positive reaction for glucose in the urine may occur. This has been observed with CLINITEST† reagent tablets.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have not been performed with cefoxitin to evaluate carcinogenic or mutagenic potential. Studies in rats treated intravenously with 400 mg/kg of cefoxitin (approximately three times the maximum recommended human dose) revealed no effects on fertility or mating ability.

Pregnancy

Pregnancy Category B. Reproduction studies performed in rats and mice at parenteral doses of approximately one to seven and one-half times the maximum recommended human dose did not reveal teratogenic or fetal toxic effects, although a slight decrease in fetal weight was observed.

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 clearly needed.

In the rabbit, cefoxitin was associated with a high incidence of abortion and maternal death. This was not considered to be a teratogenic effect but an expected consequence of the rabbit's unusual sensitivity to antibiotic-induced changes in the population of the microflora of the intestine.

Nursing Mothers

Cefoxitin is excreted in human milk in low concentrations. Caution should be exercised when cefoxitin is administered to a nursing woman.

Pediatric Use

Cefoxitin for Injection USP, Pharmacy Bulk Package bag, SmartPak® should not be used in pediatric patients who require less than the 1 gram adult dose of cefoxitin.

Safety and efficacy in pediatric patients from birth to three months of age have not yet been established. In pediatric patients three months of age and older, higher doses of cefoxitin have been associated with an increased incidence of eosinophilia and elevated SGOT.

Geriatric Use

Of the 1,775 subjects who received cefoxitin in clinical studies, 424 (24%) were 65 and over, while 124 (7%) were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out (see **CLINICAL PHARMACOLOGY**).

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (see **DOSAGE AND ADMINISTRATION** and **PRECAUTIONS**).

ADVERSE REACTIONS:

Cefoxitin is generally well tolerated. The most common adverse reactions have been local reactions following intravenous injection. Other adverse reactions have been encountered infrequently.

Local Reactions

Thrombophlebitis has occurred with intravenous administration.

Allergic Reactions
Rash (including exfoliative dermatitis and toxic epidermal necrolysis), urticaria, flushing, pruritus, eosinophilia, fever, dyspnea, and other allergic reactions including anaphylaxis, interstitial nephritis and angioedema have been noted.

Cardiovascular
Hypotension.

Gastrointestinal
Diarrhea, including documented pseudomembranous colitis, which can appear during or after antibiotic treatment. Nausea and vomiting have been reported rarely.

Neuromuscular
Possible exacerbation of myasthenia gravis.

Blood
Eosinophilia, leukopenia including granulocytopenia, neutropenia, anemia, including hemolytic anemia, thrombocytopenia, and bone marrow depression. A positive direct Coombs test may develop in some individuals, especially those with azotemia.

Liver Function
Transient elevations in SGOT, SGPT, serum LDH, and serum alkaline phosphatase; and jaundice have been reported.

Renal Function

Cefoxitin for Injection USP, Pharmacy Bulk Package bag, SmartPak® should not be used in patients with renal impairment who require less than the 1 gram adult dose of cefoxitin.

Elevations in serum creatinine and/or blood urea nitrogen levels have been observed. As with the cephalosporins, acute renal failure has been reported rarely. The role of cefoxitin in changes in renal function tests is difficult to assess, since factors predisposing to prerenal azotemia or to impaired renal function usually have been present.

In addition to the adverse reactions listed above which have been observed in patients treated with Cefoxitin for Injection, the following adverse reactions and altered laboratory test results have been reported for cephalosporin class antibiotics:

Urticaria, erythema multiforme, Stevens-Johnson syndrome, serum sickness-like reactions, abdominal pain, colitis, renal dysfunction, toxic nephropathy, false-positive test for urinary glucose, hepatic dysfunction including cholestasis, elevated bilirubin, aplastic anemia, hemorrhage, prolonged prothrombin time, pancytopenia, agranulocytosis, superinfection, vaginitis including vaginal candidiasis.

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. (See **DOSAGE AND ADMINISTRATION**.) If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

OVERDOSAGE:

The acute intravenous LD_{50} in the adult female mouse and rabbit was about 8 grams/kg and greater than 1 gram/kg, respectively. The acute intraperitoneal LD_{50} in the adult rat was greater than 10 grams/kg.

DOSAGE AND ADMINISTRATION

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Cefoxitin for Injection USP, Pharmacy Bulk Package bag SmartPak® should not be used in

patients who require less than the 1 gram dose of cefoxitin.

THE INTENT OF THIS PHARMACY BULK PACKAGE IS FOR THE PREPARATION OF SOLUTIONS FOR INTRAVENOUS INFUSION ONLY. BEFORE ADMINISTRATION, THIS PHARMACY BULK PACKAGE REQUIRES RECONSTITUTION TO A CONCENTRATION OF 100 MG/ML AND FURTHER DILUTION IN 50 mL OF A COMPATIBLE SOLUTION.

THIS IS A PHARMACY BULK PACKAGE – NOT FOR DIRECT INJECTION

USE THIS FORMULATION OF CEFOXITIN ONLY IN PATIENTS WHO REQUIRE A 1 GRAM DOSE.

Treatment

Adults

Cefoxitin for Injection, USP, Pharmacy Bulk Package bag SmartPak® should be used only in patients who require a 1 gram dose and not any fraction thereof.

Cefoxitin for Injection USP, Pharmacy Bulk Package bag SmartPak® should not be used in patients who require less than the 1 gram dose of cefoxitin.

The usual adult dosage range is 1 gram to 2 grams every six to eight hours. Dosage should be determined by susceptibility of the causative organisms, severity of infection, and the condition of the patient (see Table 1 for dosage guidelines).

If *C. trachomatis* is a suspected pathogen, appropriate anti-chlamydial coverage should be added, because cefoxitin sodium has no activity against this organism.

This formulation of Cefoxitin for Injection USP, Pharmacy Bulk Package SmartPak® should not be used in patients who require less than the 1 gram dose of cefoxitin.

Cefoxitin for Injection may be used in patients with reduced renal function with the following dosage adjustments:

In adults with renal insufficiency, **Cefoxitin for Injection, USP, Pharmacy Bulk Package bag SmartPak® should be used only in patients who require a 1 gram dose and not any fraction thereof. Cefoxitin for Injection USP, Pharmacy Bulk Package bag SmartPak® should not be used in patients with renal impairment who require less than the 1 gram dose of cefoxitin.** An initial loading dose of 1 gram to 2 grams may be given. After a loading dose, the recommendations for *maintenance dosage* (Table 2) may be used as a guide.

When only the serum creatinine level is available, the following formula (based on sex, weight, and age of the patient) may be used to convert this value into creatinine clearance. The serum creatinine should represent a steady state of renal function.

Males: $\frac{\text{Weight (kg)} \times (140 - \text{age})}{72 \times \text{serum creatinine (mg/100 mL)}}$

Females: 0.85 x above value

In patients undergoing hemodialysis, the loading dose of 1 to 2 grams should be given after each hemodialysis, and the maintenance dose should be given as indicated in Table 2.

Antibiotic therapy for group A beta-hemolytic streptococcal infections should be maintained for at least 10 days to guard against the risk of rheumatic fever or glomerulonephritis. In staphylococcal and other infections involving a collection of pus, surgical drainage should be carried out where indicated.

Pediatric Patients

Cefoxitin for Injection, USP, Pharmacy Bulk Package bag SmartPak® should be used only in

patients who require a 1 gram dose and not any fraction thereof. Cefoxitin for Injection USP, Pharmacy Bulk Package bag SmartPak® should not be used in pediatric patients who require less than the 1 gram dose of cefoxitin.

The recommended dosage in pediatric patients three months of age and older is 80 to 160 mg/kg of body weight per day divided into four to six equal doses. The higher dosages should be used for more severe or serious infections. The total daily dosage should not exceed 12 grams.

At this time no recommendation is made for pediatric patients from birth to three months of age (see **PRECAUTIONS**).

In pediatric patients with renal insufficiency, the dosage and frequency of dosage should be modified consistent with the recommendations for adults (see Table 2).

Prevention

Cefoxitin for Injection, USP, Pharmacy Bulk Package bag SmartPak® should be used only in patients who require a 1 gram dose and not any fraction thereof. Cefoxitin for Injection USP, Pharmacy Bulk Package bag SmartPak® should not be used in patients who require less than the 1 gram dose of cefoxitin.

Effective prophylactic use depends on the time of administration. Cefoxitin for Injection usually should be given one-half to one hour before the operation, which is sufficient time to achieve effective levels in the wound during the procedure. Prophylactic administration should usually be stopped within 24 hours since continuing administration of any antibiotic increases the possibility of adverse reactions but, in the majority of surgical procedures, does not reduce the incidence of subsequent infection.

For prophylactic use in uncontaminated gastrointestinal surgery, vaginal hysterectomy, or abdominal hysterectomy, the following doses are recommended:

Adults:

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Cefoxitin for Injection USP, Pharmacy Bulk Package bag SmartPak® should not be used in patients who require less than the 1 gram dose of cefoxitin.

2 grams administered intravenously just prior to surgery (approximately one-half to one hour before the initial incision) followed by 2 grams every 6 hours after the first dose for no more than 24 hours.

Pediatric Patients (3 months and older):

30 to 40 mg/kg doses may be given at the times designated above.

Cesarean section patients:

For patients undergoing cesarean section, either a single 2 gram dose administered intravenously as soon as the umbilical cord is clamped OR a 3-dose regimen consisting of 2 grams given intravenously as soon as the umbilical cord is clamped followed by 2 grams 4 and 8 hours after the initial dose is recommended. (See **CLINICAL STUDIES**.)

Table 1. Guidelines for Dosage of Cefoxitin for Injection

Type of Infection	Daily Dosage	Frequency and Route
Uncomplicated forms* of infections such as pneumonia, urinary tract infection, cutaneous infection	3 to 4 grams	1 gram every 6 to 8 hours I.V.
Moderately severe or severe infections	6 to 8 grams	1 gram every 4 hours *or* 2 grams every 6 to 8 hours I.V.

Infections commonly needing antibiotics in higher dosage (e.g., gas gangrene)	12 grams	2 grams every 4 hours *or* 3 grams every 6 hours I.V.

* Including patients in whom bacteremia is absent or unlikely.

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Renal Impairment

Cefoxitin for Injection USP, Pharmacy Bulk Package bag SmartPak® should be used only in patients who require a 1 gram dose and not any fraction thereof.

Cefoxitin for Injection USP, Pharmacy Bulk Package bag SmartPak® should not be used in patients with renal impairment who require less than the 1 gram dose of cefoxitin.

Table 2. Maintenance Dosage of Cefoxitin for Injection in Adults with Reduced Renal Function

Renal Function	Creatinine Clearance (mL/min)	Dose (grams)	Frequency
Mild impairment	50 to 30	1 to 2	Every 8 to 12 hours
Moderate impairment	29 to 10	1 to 2	Every 12 to 24 hours
Severe impairment	9 to 5	0.5 to 1	Every 12 to 24 hours
Essentially no function	<5	0.5 to 1	Every 24 to 48 hours

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Cefoxitin for Injection USP, Pharmacy Bulk Package bag SmartPak® should not be used in patients who require less than the 1 gram dose of cefoxitin.

Directions for Proper Use of a Pharmacy Bulk Package

- **NOT FOR DIRECT INFUSION.** The Pharmacy Bulk Package is for use in the hospital pharmacy admixture service only in a suitable work area, such as a laminar flow hood. Using aseptic technique, the container closure may be penetrated only one time after reconstitution using a suitable sterile dispensing set or transfer device that allows measured dispensing of the contents. Use of a syringe and needle is not recommended as it may cause leakage. The withdrawal of container contents should be accomplished without delay. However, should this not be possible, a maximum time of **4 HOURS** from initial reconstitution port closure entry is permitted to complete fluid transfer operations. This time limit should begin with the introduction of the solvent or diluent into the Pharmacy Bulk Package. Discard any unused portion after **4 HOURS**. This pharmacy bulk package is not intended to be dispensed as a unit.

- **PRIOR TO RECONSTITUTION: DO NOT USE THE INNER BAG IF PARTICULATE OR FOREIGN MATTER IS PRESENT, IF THE DRY POWDER IS DARK YELLOW OR BROWN, IF THE SEALS ARE NOT INTACT, OR IF THERE IS ANY OTHER DAMAGE TO THE BAG. IN SUCH CASES, DISCARD THE BAG IMMEDIATELY.**

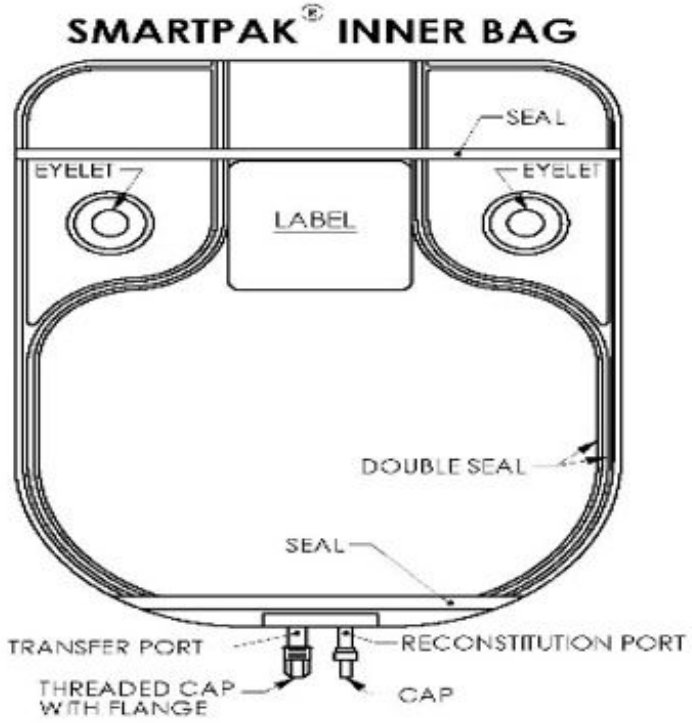
- After initial reconstitution port entry, use entire contents of the Pharmacy Bulk Package promptly. Any unused portion must be discarded after **4 HOURS**.

- Gather the following items prior to the reconstitution of the product: Appropriate number of bags of Sterile Water for Injection and, depending upon the method of filling, appropriate sterile tubing and

adapters.

INSTRUCTION FOR RECONSTITUTION OF THE PHARMACY BULK PACKAGE BAG SmartPak®

The entire contents of the bag and the preparation process (reconstitution and dilution) should be completed within **4 hours** of initial entry.



- Document the date and time reconstitution starts in the designated place on the container label. The entire contents of the bag must be used within **4 hours** from the time of initial entry.
- Remove the translucent unthreaded cap from the reconstitution (smaller) port and discard it.
- Reconstitute the powder through the reconstitution (smaller) port, using Sterile Water for Injection according to the table below.

Table 3. RECONSTITUTION TABLE

SmartPak® Bag Size	Amount of Sterile Water	Approximate Concentration
100 grams	930 mL	100 mg/mL (1 gram/10 mL)

- After reconstitution is complete, remove the transfer needle from the reconstitution port.
- Place the bag on a flat surface of a laminar flow hood and mix for at least 15 minutes by rocking gently from side to side. **CAUTION: To avoid possible leakage caused by the heavy weight of the added water, do not shake vigorously or pull strongly on the bag.**
- When foam dissipates, visually inspect the bag to verify the solution is clear, colorless to pale yellow and free of particulate matter. **DO NOT USE THE INNER BAG IF PARTICULATE OR FOREIGN MATTER IS PRESENT.**
- Unscrew the clear threaded cap from the transfer (larger) port and discard it. Attach sterile tubing

and filling adapter unit to the transfer port.

- Reconstituted solution can now be transferred using the transfer port and the filling adapter.

It should be noted that the spike placed into the transfer port of the Pharmacy Bulk Package SmartPak® is NEVER removed during this procedure and that the reconstitution port is self-sealing.

Dilution

- Hang the bag from two eyelets.
- Following reconstitution, transfer 10 mL of the reconstituted solution into transfusion bags, each containing 50 mL of one of the compatible solutions below.

Compatible solutions for dilution are the following:

Sodium Chloride Injection, USP

5% Dextrose Injection, USP

- Dilution should be completed within the **4 hour** preparation process.
- When diluted according to the instructions above, cefoxitin is stable for 18 hours at room temperature or for 48 hours if stored under refrigeration (5°C or 41°F).

After the periods mentioned above, any unused solutions should be discarded.

Administration

This formulation of Cefoxitin for Injection USP, Pharmacy Bulk Package SmartPak® is for intravenous infusion only after reconstitution.

Parenteral products should be inspected visually for particulates and discoloration prior to administration whenever solution and container permit.

Intravenous Administration

The intravenous route is preferable for patients with bacteremia, bacterial septicemia, or other severe or life-threatening infections, or for patients who may be poor risks because of lowered resistance resulting from such debilitating conditions as malnutrition, trauma, surgery, diabetes, heart failure, or malignancy, particularly if shock is present or impending.

For intermittent intravenous administration: Using an infusion system, a solution containing 1 gram or 2 grams may be given over a period of time through the tubing system by which the patient may be receiving other intravenous solutions. However, during infusion of the solution containing cefoxitin, it is advisable to temporarily discontinue administration of any other solutions at the same site.

Solutions of Cefoxitin for Injection, like those of most beta-lactam antibiotics, should not be added to aminoglycoside solutions (e.g., gentamicin sulfate, tobramycin sulfate, amikacin sulfate) because of potential interaction. However, cefoxitin and aminoglycosides may be administered separately to the same patient.

HOW SUPPLIED:

Cefoxitin for Injection, USP is a dry white to off-white powder available in the following SmartPak® Pharmacy Bulk Package:

100 grams* (1 Pharmacy Bulk Package) Product No. 4100 NDC 66288-4100-1 sold in individual bags.

*Each 100 gram Pharmacy Bulk Package contains sterile cefoxitin sodium equivalent to 100 grams of cefoxitin.

SmartPak® system components are not made with natural rubber latex.

Special storage instructions
Cefoxitin for Injection, USP in the dry state should be stored between 2-25°C (36-77°F). Avoid exposure to temperatures above 50°C. The dry material as well as solutions tend to darken, depending on storage conditions; product potency, however, is not adversely affected.

CLINICAL STUDIES:

A prospective, randomized, double-blind, placebo-controlled clinical trial was conducted to determine the efficacy of short-term prophylaxis with cefoxitin in patients undergoing cesarean section who were at high risk for subsequent endometritis because of ruptured membranes. Patients were randomized to receive either three doses of placebo (n=58), a single dose of cefoxitin (2 grams) followed by two doses of placebo (n=64), or a three-dose regimen of cefoxitin (each dose consisting of 2 grams) (n=60), given intravenously, usually beginning at the time of clamping of the umbilical cord, with the second and third doses given 4 and 8 hours post-operatively. Endometritis occurred in 16/58 (27.6%) patients given placebo, 5/63 (7.9%) patients given a single dose of cefoxitin, and 3/58 (5.2%) patients given three doses of cefoxitin. The differences between the two groups treated with cefoxitin and placebo with respect to endometritis were statistically significant ($p<0.01$) in favor of cefoxitin. The differences between the one-dose and three-dose regimens of cefoxitin were not statistically significant.

Two double-blind, randomized studies compared the efficacy of a single 2 gram intravenous dose of cefoxitin to a single 2 gram intravenous dose of cefotetan in the prevention of surgical site-related infection (major morbidity) and non-site-related infections (minor morbidity) in patients following cesarean section. In the first study, 82/98 (83.7%) patients treated with cefoxitin and 71/95 (74.7%) patients treated with cefotetan experienced no major or minor morbidity. The difference in the outcomes in this study (95% CI: –0.03, +0.21) was not statistically significant. In the second study, 65/75 (86.7%) patients treated with cefoxitin and 62/76 (81.6%) patients treated with cefotetan experienced no major or minor morbidity. The difference in the outcomes in this study (95% CI: –0.08, +0.18) was not statistically significant.

In clinical trials of patients with intra-abdominal infections due to *Bacteroides fragilis* group microorganisms, eradication rates at 1 to 2 weeks posttreatment for isolates were in the range of 70% to 80%. Eradication rates for individual species are listed below:

Bacteroides distasonis	7/10	(70%)
Bacteroides fragilis	26/33	(79%)
Bacteroides ovatus	10/13	(77%)
B. thetaiotaomicron	13/18	(72%)

Smartpak is a registered trademark of Samson Medical Technologies, L.L.C. †Registered trademark of Siemens Healthcare Diagnostics Inc.

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Printed in USA

C4100b

Manufactured for:
Samson Medical Technologies, LLC
Cherry Hill, NJ 08003

Manufactured by:

ACS Dobfar S.p.A.
20067 Tribiano (Milano) Italy

PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – Bag Label

NDC 66288-4100-1

Cefoxitin for Injection, USP

100 grams (ONE HUNDRED GRAMS) per Pharmacy Bulk

Package Bag

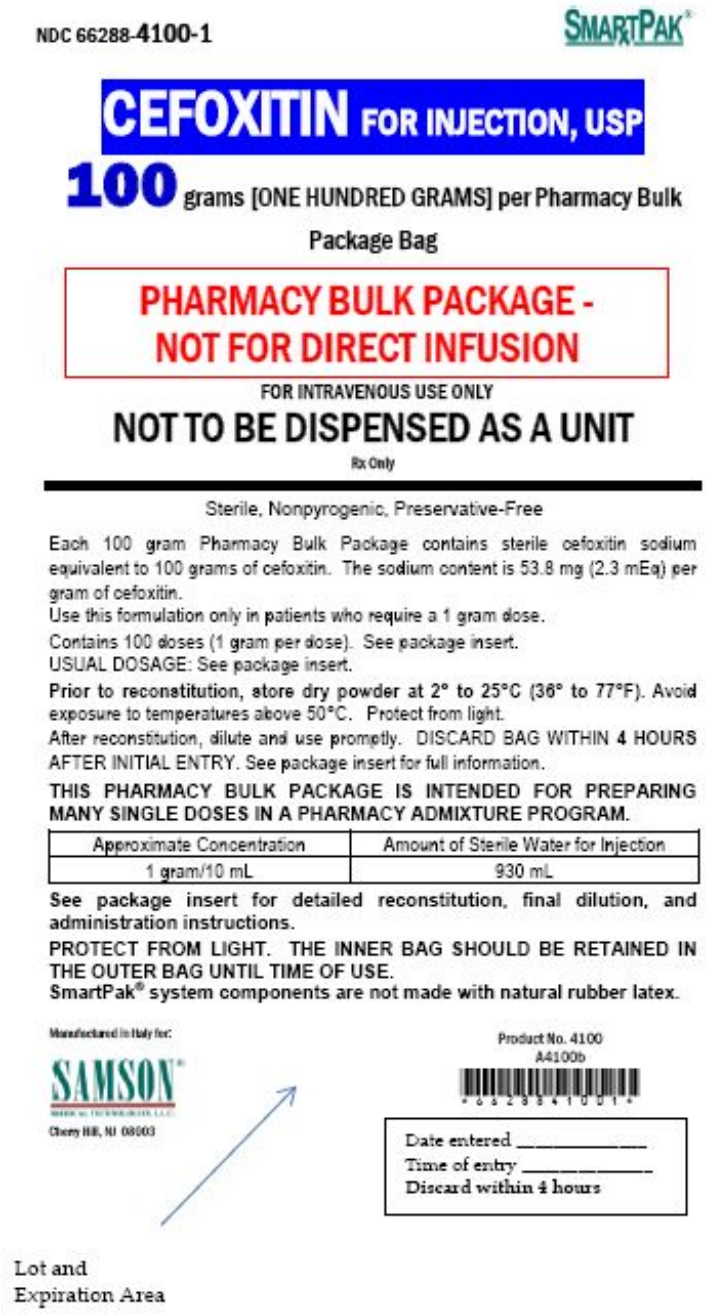
PHARMACY BULK PACKAGE -

NOT FOR DIRECT INFUSION

FOR INTRAVENOUS USE ONLY

NOT TO BE DISPENSED AS A UNIT

Rx only



CEFOXITIN

cefoxitin injection, powder, for solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:66288-4100
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**

Cefoxitin Sodium (UNII: Q68050H03T) (Cefoxitin - UNII:6OEV9DX57Y)	Cefoxitin	100 g

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:66288-4100-1	1 in 1 BAG	03/01/2016	
1		1 in 1 BAG; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA200938	03/01/2016	

Labeler - SAMSON MEDICAL TECHNOLOGIES LLC (102837429)

Registrant - SAMSON MEDICAL TECHNOLOGIES LLC (102837429)

Establishment

Name	Address	ID/FEI	Business Operations
ACS DOBFAR SPA		429243025	manufacture(66288-4100)

Revised: 11/2020 SAMSON MEDICAL TECHNOLOGIES LLC