Xtum-O

Cefpodoxime + Clavulanic Acid

Xterminator...

with Oral Power O! YES

Product Monograph

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INDEX

INTRODUCTION TO SWITCH THERAPY

In practice of critical care or hospital care, it is now well accepted that the patients on intravenous therapy should be switched over to oral therapy as soon as stability of vital signs are achieved and the patient is alert enough to take drugs by oral route. Such treatment strategy has been shown to have tremendous positive impact on health and recovery of patients. Switching the patient on oral therapy has also shown to reduce the overall cost of treatment.
(Source: Intravenous to oral antibiotic switch therapy, Burke et al, Vol 101/ No 4/ April 1997/ Postgraduate medicine.)

While intravenous or intramuscular medications may have more bioavailability and have greater effects, some oral drugs produce serum levels compatible to parenteral formulation. This pharmacokinetic profile of drugs serves a good option to convert the patients on i.v./i.m. drugs to oral use. This process of switching the patients form i.v./i.m to oral therapy is called "switch therapy, sequential therapy, transitional therapy, antibiotic streamlining or step down therapy.

INDICATIONS OF SWITCH THERAPY

Switch therapy is commonly used for analgesics, antibiotics and antiviral segment of medications. However in this article we will mainly discuss topics related to infectious diseases.

Many centres have designed their switch therapy to suit their needs for example: Winthrop-University Hospital of New York in 1997 published a guideline for empirical intravenous-to-oral switch therapy to treat various types of infections.

Guideline mentions the following
1) Clinical condition from which patient is suffering
2) Empirical Intravenous therapy which is to be administered
3) Oral medication which is best suited for switch therapy

Their recommendations are shown in Table I :-

Table I

Infection	Intravenous agent	Oral agent
Acute bacterial meningitis	Ceftriaxone sodium	Chloramphenicol
Community-acquired pneumonia		
• Typical**	Ceftriaxone or ceftizoxime sodium or levofloxacin	Doxycycline or azithromycin or levofloxacin or cefuroxime axetil or cefixime
• Atypical	levofloxacin	Doxycycline or azithromycin or levofloxacin
Intra-abdominal sepsis (excluding biliary tract)		
• Mild/moderate	Ampicillin/sulbactam or ceftizoxime	Metronidazole **PLUS** levofloxacin or Trimethoprim- sulfamethoxazole or cefixime
• Severe	Meropenem *or* metronidazole **PLUS** gentamicin *or* ceftriaxone *or* levofloxacin	Metronidazole **PLUS** levofloxacin or Trimethoprim- sulfamethoxazole or cefixime
Biliary tract sepsis	Ampicillin/sulbactam or cefoperazone sodium	Levofloxacin *or* amoxicillin **PLUS** cefixime
Urosepsis		
• Gram-negative	Aminoglycoside *or* levofloxacin*** *or* aztreonam	Trimethoprim- sulfamethoxazole *or* levofloxacin*** *or* cefixime
Gram-positive (groups B and G streptococci)	Ampicillin	Amoxicillin or erythromycin or levofloxacin
Skin and soft-tissue infections	Ceftizoxime	Cephalexin or cefuroxime or cefixime
Infection from human or animal bites	Ampicillin/sulbactam	Doxycycline or amoxicillin/potassium clavulanate

TMP-SMX, trimethoprim-sulfamethoxazole. **Therapy is same for aspiration pneumonia and in elderly, nursing home, and nonleukopenic immunocompromised patients. ***In cases of urosepsis due to urologic instrumentation, use ciprofloxacin for coverage against Pseudomonas species.

Source: Post Graduate Medicine, Intravenous to oral antibiotic switch therapy, Burke A et al, Vol 101/ No 4/ April 1997

DRUGS USED FOR ORAL CONVERSION

The last 10 years has witnessed the development of safe and effective oral antimicrobials (cephalosporins, loracarbef, clarithromycin, azithromycin, fluoroquinolones) that are well absorbed, can be administered orally, and have a proven track record in the management of many infections, including disorders previously treated exclusively by intravenous antibiotics. Experience with these have evolved a criteria of selecting oral antibiotics for switch therapy.

Criteria for selection of antibiotics to be used for oral conversion

1) Antibiotic that can be used orally for switch therapy should have pharmacokinetic profile and microbial spectrum more or less similar to that of the parenteral antibiotic used.
2) Choosing the right antibiotic depends mainly on the likely pathogen.
3) A thorough understanding of the likely microbial cause of the infection
4) Local susceptibility patterns
5) Properties of the antimicrobials, namely spectrum of activity and potency (including activity versus known resistance mechanisms)
6) Pharmacokinetic profile tolerability and safety of oral antibiotic

Below mentioned is the table giving examples of various antibiotics which can be used for switching over to oral therapy: **Table II**

Intravenous Product	Oral Conversion Product
Ampicillin	**Ampicillin** 250-500 mg po qid or **Amoxicillin** 250-500 mg tid
Ampicillin-sublactam	**Amoxicillin+clavulanic acid** 250-500 po q8h
Cefazolin	**Cefadroxil** 500 mg po q12h, **Cephalexin** 500 mg po q6h, or **Cefaclor** 500 mg po q8h
Cefotaxime	**CEFPODOXIME** 100-200 mg po q12h, **Cefixime** 400 mg po qd, or **Ceftibuten** 400 mg po qd
Cefotetan	**Cefuroxime** 250-500 mg bid, **Cefixime** 400 mg po qd
Cefoxitin	**Cefuroxime** 250-500 mg bid, **Cefixime** 400 mg po qd
Ceftizoxime	**Cefixime** 400 mg po qd
Ceftriaxone	**CEFPODOXIME** 100-200 mg po q12h, **Cefixime** 400 mg po qd
Cefuroxime	**Cefuroxime** 250-500 mg q12h

(Source: Clinical Center Pharmacy Department 1998,Intravenous to Oral Conversion)

Criteria for selection of antibiotics to be used for oral conversion

Antibiotic that can be used orally for switch therapy should have the pharmacokinetic profile and microbial spectrum more or less similar to that of the parenteral antibiotic used

Criteria to start oral drugs :

Patient's condition

Functioning gastrointestinal tract

Diet

Prognosis

Also equally important is the time at which the patients have to be started oral drugs. This mainly depends on 4 criteria:

- **Patient's condition** (Is the patient treatable by oral form of medication).
- **Functioning gastrointestinal tract** (Does the patient have a functioning GI tract for adequate absorption of drugs).
- **Diet** (Is the patient currently receiving a soft or regular diet and/or is taking other oral medications)
- **Prognosis** (Is Patient's condition improving as indicated from clinical findings (e.g., decreasing temperature and white blood cell count).

Different doctors have different approaches to switch therapy. Switch therapy is possible with a variety of oral antibiotics. Antibiotics ideal for intravenous-to-oral (IV-to-PO) switch programs include chloramphenicol, clindamycin, metronidazole, trimethoprim-sulfamethoxazole, fluconazole, itraconazole, voriconazole, doxycycline, minocycline, levofloxacin, gatifloxacin, moxifloxacin, and linezolid and oral cephalosporins.

(Source : Cunha, Drugs Today, 2001).

SWITCHING FROM CEFTRIAXONE TO ORAL CEFPODOXIME

Ceftriaxone is one of the antibiotics in community acquired pneumonia which has a good coverage for Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, E coli, Klebsella pneumoniae, Proteus mirabilis.

Cefpodoxime has equally good coverage as ceftriaxone

- The patient once stabilized can be switched over to cefpodoxime which has equally good coverage for the above mentioned pathogens. The comparison is as shown below in table:

Organisms	Cefpodoxime	Ceftriaxone
	MIC_{90} (mcg/ml)	MIC_{90} (mcg/ml)
S. aureus	2	2
S. pneumoniae	≤ 0.06	≤ 0.06
H .influenzae	≤ 0.06	≤ 0.06
E. coli	≤ 0.06	≤ 0.06
K. pneumoniae	≤ 0.06	≤ 0.06

Antimicrobial Agents and Chemotherapy, Dec 1988, 1896-1898

NCCLS criteria: Upto 2 mcg/ml: sensitive, 2-4 mcg/ml: intermediate, >8: resistant

Thus from the above table it is clear that most of the organisms covered by ceftriaxone are also covered by cefpodoxime, hence cefpodoxime form a good alternative for the patients of CAP who have to be switched over to oral drugs.

- Cefpodoxime also finds use as oral continuation therapy when parenteral cephalosporins (such as ceftriaxone) are no longer necessary for continued treatment.
  http://en.wikipedia.org/wiki/Cefpodoxime

- An oral regimen of cefpodoxime proxetil was as efficacious as parenterally administered ceftriaxone for the treatment of bronchopneumonia in hospitalised patients
  Drugs. 1992 Nov;44(5):889-917.

- Clinical and bacteriological results obtained with cefpodoxime proxetil were comparable with those obtained with ceftriaxone in the treatment of community – acquired bronchopneumonia

  The percentage of overall success (cured or improved) was 97.7% (43/44) in the cefpodoxime proxetil group and 95.1% (39/41) in the ceftriaxone group. The bacteriological efficacy was 94.3% in the cefpodoxime proxetil group and 97.4% in the ceftriaxone group
  J Antimicrob Chemother. 1990 Dec; 26 Suppl E: 71-7

Cefpodoxime proxetil was as efficacious as parenterally administered ceftriaxone

Clinical and bacteriological results obtained with cefpodoxime proxetil were comparable with those obtained with ceftriaxone

SWITCH THERAPY IN COMMUNITY ACQUIRED PNEUMONIA (CAP)

In patients with community-acquired pneumonia it is possible to switch treatment from intravenous (IV) to oral cephalosporin therapy early and still achieve a cure. Early use of oral therapy enables patients to be discharged from hospital sooner than if they were receiving IV therapy and is thus associated with significant cost savings.

IV to Oral Switch Therapy

The length of hospital stay is a major factor in the total medical costs for a hospitalised patient with CAP. Consequently, regimens which allow early switch to oral therapy and subsequent discharge could be expected to substantially reduce costs without compromising efficacy and safety.

Ideally, the oral agent chosen after parenteral therapy would merely be a different formulation of the same drug and would have good oral bioavailability. In those instances where there is no equivalent oral formulation, a different oral agent must be considered - preferably one from the same antibacterial class.

When to Initiate Switch Therapy in CAP ?

Cough and respiratory distress are improving

Patient is afebrile

White blood cell count is returning to normal

No evidence of abnormal gastrointestinal absorption

When to Initiate Switch Therapy

Table III

Patient reports that cough and respiratory distress (shortness of breath) are improving satisfactorily
Patient is afebrile
The white blood cell count is returning to normal
There is no evidence of abnormal gastrointestinal absorption

Time to consider switch therapy

For most patients with CAP, the period of early improvement occurs within 72 hours of admission. At this stage, the patient will meet the criteria for switch therapy shown in table III and is then eligible for oral treatment.

Benefits of switch therapy

Patient Benefits
Improved comfort and clinical outcome from: • More rapid mobilisation • Avoidance of pain/phlebitis associated with indwelling intraveneous (IV) catheter • Reduced likelihood of catheter sepsis/bacteremia
Hospital Benefits
Reduced costs secondary to: • Lower drug acquisition costs • Reduction in pharmacy drug preparation • No need for IV delivery systems to administer antibacterials • Shorter hospital stays • Reduction in nosocomial infections (especially bacteraemia associated with line sepsis) • Decreased nursing time associated with IV line care/IV drug administration

ROLE OF CEFPODOXIME IN SWITCH THERAPY

According to a 1988 survey of antibacterial utilisation, the treatment of CAP with third-generation cephalosporins is a common practice among US hospitals.

Unlike various other classes of antibacterial, third-generation cephalosporins do not include drugs that are available in both parenteral and oral formulations. How-ever, the spectrum of activity of the various members of this class are similar indeed; switch therapy from an IV to a different oral third-generation antibacterial has been successfully achieved in CAP.

Cefpodoxime is a good alternative for switching over from intravenous agents to oral therapy. It has a good sensitivity against the common pathogens causing CAP. Antibacterial activity of cefpodoxime is comparable with Ceftriaxone/ Cefotaxime the most commonly used parenteral antibiotic.

Antibacterial activity of cefpodoxime is comparable with Ceftriaxone the most commonly used parenteral antibiotic

Table IV

Common bacteria in CAP	Intravenous agents					Oral agents
	Cefotaxime	Ceftizoxime	Ceftriaxone	Cefoperazone*	Ceftazidime	CEFPODOXIME*
Streptococcus pneumoniae[a]	S	S	S	S	S/R	S
Haemophilus influenzae[b]	S	S	S	S	S	S
Klebsiella pneumoniae[c]	S	S	S	S/R	S	S
Escherichia coli[c]	S	S	S	S/M	S	S
Pseudomonas aeruginosa[c,d]	R	R	M/R	S/R	S/R	R
Staphylococcus aureus	S	S	S	S	S/M	M
Moraxella catarrhalis[b]	S	?S	S	?S	S	S

[a] enicillin sensitive.
[b] Includes both ß-lactamase-negative and -positive strains.
[c] More likely in elderly patients.
[d] More likely in nursing home patients.

Abbreviations:
CAP = community-acquired pneumonia;
M = moderately sensitive;
R = resistant;
S = sensitive.

Adapted from Medscape, Early Intravenous to Oral Switch Therapy in Community-Acquired Pneumonia Is Advantageous, Drug Ther Perspect 10(3):10-13, 1997.

ANTIBIOTIC RESISTANCE

Resistance to antibiotics constitutes a major threat to public health. It is therefore critical to treat severe bacterial infections appropriately by starting antimicrobial treatment early in the course of infection, using the correct agent, at the most appropriate dose, and for an adequate duration.

THE NEED FOR A BETA-LACTAM-BETA LACTAM INHIBITOR COMBINATION ANTIBIOTIC

Among different antibiotics, beta lactam antibiotics account for approximately 50% of global antibiotic consumption because of their proven efficacy and safety. It is well documented fact that bacterial resistance to this group of antibiotic increased parallely with increasing use of these antibiotics. Strategy for overcoming bacterial resistance with newer cephalosporins has been successfully employed as it was possible to modify structure of a cephalosporin nucleus easily to confer an additional advantage. However, it has become clear that such attempts have been not only short lived but has created an alarming situation that currently available antibiotics are not adequate to control infection due to resistant bacteria.

Reintroduction of currently available penicillins and cephalosporins with other agents such as beta lactamase inhibitors is an attractive preposition for many reasons;

1) Well established safety and efficacy profile
2) Production of beta lactamase is the most common mechanism of resistance to beta lactam antibiotics, especially in gram negative bacteria
3) Convenience of use, and more essentially an understanding that using such combination empirically may help in not only overcome therapeutic failures due to resistant bacteria but will also delay resistance development in susceptible bacteria
4) Minimize use of newer antibacterials so that they remain effective antibacterial for specific use

Desired Properties of a Beta Lactam / Beta Lactamase Combination

Since the objective of a beta lactam / beta lactamase combination is to provide an empiric therapy without increasing risk of development of bacterial resistance the combination should possess the following properties:

1) The combination should have low MIC values
2) It should have intrinsic broad spectrum of activity
3) Blood and tissue levels above MIC values should be maintained for long duration to inhibit bacterial growth between two doses during the treatment period
4) Should inhibit broad range of beta lactamase
5) Should be suicidal inhibitor of beta lactamase
6) Should be well tolerated

ADVANTAGE OF CEFPODOXIME CLAVULANIC ACID COMBINATION

Cefpodoxime is a 3rd generation cephalosporin active against many gram positive and gram negative organisms and is beta lactamase stable. It exhibits excellent activity against Streptococcus pneumoniae, methicillin susceptible Staphylococci, Haemophilus influenzae, Moxaxella catarrhalis and Nesseria spp which are the most common community acquired and hospital acquired infections.

However in recent past it observed that due to production of Beta lactamase enzyme MIC values of cefpodooxime has increased for certain micro-organism. As a result, cefpodoxime may be less effective in treating infections.

Reference: Drugs. 1991;42 Suppl 3:6-12.

Protective role of Clavulanic acid:

Clavulanic acid is a naturally derived beta lactamase inhibitor produced by Streptomyces clavuligerus. *Clavulanic acid binds to and inactivates them thus preventing the destruction of cefpodoxime that is a substrate for this enzyme.*
It has poor intrinsic antimicrobial activity , but it is a 'suicide' inhibitor (irreversible binder) of ß-lactamases produced by a wide range of gram positive and gram negative microorganism. Clavulanic acid is well absorbed by mouth.

The combination of Cefpodoxime (3rd generation cephalosporin) and Clavulanic acid (beta-lactamase inhibitor) provides a solution for treatment of bacterial infections caused by beta lactam resistant pathogens.

Properties of Beta Lactam / Beta Lactamase Combination

Combination should have low MIC values

Intrinsic broad spectrum of activity

Blood and tissue levels above MIC values should be maintained for long duration

Addition of clavulanic acid to cefpodoxime reduces MIC level of cefpodoxime dramatically if bacteria is producing ß-lactamase

SYNERGY OF CEFPODOXIME CLAVULANIC ACID COMBINATION

Micro-organism	MIC values in µg /ml	
	Cefpodoxime	**Cefpodoxime + Clavulanic acid**
Citrobacter amalonaticus ***4026***	8 (Resistant)	2
Citrobacter freundii ***3757***	128 (Resistant)	8
Enterobacter aerogenes ***3701***	32 (Resistant)	≤0.06
Enterobacter cloacae ***53***	32 (Resistant)	0.5
Enterobacter cloacae ***3146***	64 (Resistant)	2
Proteus mirabilis ***3750***	8 (Resistant)	≤0.06
Proteus penneri ***1767***	32 (Resistant)	≤0.06
Proteus vulgaris ***1781***	1 (Susceptible)	0.12
Proteus vulgaris ***1405***	128 (Resistant)	≤0.06
Proteus vulgaris ***1699***	128 (Resistant)	≤0.06
Proteus vulgaris ***1765***	>128 (Resistant)	0.12
Serratia marcescens ***91***	>128 (Resistant)	4
Serratia marcescens ***167***	>128 (Resistant)	4
Serratia rubidaea ***3139***	4 (Intermediate)	0.25
Serratia rubidaea ***3134***	2 (Susceptible)	0.5

Adapted From : Journal Of Clinical Microbiology Jan 2004 p294 -298

2:1 to 1:1 is the ideal ratio of cepodoxime: clavulanic acid

IDEAL RATIO:

1) Peak plasma concentration of Cefpodoxime 200 mg single dose is 2.18 mcg/ml
(Antimicrobial Agents and Chemotherapy ,June 1990 ,p.1094-1099)

2) Peak plasma concentration of Clavulanic acid 125 mg single dose is 2.2 mcg/ml
(Physicians' Desk Reference 54 the edition,2000 p2978-2980)

3) Microbiological studies have shown that Antibiotic: Clavulanate ratio ranging from 1:1 to 16:1 improves sensitivity of antibiotic. Further these studies concluded that the ratio of 1:1 to 2:1 is the ideal ratio.
(Adapted from :Antimicrobial Agents and Chemotherapy, Nov 1995 p2591-2592)

4) The ratio of Cefpodoxime and Clavulanic acid used in Xtum-O 200mg: 125mg. Moreover the ratio of peak plasma concentration lies within the ratio of 1:1 to 2:1

To conclude 100/200 mg Cefpodoxime and 62.5/125 mg Clavulanic acid combination is most appropriate ratio for maximum clinical efficacy.

The benefits of such combination are:

- Prevention of resistance to Cefpodoxime which may increase over a period of time due to its extensive use.
- Cefpodoxime-Clavulanic acid combination has the unique property of a broad spectrum antibiotic with the added advantage of a wide spectrum beta lactamase inhibitor.
- Highly effective combination in SWITCH THERAPY

CEFPODOXIME SCORES OVER CEFIXIME

Plasma concentrations may not be the ideal parameter on which to base antibiotic dosing schedules. Most infections do not occur in plasma but in tissues, therefore the ability of antibiotics to reach the target sites is a key determinant of clinical outcome. One such study was done to determine the tissue concentrations of cefpodoxime. In the study the tissue concentrations of cefodoxime were compared to cefixime with showed the following results as mentioned below in table.

It was seen that tissue penetration of cepfodoxime if substantially higher than that of cefixime, as demonstrated by its higher peak free tissue concentrations and AUC

Parameter	Cefpodoxime	Cefixime
AUC_p (mg.h/L)	22.4 +or- 8.7	25.6 =or- 8.5
AUC_t (mg.h/L)	**15.4 =or- 5.1**	7.3 =or- 2.2
C_{maxp} mg/L	3.9 +or- 1.2	3.4 +or- 1.1
C_{maxt} mg/L	**2.1 +or- 1.1**	0.9 +or- 0.3

AUC, area under curve: p, total plasma: t, free tissue: C_{max}, maximum concentration (average of individual C_{max})

Ref- Intestinal Tissue concentration of cefpodoxime, Ping liu et al, Journal of antimicrobial chemotherapy (2002) 50, Topic T1, 19-22

This finding indicates that, taking into account pharmacokinetic/pharmacodynamic considerations, cefpodoxime is likely to be more efficacious than cefixime, due to its greater tissue penetration.

Enhanced antistaphylococcal activity of cefpodoxime, distinguishes it from other orally active third generation cephalosporins such as cefixime.

Drugs. 1992 Nov;44(5):889-917.

Cefpodoxime scores over cefixime

Cefpodoxime is likely to be more efficacious than cefixime, due to its greater tissue penetration

Cefpodoxime has enhanced antistaphylococcal activity compared to cefixime

Xtum-O OVERVIEW

This is an oral antibiotic combination consisting of the cephalosporin antibiotic (Cefpodoxime) and the beta lactamase inhibitor Clavulanic Acid

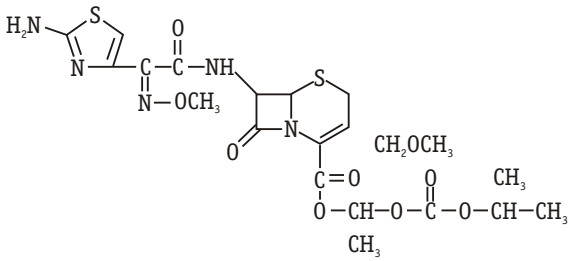
COMPOSITION

Each tablet of Xtum-O (325) contains	
Cefpodoxime Proxetil	USP 200 mg
Clavulanic acid	USP 125 mg

Each tablet of Xtum-O (162.5) contains	
Cefpodoxime Proxetil	USP 100 mg
Clavulanic acid	USP 62.5 mg

DESCRIPTION

Cefpodoxime is an orally administered extended spectrum, semi-synthetic antibiotic of the cephalosporin class. It is a third generation cephalosporin.



Cefpodoxime proxetil is a prodrug; its active metabolite is cefpodoxime. All doses of cefpodoxime proxetil in this combination are expressed in terms of the active cefpodoxime moiety.

Clavulanic acid is produced by the fermentation of Streptomyces clavuligerus. It is a beta-lactam structurally related to the penicillins and possesses the ability to inactivate a wide variety of beta-lactamases by blocking the active sites of these enzymes. Clavulanic acid is particularly active against the clinically important plasmid-mediated beta-lactamases frequently responsible for transferred drug resistance to penicillins and cephalosporins.

MICROBIOLOGY

The bactericidal action of cefpodoxime results from inhibition of cell wall synthesis.

Cefpodoxime is usually active against the following organisms in vitro and in clinical infections

Gram-positive Aerobes:
Staphylococcus aureus (including penicillinase-producing strains)
Staphylococcus saprophyticus
Streptococcus pneumoniae (excluding penicillin resistant strains)
Streptococcus pyogenes
Streptococcus agalactiae
Streptococcus spp. (Groups C, F, G)

Aerobic Gram-negative microorganisms
Escherichia coli
Klebsiella pneumoniae
Proteus mirabilis
Haemophilius influenzae (including beta lactamase strains)
Moraxella (Branhmella) catarrhalis
Nesseria gonorrhoeae (including penicillinase-producing strains)
Citrobacter diversus
Klebsiella oxytoca
Proteus vulgaris
Providencia rettgeri
Haemophilus parainfluenzae

Anaerobic Gram-positive microorganisms:
Peptostreptococcus magnus

Reference :Physicians' Desk Reference,54 th edition 2000 p2488-2492

RATIONALE OF COMBINING CLAVULANIC ACID WITH CEFPODOXIME

Cefpodoxime is ineffective in the presence of beta lactamase producing micro organisms. Clavulanic acid which is a beta lactamase inhibitor protects cefpodoxime from hydrolysis by beta lactamases thus enhances the spectrum of cefpodoxime.

PHARMACOKINETICS

Cefpodoxime proxetil is a prodrug that is absorbed from the gastrointestinal tract and de-esterified to its active metabolite, cefpodoxime.

Absorption: Bioavailability of cefpodoxime is 50% in fasting subjects and it increases in presence of food.

Distribution: Well distributed after oral administration. Cefpodoxime reaches therapeutic concentrations in respiratory tract and genito-urinary tracts and bile. Protein binding of cefpodoxime ranges from 20 to 30 %. The plasma half life of cefpodoxime is about 2 to3 hours and is prolonged in patients with impaired renal function.

Excretion: Cefpodoxime is excreted unchanged in urine

Reference: Martindale 32 nd edition p172

Clavulanic acid

Absorption: Well absorbed after oral administration.

Distribution: Well distributed after oral administration. Protein binding of clavulanic acid is about 30 %.The plasma half life of clavulanic acid is one hour.

Excretion: About 60 % of clavulanic acid is excreted unchanged in urine.

Reference: Martindale 32 nd edition p190

The clavulanic acid component in Xtum-O protects cefpodoxime from degradation by ß-lactamase enzymes and effectively extends the antibiotic spectrum of cefpodoxime to include many bacteria normally resistant to cefpodoxime and other ß-lactam antibiotics. Thus, Xtum-O possesses the distinctive properties of a broad-spectrum antibiotic and a ß-lactamase inhibitor.

INDICATIONS

Cefpodoxime is indicated in the following infections when caused by susceptible organisms

- As a switch therapy after parenteral cephalosporins
- Upper and lower respiratory tract infections
- Skin and soft tissue infections
- Urinary tract infections

DOSAGE AND ADMINISTRATION

ADULTS: **Table V**

Adults (age 12 years and older):			
Type of Infection	**Total Daily Dose**	**Dose Frequency**	**Duration**
Pharyngitis and/ or tonsillitis	200 mg	100 mg Q 12 hrs	5 to 10 days
Acute community-acquired pneumonia	400 mg	200 mg Q 12 hrs	14 days
Acute bacterial exacerbations of chronic bronchitis	400 mg	200 mg Q 12 hrs	10 days
Uncomplicated gonorrhea (men and women) and rectal gonococcal infections (women)	200 mg	Single dose	
Skin and skin structure	800 mg	400 mg Q 12 hrs	7 to 14 days
Acute maxillary sinusitis	400 mg	200 mg Q 12 hrs	10 days
Uncomplicated urinary tract infection	200 mg	100 mg Q 12 hrs	7 days

PEDIATRIC PATIENTS:

Children 2 months to 12 years- 10 mg/kg/day divided every 12 hours

SIDE EFFECTS

Cefpodoxime is well tolerated.
Most common gastrointestinal adverse effects seen is diarehoea,vomiting and abdominal pain.

PREGNANCY: Category B

SUPERIORITY OF CEFPODOXIME

Table VI

Patients suffering from Lower Respiratory Tract Iinfections • *Acute Exacerbations of Chronic Bronchitis* • *Community Acquired Pneumonia*				
Name of the Investigator	**Treatment regimen**	**Mean age**	**Clinical end point**	**Clinical efficacy at the end of treatment**
Sengupta (2004)	**CEFPODOXIME** 5mg/kg twice daily for 10 -14 days	10 years	Cure + improvement	97%
	Cefixime 4mg/kg daily for 10 -14 days	10 years	Cure + improvement	86.8 %

Reference: Indian J Pediatrics 2004;71:517-521

Patient suffering from Acute Otitis Media				
Cohen et al (1994	**CEFPODOXIME** 8mg/kg/day for 8 days	1.9 years	Cure + improvement	88 %
	Cefixime 8mg/kg/ day for 8 days	2.1 years	Cure + improvement	73 %

Reference: Journal of antimicrobial chemotherapy (2002) 50 ,Topic T1,23-27

UNIQUE FEATURES

- Broad spectrum antibiotic
- Effective against ß-lactamase producing pathogens
- Well tolerated
- Administered only once or twice daily therefore good patient compliance

NOTES

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

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