DADS/DSHS EXECUTIVE FORMULARY COMMITTEE MINUTES
October 21, 2005

The Executive Formulary Committee convened on Friday, October 21, 2005 in Room 240 - CO Building 2. The meeting was called to order by Dr. Ward, Interim Chair at 9:40 a.m.

Janet Adams, MSN, RN, CNS	√	Kenny Dudley	Absent
Rosha Chadwick, R.Ph.	√	Mike Maples	Absent
Jeanna Heidel, Pharm.D.	√	Michael Woolsey	Absent
J. Brett Hood, M.D.	√	Barbara Otting, RN	Absent
Connie Millhollon, RN,	√	Camille Hemlock, M.D.	√
Victoria B. Morgan, M.D.	√	Nina Muse, M.D.	√
Ann L. Richards, Pharm.D.	√	Steven P. Shon, M.D.	Absent
Dan Still, Pharm.D.	√	Vacant Center Position	
Bernardo C. Tarin-Godoy, M.D.	√	Vacant Center Position	
Robert L. Ward, D.O.	√	Vacant Center Position	
Scott Schalchlin	Absent	Vacant State School Position	

Guest Present: Sharon Tramonte, Pharm.D., San Antonio State School

Roll Call, Introductions and Announcements

Dr. Jack McCoy has retired from Lufkin State School and Dr. Robin Mallett resigned from her position on the Executive Formulary Committee.

Dr. J. Brett Hood, physician at Brenham State School was introduced as a new member.

Approval of Minutes of April 29, 2005

On a motion of Dr. Tarin-Godoy, seconded by Ms. Chadwick, the minutes of the April 29th meeting were approved as previously distributed. The Committee did not meet in July.

Adverse Drug Reaction Reports

The Executive Formulary Committee received three adverse drug reaction reports. In the first

case, a 24-year-old male developed a fine, follicular itchy rash secondary to oxcarbazepine (Trileptal®). The rash cleared when the medication was discontinued.

In the second case, a patient receiving clozapine (Clozaril®), olanzapine (Zyprexa®) and risperidone (Risperdal®) developed neuroleptic malignant syndrome. The patient was found to be sweating profusely. Patient was confused and had problems with responding to questions as the patient moves lips without producing a sound. The patient had significant cogwheel and muscle rigidity in arms with medium-sized tremors. CPK is 1754 units (normal range is 37-289) and temperature is 99 degrees.

In the other case, a 61-year-old female patient on olanzapine and risperidone died. A patient with paranoid schizophrenia was refusing treatment and refusing to eat. After initiation of court ordered medication, the patient received olanzapine 10 mg IM on 4/12/05 at 10:45 a.m. She then complied with laboratory testing and vital signs and on 4/12/05 at 9 p.m. she took one risperidone 2 mg M-tab. On 4/13/05 at 8 a.m. she refused the oral risperidone and was giving olanzapine 10 mg IM. At 10:30 a.m. she refused to go to lunch since she did not feel like eating but she did drink a glass of ice water. At 11:40 a.m. she state that she wasn't feeling well and shortly afterwards she lost consciousness. CPR was initiated and an AED was used. She was transported to the nearest emergency room via ambulance where she was pronounced dead at 12:22 p.m. The autopsy reports cause of death as arthrosclerotic heart disease. The patient has a history of hypertension that the patient denied and refused treatment for. In addition, the patient had a family history of cardiovascular disease and diabetes.

Medication Audit Criteria/Audit Checklist

The Medication Audit Criteria were modified at the meeting in April. Those changes were incorporated into the medication audit criteria and guidelines presented at this meeting. On the motion of Dr. Heidel, seconded by Ms. Chadwick, the recommendation to approve the revised guidelines was approved. Dr. Richards will distribute the approved guidelines to the field.

In reviewing the audit criteria, it was discovered that the audit criteria for duloxetine (Cymbalta®) was not developed. This audit criteria will be developed for presentation at the next meeting.

FDA Alerts

The FDA has issued numerous alerts in the past several months.

> The FDA approved a risk management program for isotretinoin (Accutane®) and its generics called iPLEDGE. In this program, wholesalers, prescribers, pharmacies and patients must register with this program. By registering one accepts specific responsibilities designed to minimize pregnancy exposures in order to distribute, prescribe, dispense and use isotretinoin. Isotretinoin is approved for the treatment of the most severe form of acne (nodular acne) that has not responded to other acne treatments and that can leave permanent scars. As a result of the implementation of this program,

the Committee recommended to change isotretinoin to the reserve category. The criteria for use shall be:

- The patient, prescriber and pharmacy must register with iPLEDGE and comply with all the requirements for the use of isotretinoin.

The Committee recommended that the information regarding iPLEDGE be distributed to the field (clinical/medical directors and pharmacy directors). It was suggested that this memo include a statement that this issue be discussed with the medical staff. In addition, it was recommended that patients currently on isotretinoin sign a new consent form.

As a means to prevent dispensing errors, color branded labeling has been introduced for NovoLog Mix 70/30, a premixed insulin analog, and NovoLog, a rapid-acting insulin analog. Previously, both packaging were white with blue bands. NovoLog Mix 70/30 will have similar packaging and remains white with a blue band. The NovoLog will change to a white with orange band.

A Dear Healthcare Professional and Dear Pharmacist letters were distributed regarding dispensing or prescribing errors associated with Toprol-XL®, Topamax®, Tegretol® and Tegretol-XR®.

The FDA issued a warning that a study has suggested that paroxetine (Paxil®) may be associated with birth defects. A retrospective study found increased numbers of babies born with birth defects to women who were taking paroxetine during the first trimester of pregnancy, as compared with women on other antidepressants. The drug is already classified as a Category C drug for pregnant women – meaning comprehensive studies of is effects on a pregnancy have not been performed.

Atomoxetine (Strattera®) has added a black box warning and additional warning statements that alert health care providers of an increased risk of suicidal thinking in children and adolescents being treated with this medication. The FDA also informed Lilly that a Patient Medication Guide (MedGuide) should be provided when atomoxetine is dispensed.

Eli Lilly has distributed a Dear Health Care Professional letter regarding the hepatic effects of duloxetine (Cymbalta®). The following has been added to the general precaution section of duloxetine: “Postmarketing reports have described cases of hepatitis with abdominal pain, hepatomegaly and elevation of transaminase levels to more than twenty times the upper limit of normal with or without jaundice, reflecting a mixed or hepatocellular pattern of liver injury. Cases of cholestatic jaundice with minimal elevation of transaminase levels have also been reported.” The package insert further states “Postmarketing reports indicated that elevated transaminases, bilirubin and alkaline phosphatase have occurred n patients with chronic liver disease or cirrhosis. Because it is possible that duloxetine and alcohol may interact to cause liver injury or that duloxetine may aggravate pre-existing liver disease; duloxetine should ordinarily not be prescribed to patients with substantial alcohol use or evidence of chronic liver disease.”

A memo regarding these FDA alerts will be distributed to the field. The issue of isotretinoin will be sent separately.

Medicare D

An update on Medicare Part D was provided. Medicare Part D goes into effect on January 1, 2006 and will affect about two thirds of the State School population and one third of the State Hospital population. The plan is to have each facility pharmacy serve as a network pharmacy for each PDP that the patients select. It appears that both DADS and DSHS will utilize HHSC to negotiate the contract with these PDPs. Each facility will need to implement a process to assist consumers and patients in selecting a PDP that is the best for the individual. At this time, a decision has not been made on the process for billing. The vendor for the new Pharmacy system is working on an on-line adjudication program. Last week, a demo of this program was presented to several key individuals in both DADS and DSHS organizations.

New Drug Applications

The Committee did not receive any new drug applications.

Non-Formulary Drug Justification Report

The Quarterly Non-Formulary Drug Justification Report and the Top 10 Non-Formulary Drug purchases for FY05 were reviewed. The top ten non-formulary drug items were also reviewed. The top agent purchased was celecoxib (Celebrex®). Over the years, the Committee has turned down several applications to add a COX-2 inhibitor like celecoxib to the Drug Formulary. It was noted that ofloxacin (Floxin®) Otic made the top ten list. This may be due to the fact that the ciprofloxacin otic product contains hydrocortisone. However, the ophthalmic ciprofloxacin product could be used in the ear. At the next meeting, the Committee will consider the addition of an angiotensin II receptor blocker to the Formulary.

Psychotropic Drug Tables

Dr. Still presented his recommendations for changes to the psychotropic drug tables that are included in the Drug Formulary. His recommendations are:

- For the antipsychotic table - add risperidone (Risperdal®) Consta with a maximum dose of 50 mg every two weeks
- For the antidepressant table - add duloxetine (Cymbalta®) with a maximum dose of 60 mg/day
- For the sedatives and hypnotics table - remove mirtazapine (Remeron®)

On a motion of Dr. Heidel, seconded by Ms. Chadwick, the recommended changes were approved.

Reserve Criteria for Dementia Agents

Currently, donepezil (Aricept®) and rivastigmine (Exelon®) are in the reserve category. Galantamine (Razadyne®) and memantine (Namenda®) are not in the reserve category. Dr. Tramonte presented several options for this category. After much discussion, on a motion of Dr. Heidel, seconded by Dr. Tarin-Godoy, it was recommended that donepezil and rivastigmine be removed from the reserve category.

The Committee recommended that the purchases for these agents be reviewed at the next meeting.

Addition of Dosage Forms and Strengths

Dr. Tramonte recommended that the following items be added to the Formulary:

Aripiprazole (Abilify®) oral solution 1 mg/ml
Atorvastatin (Lipitor®) 80 mg tablet
Citalopram (Celexa®) oral solution 10 mg/5 ml
Hydrochlorothiazide (Oretic®) 12.5 mg capsule
Lamotrigine (Lamictal®) disperse tablets 2 mg, 5 mg, 25 mg
Levofloxacin (Levaquin®) 750 mg tablet
Metronidazole 0.75% cream
Mupirocin (Bactroban®) 2% cream
Vitamin D 50,000 IU capsule
Zafirlukast (Accolate®) 10 mg tablet

On a motion of Dr. Tarin-Godoy, seconded by Dr. Heidel, the recommendation to add these products to the Formulary was approved.

Proposed Drug Deletion List -

Muscle Relaxants
Antiparkinson Agents
Migraine Agents
Miscellaneous CNS Agents
Endocrine Agents

The Committee did not receive any comments from the field about the proposed deletions for the muscle relaxant, antiparkinson, migraine, miscellaneous CNS and endocrine agents. On a motion of Dr. Heidel, seconded by Dr. Tarin-Godoy, the motion to delete these agents was approved.

Drug Formulary Sectional Review- Infectious Disease Agents

Dr. Tramonte provided the review of the infectious disease agents with her recommendation. Attachment A. The comparative cost index and dosage availability of these agents was reviewed (included in Attachment A).

Dr. Tramonte recommended that the following agents be added to the Formulary.

Piperacillin/tazobactam (Zosyn®) is an injectable antibacterial combination product indicated for the treatment of infections of the lower respiratory tract, urinary tract, skin and skin structures, gynecologic, bone and joint infections and septicemia caused by piperacillin resistant, piperacillin/tazobactam-susceptible, β- lactamase producing micro-organisms. Piperacillin sodium exerts bactericidal activity by inhibiting septum formation and cell wall synthesis of susceptible bacteria. *In vitro,* piperacillin is active against a variety of gram-positive and gram-negative aerobic and anaerobic bacteria. Tazobactam is β-lactamase inhibitor of penicillinases and cephalosporinases. It varies in its ability to inhibit class II and IV (2a & 4) penicillinases. It is administered by IV infusion over 30 minutes. See Attachment B.

Cefepime (Maxipime®) is a cephalosporin indicated for the treatment of uncomplicated and complicated urinary tract infections, uncomplicated skin and skin structure infections, pneumonia, and complicated intra-abdominal infections (in combination with metronidazole). It inhibits bacterial cell wall synthesis by binding to one or more of the penicillin-binding proteins (PBPs) which in turn inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell walls, thus inhibiting cell wall biosynthesis. Bacteria eventually lyse due to ongoing activity of cell wall autolytic enzymes (autolysis and murein hydrolases) while cell wall assembly is arrested. It is also active against methicillin-susceptible staphylococci, Enterobacter sp. and many other gram-negative bacilli. See Attachment C.

Moxifloxacin (Avelox®) has *in vitro* activity against a wide range of gram-positive and gram-negative micro-organisms. The bactericidal action of moxifloxacin results from inhibition of the topoisomerase II (DNA gyrase) and topoisomerase IV required for bacterial DNA replication, transcription, repair, and recombination. Moxifloxacin is used in the treatment of infections caused by susceptible organisms. It is used in the treatment of respiratory tract infections, infections of the skin and skin structure; sinusitis, and chronic acute bronchitis. See Attachment D.

Minocycline (Minocin®) is a semisynthetic derivative of tetracycline. The tetracyclines are primarily bacteriostatic and are thought to exert their antimicrobial effect by the inhibition of protein synthesis. The tetracyclines, including minocycline, have similar antimicrobial spectra of activity against a wide range of gram-positive and gram-negative organisms. Cross- resistance of these organisms to tetracyclines is common. Minocycline is indicated for the treatment of susceptible infections of both gram-negative and gram-positive organisms. See Attachment E.

Amikacin (Amikin®) is a semisynthetic aminoglycoside antibiotic derived from

kanamycin. It is bactericidal and interferes with protein synthesis by binding to the 30S ribosomal subunits of susceptible organisms. Its activity spectrum covers gram-negative bacilli and some gram-positive organisms. It is indicated for the short-treatment of serious infections due to organisms resistant to gentamicin and tobramycin including Pseudomonas, Serratia, Proteus and other gram-positive bacilli. See Attachment F.

Terbinafine (Lamisil®) is a synthetic allylamine derivative. Terbinafine is hypothesized to act by inhibiting squalene epoxidase, thus blocking the biosynthesis of ergosterol, an essential component of fungal cell membranes. Terbinafine has been shown to be active against most strains of *Trichophyton mentagrophytes* and *Trichophyton rubrum*. Oral terbinafine is indicated for the treatment of onychomycosis of the toenail or fingernail due to dermatophytes (tinea unguium). See Attachment G.

Rifabutin (Mycobutin®) is a semisynthetic ansamycin antibiotic derived from rifamycin S. Rifabutin inhibits DNA-dependent RNA polymerase which prevents chain initiation. Rifabutin is indicated for the prevention of disseminated *Mycobacterium avium* complex (MAC) disease in patients with advanced HIV infection. See Attachment H.

Oseltamivir (Tamiflu®) is a prodrug. Once hydrolyzed to the active drug, oseltamivir carboxylate, it is thought to inhibit influenza virus neuraminidase, with the possibility of alteration of virus particle aggregation and release. Oseltamivir is used in the treatment of uncomplicated acute illness due to influenza (A or B) infection in adults and children > 1 year of age who have been symptomatic for no more than 2 days or for prophylaxis against influenza (A or B) infection. See Attachment I.

Zanamivir (Relenza®) is for administration to the respiratory tract by oral inhalation only. Each Relenza® Rotadisk contains 4 regularly spaced double-foil blisters with each blister containing a powder mixture of 5 mg of zanamivir and 20 mg of lactose (which contains milk proteins). The contents of each blister are inhaled using a specially designed breath-activated plastic device for inhaling powder called he Diskhaler. After a Relenza® Rotadisk is loaded into the Diskhaler, a blister that contains medication is pierced and the zanamivir is dispersed into the air stream created when the patient inhales through the mouthpiece. The amount of drug delivered to the respiratory tract will depend on patient factors such as inspiratory flow. The proposed mechanism of action of zanamivir is via inhibition of influenza virus neuraminidase with the possibility of alteration of virus particle aggregation and release. No studies have been performed o assess risk of emergence of cross-resistance during clinical use. Zanamivir is indicated for treatment of uncomplicated acute illness due to influenza A and B virus in adults and pediatric patients 7 years and older who have been symptomatic for no more than 2 days. Zanamivir is not recommended for treatment of patients with underlying airway disease (such as asthma or chronic obstructive pulmonary disease). See Attachment J.

Valacyclovir (Valtrex®) is the hydrochloride salt of L-valyl ester of the antiviral drug acyclovir. Valacyclovir is rapidly converted to acyclovir which has demonstrated antiviral activity against herpes simples virus types 1 (HSV-1) and 2 (HSV-2) and varicella zoster virus (VZV) both *in vitro* and *in vivo*. The inhibitory activity of acyclovir is highly selective due to its affinity for the enzyme thymidine kinase (TK) encoded by

HSV and VZV. This viral enzyme converts acyclovir into acyclovir monophosphate, a nucleotide analogue. The monophosphate is further converted into diphosphate by cellular guanylate kinase and into triphosphate by a number of cellular enzymes. *In vitro*, acyclovir stops replication of herpes viral DNA. This is accomplished in 3 ways: 1) competitive inhibition of viral DNA polymerase, 2) incorporation and termination of the growing viral DNA chain, and 3) inactivation of the viral DNA polymerase. The greater antiviral activity of acyclovir against HSV compared to VZV is due to its more efficient phosphorylation by the viral TK. Valacyclovir is indicated for the treatment of herpes zoster (shingles), for the treatment or suppression of genital herpes in immunocompetent individuals and for the suppression of recurrent genital herpes in HIV-infected individuals and for the treatment of cold sores (herpes labialis). See Attachment K.
Ivermectin (Stromectol®) is a semisynthetic antihelmintic agent that binds selectively to glutamate-gated chloride ion channels which occurs in invertebrate nerve and muscle cells. This leads to increased permeability of cell membranes to chloride ions leading to hyperpolarization of the nerve and muscle cell which results in the parasites death. Ivermectin is used in the treatment of infections due to *Strongyloides stercoralis* and *Onchocerca volvulus*. Ivermectin has been used for other parasitic infections including *Ascaris lumbicoides, Bancroftian filariasis, Brugia malayi*, scabies, *Enterobius vermicularis, Mansonella ozzardi* and *Trichuris trichiura*. See Attachment L.

On a motion by Dr. Heidel, seconded by Dr. Tarin-Godoy, the recommendation to add these drugs to the formulary was approved. The Formulary CheckLists were completed.

Dr. Tramonte recommended the deletion of the following dosage strengths/formulations.

Generic Name	Brand Name	Dosage forms to be deleted	Dosage forms still available
Cefoperazone	Cefobid®	Infusion, premixed in dextrose: 1 g, 2 g Powder for injection: 1 g, 2 g	None
Chloroquine	Aralen®	Tablet: 250 mg, 500 mg	None
Cloxacillin	Cloxapen®, Tegopen®	Capsule: 250 mg, 500 mg Powder for oral suspension: 125 mg/5 ml	None
Ethionamide		Tablet, sugar-coated: 250 mg	None
Pentamidine	Pentam®	Inhalation:300 mg Powder for injection: 300 mg	None
Pyrantel	Antiminth®	Capsule: 180 mg Liquid, oral: 50 mg/ml Suspension, oral: 50 mg/ml	None
Thiabendazole	Mintezol®	Suspension, oral: 500 mg/5 ml Tablet, chewable: 500 mg	None
Ticarcillin	Ticar®	Powder for injection: 1 g, 3 g, 6 g, 20 g, 30 g	None
Ticarcillin/ clavulanate	Timentin®	Powder for injection: 3.1 g	None

On a motion of Dr. Heidel, seconded by Dr. Tarin-Godoy, the motion to delete these products was approved. Feedback will be obtained from the field.

The Committee reviewed the recommendations by Dr. Tramonte regarding the antiretroviral agents used in the treatment of HIV-AIDS. On a motion of Dr. Tarin-Godoy, seconded by Ms. Chadwick, it was recommended that all commercially available antiviral agents used in the treatment of HIV-AIDS be on Formulary since any treatment a patient is receiving for HIV-AIDS would be continued when the patient is admitted to a State Facility.

Sectional Review for February 2006

The gastrointestinal and genitourinary agents will be reviewed at the next meeting.

DADS/DSHS 2006 Drug Formulary

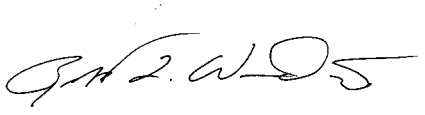
The DADS/DSHS 2006 Drug Formulary was presented for review. The Formulary has been reviewed for emerging safety and efficacy information on an ongoing basis throughout the year. In addition, specific in-depth sectional reviews have been completed at each meeting. On a motion of Dr. Heidel, seconded by Dr. Tarin-Godoy, the DADS/DSHS 2006 Drug Formulary was approved.

Next Meeting Date

The next scheduled EFC meeting is February 10, 2006.

Adjourn

There being no further business, the meeting was adjourned at 1:33 p.m.



Approved: Robert Ward, D.O., Interim Chairman

Attachments

- Attachment A - Infectious Agents Class Review & Cost Review and Alphabetical Listing
- Attachment B - Piperacillin/tazobactam (Zosyn®) Monograph
- Attachment C - Cefepime (Maxipime®) Monograph
- Attachment D - Moxifloxacin (Avelox®) Monograph
- Attachment E - Minocycline (Minocin®) Monograph
- Attachment F - Amikacin (Amikin®) Monograph
- Attachment G - Terbinafine (Lamisil®) Monograph
- Attachment H - Rifabutin (Mycobutin®) Monograph
- Attachment I - Oseltamivir (Tamiflu®) Monograph
- Attachment J - Zanamivir (Relenza®) Monograph
- Attachment K - Valacyclovir (Valtrex®) Monograph
- Attachment L - Ivermectin (Stromectol®) Monograph

Minutes Prepared by:
Ann L. Richards, Pharm.D.
Rosha Chadwick

Attachment A

Memorandum

To: Executive Formulary Committee

From: Sharon M. Tramonte, Pharm.D.

Through: Ann L. Richards, Pharm.D.

Subject: Class Review – Infectious Disease Agents

Date: 20 October 2005

Upon review, the following is a synopsis of recommended changes to the DSHS/DADS Formulary.

Recommended for addition:

- Pipracillin/Tazobactam (Zosyn)
- Cefepime (Maxipime)
- Moxifloxacin (Avelox)
- Minocycline (Dynacin, Minocin)
- Amikacin (Amikin)
- Terbenafine (Lamisil)
- Rifabutin (Mycobutin)
- Oseltamivir (Tamiflu)
- Zanamivir (Relenza)
- Valacyclovir (Valtrex)
- Ivermectin (Stromectol)

Recommended for deletion:

- Cloxacillin (Cloxapen, Tegopen)
- Ticarcillin (Ticar)
- Ticarcillin/Clavulanate (Timentin)
- Cefoperazone (Cefobid)
- Chloroquine (Aralen)
- Ethionamide (Trecator-SC)

- Pentamidine (Pentam)
- Thiabendazole (Mintezol)
- Pyrantel (Pin-Rid, Amtimenth)

Other Recommendations:

- Remove the individual antiretroviral agents used in the treatment of HIV-AIDS for the following reasons:
  - The infectious disease agents are systematically reviewed every three years which is not frequent enough to provide timely assessment of the agents.
  - The vast majority of patients treated with these agents come into our facilities with their therapy already determined and we are merely continuing their therapy.
  - Those patients who would initiate therapy while in one of our facilities will most likely be seen by an infectious disease specialist who will determine the therapy.
- Add a "disclaimer statement" for the antiretroviral agents such as "The use of antiretroviral agents in the treatment of HIV-AIDS should be determined by an infectious disease specialist"
- Add a "disclaimer statement" to ensure all facilities stock agents needed for HIV postexposure prophylaxis such as " Each facility should ensure timely access to agents needed for HIV postesposure prophylaxis regimens as determined by the CDC and the facility infection control policies."

Infectious Disease Agents

Antibiotics

Penicillins

Amoxicillin (Amoxil, Polymox)	$ - $$$$
Amoxicillin/Clavulanate (Augmentin)	$$$ - $$$$$
Ampicillin (Polycillin, Omnipen)	$ - $$$$
~~Cloxacillin (Cloxapen, Tegopen or~~ Dicloxacillin (Dycill, Dynapen, Pathocil)	$ - $$$$$$
Nafcillin (Unipen) or Oxacillin (Prostaphlin)	$ - $$$$$
Penicillin G Benzathine (Bicillin)	$$$ - $$$$$$$
Penicillin G Benzathine/Penicillin G Procaine (Bicillin C-R)	$$$$
Penicillin G Procaine (Wycillin)	$$ - $$$$$$
Penicillin G Sodium	$$ - $$$$
Penicillin V Potassium (Pen-Vee K, V-Cillin K)	$ - $$
~~Ticarcillin (Ticar)~~	~~$$$$$ - $$$$$$$~~
~~Ticarcillin/Clavulanate (Timentin)~~	~~$$$$$$$~~

Cephalosporins

Cefazolin (Kefzol, Ancef)	$$$$ - $$$$$
~~Cefoperazone (Cefobid)~~	~~$$$$$$$~~
Ceftriaxone (Rocephin)	$$$$$$
Cefuroxime Axetil (Ceftin) - Oral form only - **RESERVE USE**	$$$ - $$$$$
Cephalexin (Keflex)	$ - $

Macrolides

Azithromycin (Zithromax) - **RESERVE USE**	$$$$$$
Clarithromycin (Biaxin) - **RESERVE USE**	$$$ - $$$$
Erythromycin (Erythrocin)	$ - $
Erythromycin Ethylsuccinate/Sulfisoxazole Suspension (Pediazole)	$ - $$

Tetracyclines

Doxycycline (Vibramycin)	$ - $$$$$
Tetracycline (Achromycin, Panmycin)	$ - $$

Quinolones

Ciprofloxacin (Cipro)	$$$$ - $$$$$$
Levofloxacin (Levaquin)	$$$$$ - $$$$$$

Aminoglycosides

Gentamicin (Garamycin)	$$
Neomycin (Mycifradin)	$$ - $$$$
Tobramycin (Nebcin)	$$$ - $$$$

Miscellaneous Antibiotics

Clindamycin (Cleocin)	$ - $$$$$$
Metronidazole (Flagyl)	$ - $$$$$$
Trimethoprim/Sulfamethoxazole (Co-Trimoxazole, Bactrim, Septra)	$ - $$$$$$
Vancomycin (Vancocin)	$$$$ - $$$$$$

Antifungals

Fluconazole (Diflucan)	$$$$ - $$$$$
Griseofulvin (Fulvicin)	$
Ketoconazole (Nizoral)	$$ - $$$
Nystatin (Mycostatin)	$$ - $$

~~Antimalarials~~

~~Chloroquine (Aralen)~~	~~$$$~~

Antituberculars

Ethambutol (Myambutol)	$$ - $$$$
~~Ethionamide~~	~~$$$~~
Isoniazid (INH)	$
Pyrazinamide	$ - $$$
Rifampin (Rifadin)	$$ - $$$$$$$
Rifampin/Isoniazid (Rifamate)	$$

Antivirals

Acyclovir (Zovirax)	$$ - $$$$
Amantadine (Symmetrel)	$$ - $$
~~Delavirdine (DLV, Rescriptor)~~	~~$$$$~~
~~Didanosine (ddI, Videx)~~	~~$$$$~~
~~Indinavir (Crixivan)~~	~~$$$$$~~
~~Lamivudine (Epivir)~~	~~$$$$~~
~~Lamivudine/Zidovudine (Combivir)~~	~~$$$$$$~~
~~Nelfinavir (Viracept)~~	~~$$$$$$~~
~~Nevirapine (NVP, Viramune)~~	~~$$$$~~
~~Ritonavir (Norvir)~~	~~$$$$ - $$$$$$~~
~~Saquinavir (Invirase, Fortovase)~~	~~$$$$~~
~~Stavudine (d4T, Zerit)~~	~~$$$$~~
~~Zidovudine (AZT, Retrovir)~~	~~$$$$ - $$$$$~~

Antihelmintics

Mebendazole (Vermox)	$$$ - $$$$$
~~Pyrantel (Antiminth)~~	~~$ - $$$$~~
~~Thiabendazole (Mintezol)~~	~~$$$$~~

Urinary Anti-Infectives

Nitrofurantoin (Macrodantin)	$$ - $$$$

~~Miscellaneous Anti-Infectives~~

~~Pentamidine (Pentam) - Reserve Use~~	~~$$$$$$~~

Acyclovir (Zovirax)

Capsule: 200 mg
Powder for injection: 500 mg, 1000 mg
Ointment, topical 5% [50 mg/g]: 3 gm, 15 gm
Suspension, oral: 200 mg/5 mL
Tablet: 400 mg, 800 mg

Amantadine (Symmetrel)
Capsule: 100 mg
Syrup: 50 mg/5 mL

Amoxicillin (Amoxil, Polymox)
Capsule: 250 mg, 500 mg
Powder for oral suspension: 50 mg/mL, 125 mg/5 mL, 250 mg/5 mL
Tablet: 500 mg, 875 mg
Tablet, chewable: 125 mg, 250 mg

Amoxicillin/Clavulanate (Augmentin)
Tablet: 200 mg (contains 28.5 mg Clavulanate), 250 mg (contains 125 mg Clavulanate), 400 mg (contains 57 mg Clavulanate), 500 mg (contains 125 mg Clavulanate), 875 mg (contains 125 mg Clavulanate)
Tablet, chewable: 125 mg (contains 31.25 mg Clavulanate), 250 mg (contains 62.5 mg Clavulanate)

Ampicillin (Polycillin, Omnipen)
Capsule, as anhydrous: 250 mg, 500 mg
Capsule, as trihydrate: 250 mg, 500 mg
Powder for injection: 125 mg, 250 mg, 500 mg, 1 g, 2 g, 10 g
Powder for oral suspension, as trihydrate: 125 mg/5 mL, 250 mg/5 mL

Azithromycin (Zithromax)- RESERVE USE
Powder for oral solution: 200 mg/5 mL, 400 mg/5 mL
Tablet: 250 mg, 600 mg

Cefazolin (Kefzol, Ancef)
Injection: 500 mg, 1 g
Powder for injection: 250 mg, 500 mg, 1 g, 5 g, 10 g, 20 g

~~**Cefoperazone (Cefobid)**~~
~~Infusion, premixed in dextrose: 1 g, 2 g~~
~~Powder for injection: 1 g, 2 g~~

Ceftriaxone (Rocephin)
Infusion, premixed in dextrose: 1 g, 2 g
Powder for injection: 250 mg, 500 mg, 1 g, 2 g, 10 g

Cefuroxime Axetil (Ceftin) - Oral form only - RESERVE USE
Powder for oral suspension: 125 mg/5 mL, 250 mg/5 mL
Tablet: 125 mg, 250 mg, 500 mg

Cephalexin (Keflex)
Capsule: 250 mg, 500 mg
Powder for oral suspension: 100 mg/mL, 125 mg/5 mL, 250 mg/5 mL
Tablet: 250 mg, 500 mg, 1 g
Tablet: 500 mg

~~**Chloroquine (Aralen)**~~
~~Tablet: 250 mg, 500 mg~~

Ciprofloxacin (Cipro, Ciloxan)
Injection: 200 mg, 400 mg
Solution, ophthalmic: 0.3%
Suspension, oral: 5 gm/100 mL, 10 gm/100 mL
Tablet: 100 mg, 250 mg, 500 mg, 750 mg

Clarithromycin (Biaxin) - RESERVE USE
Granules for oral suspension: 125 mg/5 mL, 250 mg/5 mL
Tablet, film coated: 250 mg, 500 mg

Clindamycin (Cleocin, Cleocin T)
Capsule: 75 mg, 150 mg, 300 mg
Gel, topical: 1% [10 mg/g]
Granules for oral solution: 75 mg/5 mL
Injection: 150 mg/mL
Lotion: 1% [10 mg/mL]
Solution, topical: 1% [10 mg/mL]

~~**Cloxacillin (Cloxapen, Tegopen)**~~
~~Capsule: 250 mg, 500 mg~~
~~Powder for oral suspension: 125 mg/5 mL~~

~~**Delavirdine (DLV, Rescriptor)**~~
~~Tablet: 100 mg, 200 mg~~

Dicloxacillin (Dycill, Dynapen, Pathocil)
Capsule: 125 mg, 250 mg, 500 mg
Powder for oral suspension: 62.5 mg/mL

~~**Didanosine (ddI, Videx)**~~
~~Capsule, delayed release: 250 mg~~
~~Powder for oral solution: 100 mg, 167 mg, 250 mg, 375 mg, 2 gm, 4 gm~~
~~Tablet, chewable: 25 mg, 50 mg, 100 mg, 150 mg, 200 mg~~

Doxycycline (Vibramycin, Periostat)
- Capsule: 50 mg, 100 mg
- Powder for injection: 100 mg, 200 mg
- Powder for oral suspension: 25 mg/5 mL
- Syrup: 50 mg/5 mL
- Tablet: 20 mg, 50 mg, 100 mg

Erythromycin (Erythrocin)
- Erythromycin base(Eryc, E-Mycin, Ery-Tab, E-Base, PCE):
  - Capsule, delayed release: 250 mg
  - Tablet, enteric coated: 250 mg, 333 mg, 500 mg
  - Tablet, film coated: 250 mg, 500 mg
  - Tablet, polymer coated particles: 333 mg, 500 mg
- Erythromycin Ethylsuccinate (EryPed, E.E.S.):
  - Granules/Powder for oral suspension: 200 mg/5 mL, 400 mg/5 mL
  - Suspension, oral: 200 mg/5 mL, 400 mg/5 mL
  - Suspension, oral (drops): 100 mg/2.5 mL
  - Tablet: 400 mg
  - Tablet, chewable: 200 mg
- Ointment, ophthalmic: 5%

Erythromycin Ethylsuccinate/Sulfisoxazole Suspension (Pediazole)
- Suspension, oral: 200 mg/600 mg per 5 mL

Ethambutol (Myambutol)
- Tablet: 100 mg, 400 mg

~~**Ethionamide**~~
- ~~Tablet, sugar coated: 250 mg~~

Fluconazole (Diflucan)
- Tablet: 100 mg, 150 mg, 200 mg, 250 mg, 500 mg

Gentamicin (Garamycin)
- Cream, topical: 0.1%
- Infusion, premixed in D5W: 60 mg, 80 mg, 100 mg
- Infusion, premixed in NS: 40 mg, 60 mg, 80 gm, 90 mg, 100 mg, 120 mg
- Injection: 10 mg/mL, 40 mg/mL
- Injection, intrathecal (preservative free): 2 mg/mL
- Ointment, ophthalmic: 0.3% [3 mg/g]
- Ointment, topical: 0.1%
- Solution, ophthalmic: 0.3% [3 mg/mL]

Griseofulvin (Fulvicin)
- Microsize:
  - Capsule: 125 mg, 250 mg
  - Suspension, oral: 125 mg/5 mL with 0.2% alcohol
  - Tablet: 250 mg, 500 mg
- Ultramicrosize:
  - Tablet: 125 mg, 165 mg, 250 mg, 330 mg

~~**Indinavir (Crixivan)**~~
- ~~Capsule: 400 mg~~

Isoniazid (INH)
- Injection: 100 mg/mL
- Syrup: 50 mg/5 mL
- Tablet: 50 mg, 100 mg, 300 mg

Ketoconazole (Nizoral)
- Cream, topical: 2%
- Shampoo: 2%
- Tablet: 200 mg

~~**Lamivudine (Epivir)**~~
- ~~Solution, oral: 10 mg/mL~~
- ~~Tablet: 150 mg~~

~~**Lamivudine/Zidovudine (Combivir)**~~
- ~~Tablet: Lamivudine 150 mg/Zidovudine 300 mg~~

Levofloxacin (Levaquin)
- Infusion: 250 mg, 500 mg
- Tablet: 250 mg, 500 mg

Mebendazole (Vermox)
- Tablet, chewable: 100 mg

Metronidazole (Flagyl, Noritate, MetroGel)
- Capsule: 375 mg
- Cream, topical: 1%
- Gel, topical: 0.75% [7.5 mg/mL]
- Gel, vaginal: 0.75%
- Injection: 5 mg/mL
- Powder for injection: 500 mg
- Tablet: 250 mg, 500 mg

Nafcillin (Unipen)
Capsule: 250 mg
Powder for injection: 500 mg, 1 g, 2 g, 4 g, 10 g
Solution: 250 mg/5 mL
Tablet: 500 mg

~~**Nelfinavir (Viracept)**~~
~~Powder for oral solution: 50 mg/g~~
~~Tablet: 250 mg~~

Neomycin (Mycifradin)
Tablet: 500 mg

~~**Nevirapine (NVP, Viramune)**~~
~~Tablet: 200 mg~~

Nitrofurantoin (Macrodantin)
Capsule: 50 mg, 100 mg
Capsule, extended release: 100 mg
Capsule, macrocrystal: 25 mg, 50 mg, 100 mg
Capsule, macrocrystal/monohydrate: 100 mg
Suspension, oral: 25 mg/mL

Nystatin (Mycostatin)
Cream, topical: 100,000 units/g
Ointment, topical: 100,000 units/g
Powder for oral suspension: 50 million units, 1 billion units, 2 billion units, 5 billion units
Powder, topical: 100,000 units/g
Suspension, oral: 100,000 units/mL
Tablet, oral: 500,000 units
Troche: 200,000 units

Oxacillin (Prostaphlin)
Capsule: 250 mg, 500 mg
Powder for injection: 250 mg, 500 mg, 1 g, 2 g, 4 g, 10 g
Powder for oral solution: 250 mg/5 mL

Penicillin G Benzathine (Bicillin)
Injection: 300,000 units/mL, 600,000 units/mL

Penicillin G Benzathine/Penicillin G Procaine (Bicillin C-R)
Injection: Penicillin G Benzathine 150,000 units/Penicillin G Procaine 150,000 units, Penicillin G Benzathine 900,000 units/Penicillin G Procaine 300,000 units

Penicillin G Procaine (Wycillin)
Injection (suspension): 300,000 units/mL, 500,000 units/mL, 600,000 units/mL

Penicillin G Sodium
Injection: 5 million units

Penicillin V Potassium (Pen-Vee K, V-Cillin K)
Powder for oral solution: 125 mg/5 mL, 250 mg/5 mL
Tablet: 125 mg, 250 mg, 500 mg

~~**Pentamidine (Pentam) - Reserve Use**~~
~~Inhalation: 300 mg~~
~~Powder for injection: 300 mg~~

~~**Pyrantel (Antiminth)**~~
~~Capsule: 180 mg~~
~~Liquid, oral: 50 mg/mL~~
~~Suspension, oral: 50 mg/mL~~

Pyrazinamide
Tablet: 500 mg

Rifampin (Rifadin)
Capsule: 150 mg, 300 mg
Injection: 600 mg

Rifampin/Isoniazid (Rifamate)
Capsule: Rifampin 300 mg/Isoniazid 150 mg

~~**Ritonavir (Norvir)**~~
~~Capsule: 100 mg~~
~~Solution, oral: 80 mg/mL~~

~~**Saquinavir (Invirase, Fortovase)**~~
~~Capsule: 200 mg~~

~~**Stavudine (d4T, Zerit)**~~
~~Capsule: 15 mg, 20 mg, 30 mg, 40 mg~~
~~Solution, oral: 1 mg/mL~~

Tetracycline (Achromycin, Panmycin)
Capsule: 100 mg, 250 mg, 500 mg
Suspension, oral: 125 mg/5 mL
Tablet: 250 mg, 500 mg

~~**Thiabendazole (Mintezol)**~~
~~Suspension, oral: 500 mg/5 mL~~
~~Tablet, chewable: 500 mg~~

~~**Ticarcillin (Ticar)**~~
~~Powder for injection: 1 g, 3 g, 6 g, 20 g, 30 g~~

~~**Ticarcillin/Clavulanate (Timentin)**~~
~~Powder for injection: 3.1 g~~

Tobramycin (Nebcin, Tobrex)
Injection: 10 mg/mL, 40 mg/mL
Ointment, ophthalmic: 0.3%
Powder for injection: 40 mg/mL
Solution, ophthalmic: 0.3%

Trimethoprim/Sulfamethoxazole (Co-Trimoxazole, Bactrim, Septra)
The 5:1 ratio of Sulfamethoxazole (SMX) to Trimethoprim (TMP) is constant in all dosage forms
Injection: 80 mg SMX/16 mg TMP per mL
Suspension, oral: 200 mg SMX/40 mg TMP per 5 mL
Tablet: 400 mg SMX/80 mg TMP, 800 mg SMX/160 mg TMP

Vancomycin (Vancocin)
Capsule: 125 mg, 250 mg
Powder for oral solution: 1 g, 10 g
Powder for injection: 500 mg, 1 g, 2 g, 5 g, 10 g

~~**Zidovudine (AZT, Retrovir)**~~
~~Capsule: 100 mg~~
~~Injection: 10 mg/mL~~
~~Syrup: 50 mg/5 mL~~
~~Tablet: 300 mg~~

Piperacillin/Tazobactam

Zosyn®, Wyeth- Ayerst Laboratories)

Classification: Infectious Disease Agents; Antibiotics; Penicillins

Description: Zosyn (piperacillin and tazobactam for injection) is an injectable antibacterial combination product consisting of the semisynthetic antibiotic piperacillin sodium and the ß- lactamase inhibitor tazobactam sodium for IV administration.

Pharmacology: Piperacillin sodium exerts bactericidal activity by inhibiting septum formation and cell wall synthesis of susceptible bacteria. *In vitro,* piperacillin is active against a variety of gram- positive and gram- negative aerobic and anaerobic bacteria. Tazobactam is ß- lactamase inhibitor of penicillinases and cephalosporinases. It varies in its ability to inhibit class II and IV (2a & 4) penicillinases.

Pharmacokinetics:

Absorption: N/A, administered intravenously

Distribution: Piperacillin and tazobactam are widely distributed into tissues and body fluids with mean tissue concentrations are generally 50- 100% of those in plasma.

Metabolism: Piperacillin is metabolized to a minor microbiologically active desethyl metabolite. Tazobactam is metabolized to a single metabolite that lacks pharmacological and antibacterial activities.

Excretion: Piperacillin is excreted rapidly primarly as the unchanged drug in the urine. Tazobactam and its metabolite are eliminated primarily in the urine. Piperacillin, tazobactam, and desethyl piperacillin are also secreted into the bile.

Indications: Treatment of infections of the lower respiratory tract, urinary tract, skin and skin structures, gynecologic, bone and joint infections and septicemia caused by piperacillin resistant, piperacillin/ tazobactam- susceptible, β- lactamase producing micro-organisms

Dosage:

- Zosyn should be administered by IV infusion over 30 minutes.
- The usual total daily dose of Zosyn for adults is 3.375 g every 6 hours for 7 to 10 days
- Initial presumptive treatment of patients with nosocomial pneumonia should start with Zosyn at a dosage of 4.5 g every 6 hours plus an aminoglycoside for 7 to 14 days
- Doses should be reduced in patients with renal dysfunction

Cl_{Cr} ml/ min	All Indications (Except Nosocomial Pneumonia)	Nosocomial Pneumonia
>40 ml/ min	3.375 q6h	4.5 q6h
20- 40 ml/ min	2.25 q6h	3.375 q6h
<20 ml/ min	2.25 q8h	2.25 q6h
Hemodialysis	2.25 q12h	2.25 q8h

Contraindications and Precautions:

- Pregnancy category B
- contraindicated in patients with a history of allergic reactions to any of the penicillins, cephalosporins, or β- lactamase inhibitors
- Anaphylactic reactions have been reported with Piperacillin/Tazobactam
- As with other penicillins, the administration of Zosyn may result in a false-positive reaction for glucose in the urine using a copper- reduction method (Clinitest).
- Due to the sodium load, dosage modification is required in patients with renal dysfunction

Interactions:

Increased effect/toxicity: Probenecid may increase penicillin levels.

Decreased effect: Tetracyclines may decrease penicillin effectiveness. Efficacy of oral contraceptives may be reduced. Aminoglycosides may cause physical inactivation of aminoglycosides in patients with mild to moderate renal dysfunction due to the elevated concentrations of piperacillin.

Adverse Reactions:

The most common adverse reaction (>10%) is diarrhea. Less common adverse reactions (1% to 10%) include: hypertension, insomnia, headache, agitation, dizziness, rash, Pruritus constipation, nausea, vomiting/dyspepsia or dyspnea.

Laboratory abnormalities associated with the administration of Pipracillin/Tazobactam include: eosinophilia, neutropenia, positive direct Coombs' test, prolonged PT and aPTT, transient elevations of liver function tests and increases in creatinine.

Costs and Monitoring:

Monitoring should include liver enzymes, creatinine, BUN, CBC with differential, serum electrolytes, urinalysis, PT, PTT and signs or symptoms of anaphylaxis. Cost of therapy is $ 54.92 per day.

Product Identification:

Injection: 2.25 g, **3.375 g and 4.5 g**

Recommendation: Add to formulary

References:

1. Pipracillin/Tazobactam Monograph. Mosby's Drug Consult. Mosby's Inc., St. Louis Mo. 2003.

2. Pipracillin/Tazobactam Monograph. APhA Drug Information Handbook. Lexi-Comp, Inc. Hudson Ohio. 2002-2003.

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Cefepime

(Maxipime®, Elan pharmaceuticals)

Classification: Infectious Disease Agents; Antibiotics; Cephalosporins

Pharmacology: Cefepime inhibits bacterial cell wall synthesis by binding to one or more of the penicillin-binding proteins (PBPs) which in turn inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell walls, thus inhibiting cell wall biosynthesis. Bacteria eventually lyse due to ongoing activity of cell wall autolytic enzymes (autolysis and murein hydrolases) while cell wall assembly is arrested.

Pharmacokinetics:

Absorption: IM absorption is rapid and complete
Distribution: Penetrates well into inflammatory fluid; crosses the blood brain barrier; minimally protein bound
Metabolism: Undergoes minimal hepatic metabolism
Elimination: Excreted in the urine, primarily as the unchanged drug

Indications: Used in the treatment of uncomplicated and complicated urinary tract infections, uncomplicated sin and skin structure infections, pneumonia, complicated intra-abdominal infections (in combination with Metronidazole). Also active against methicillin-susceptible staphylococci, Enterobacter sp. and many other gram-negative bacilli.

Dosage:

- Administer IM or IV
- Most infections can be treated with 1 – 2 grams every 12 hours for 5 to 10 days
- Higher doses or more frequent administration may be required in pseudomonal infections
- Urinary tract infections can be treated with 500 mg every 12 hours
- Reduce dose in renal impairment

Cl_{Cr} (mL/min)	Recommended Maintenance Schedule	
> 60	500 mg q12h	1 – 2 gm q12h
30 – 60	administer every 24 hours	administer every 24 hours
11 – 29	administer every 24 hours	administer ½ dose every 24 hours
< 11	administer ½ dose every 24 hours	administer ¼ dose every 24 hours

- Hemodialysis: Removed by dialysis. Administer supplemental dose of 250 mg

after each dialysis session.

Contraindications and Precautions:

- Pregnancy category: B
- Hypersensitivity to Cefepime or other cephalosporins
- Modify dose in patients with severe renal impairment

Interactions:

High dose Probenecid decreases clearance and increases the effects of Cefepime. Aminoglycosides increase the nephrotoxic potential of Cefepime.

Adverse Reactions:

The most common reaction is the development of a positive Coombs' test without hemolysis. Less common adverse reactions (1% to 10%) include: fever, headache, rash, pruritus, diarrhea, nausea, vomiting and injection site pain or erythema.

Costs and Monitoring:

Monitoring: obtain C & S prior to the first dose; monitor for signs or symptoms of anaphylaxis during the first dose.

Cost is determined by the dose required to treat the infection. Cost will range from $ 15.64 to $ 61.88 per day.

Product Identification:

Injection: 500 mg, 1 gm, 2 gm

Recommendation: Add to formulary

References:

3. Cefefpime Monograph. APhA Drug Information Handbook. Lexi-Comp, Inc. Hudson Ohio. 2003-2004.

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Moxifloxacin

(Avelox®, Bayer Pharmaceutical)

Classification: Infectious Disease Agents; Antibiotics; Quinolones

Pharmacology: Moxifloxacin has in vitro activity against a wide range of gram- positive and gram- negative microorganisms. The bactericidal action of moxifloxacin results from inhibition of the topoisomerase II (DNA gyrase) and topoisomerase IV required for bacterial DNA replication, transcription, repair, and recombination.

Pharmacokinetics:

Absorption: The oral tablet is well absorbed from the gastrointestinal tract with an absolute bioavailability of 90%

Distribution: Widely distributed throughout the body, with tissue concentrations often exceeding plasma concentrations.

Metabolism: Approximately 52% of an oral or IV dose of moxifloxacin is metabolized via glucuronide and sulfate conjugation. The cytochrome P450 system is not involved in moxifloxacin metabolism, and is not affected by moxifloxacin

Elimination: Approximately 45% of an oral or IV dose of moxifloxacin is excreted as unchanged drug.The sulfate conjugate (38%) is eliminated primarily in the feces. The glucuronide conjugate (14%) is excreted exclusively in the urine.

Indications: Used in the treatment of infections caused by susceptible organisms. Used in the treatment of respiratory tract infections, infections of the skin and skin structure; sinusitis, and chronic or acute bronchitis.

Dosage: The dose of moxifloxacin HCl is 400 mg (oral or IV) once every 24 hours. The duration of therapy ranges from 5 to 14 days and depends on the type of infection.

Contraindications and Precautions:

- Pregnancy category C
- hypersensitivity to moxifloxacin
- Moxifloxacin has been shown to prolong the QT interval of the electrocardiogram in some patients.
- used with caution in patients with ongoing proarrhythmic conditions
- Use with caution in patients at risk of seizures
- Not recommended in patients with moderate to sever hepatic insufficiency
- Use with caution in patients with diabetes; glucose regulation may be altered
- Severe hypersensitivity, including anaphylaxis, reactions have been reported;

monitor the patient for these reactions

- Quinolones may exacerbate myasthenia gravis

Interactions:

Increased risk of QT prolongation with other agents that prolong the QT interval. Cimetidine and Probenacid and loop diuretics increases serum levels of Moxifloxacin. Foscarnet and NSAIDs increase the seizure risk when given with Moxifloxacin.

Oral doses of moxifloxacin should be administered at least 4 hours before or 8 hours after antacids containing magnesium or aluminum, as well as sucralfate, metal cations such as iron, and multivitamin preparations with zinc

Adverse Reactions:

The most common adverse reactions (3% to 10%) include: dizziness, nausea and diarrhea. Less common adverse reactions (up to 3%) include: chest pain, hypertension, pal

Costs and Monitoring:

Monitor for signs of infection and CBC.

Cost of therapy per day ranges from $ 8.62 for oral therapy and $ 33.93 for intravenous therapy.

Product Identification:

Infusion: 400 mg/250 mL
Tablet: 400 mg

Recommendation: Add to formulary

References:

4. Moxifloxacin Monograph. Mosby's Drug Consult. Mosby's Inc., St. Louis Mo. 2003.

5. Moxifloxacin Monograph. APhA Drug Information Handbook. Lexi-Comp, Inc. Hudson Ohio. 2003-2004.

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Minocylcine

(various manufacturers)

Classification: Infectious Disease Agents; Antibiotics; Tetracyclines

Pharmacology: Minocycline is a semisynthetic derivative of tetracycline. The tetracyclines are primarily bacteriostatic and are thought to exert their antimicrobial effect by the inhibition of protein synthesis. The tetracyclines, including minocycline, have similar antimicrobial spectra of activity against a wide range of gram- positive and gram- negative organisms. Cross- resistance of these organisms to tetracyclines is common.

Pharmacokinetics:

Absorption: Well absorbed from the GI tract

Distribution: Majority deposits for extended periods in fat; crosses the placenta and enters the breast milk

Metabolism: metabolized to a significant degree, however, the nature of the metabolic products or sites of metabolism have not been elucidated with certainty

Elimination: Excreted in the urine

Indications: Treatment of susceptible infections of both gram-negative and gram-positive organisms.

Dosage: Doses range from 50 mg every other day to 200 mg daily. Ingestion of adequate amounts of fluids along with capsules and tablets is recommended to reduce the risk of esophageal irritation and ulceration.

Contraindications and Precautions:

- Pregnancy category D
- Hypersensitivity to minocycline or other tetracyclines
- Do not use in pregnancy
- Avoid use during tooth development (children <8 years)
- May be associated with increases in BUN secondary to anti-anabolic effects
- Avoid in renal insufficiency
- May cause photosensitivity
- Hepatotoxicity has been reported; use with caution in patients with hepatic dysfunction and in conjunction with other hepatotoxic drugs.

Interactions:

Minocycline increases the anticoagulant effects of Warfarin. The effects of Minocycline are decreased in the presence of antacids (aluminum, calcium, zinc or

magnesium), iron or dairy products, bismuth salts, barbiturates, Carbamazepine and Phenytoin.

Adverse Reactions:

The most common (>10%) adverse effect is discolorization of teeth in children. Less common (1%-10%) adverse effects include: lightheadedness, vertigo, photosensitivity, nausea and diarrhea.

Costs and Monitoring:

Cost of therapy ranges from $ 0.25 every other day to $ 9.62 per day.

Product Identification:

Capsule: 50 mg, 75 mg, 100 mg
Capsule, pellet filled: 50 mg, 100 mg

Conclusions: Minocycline effectively suppresses Propionibacterium acnes and is clinically effective in treating severe acne.

Recommendation: Add to formulary

References:

6. Minocycline Monograph. Mosby's Drug Consult. Mosby's Inc., St. Louis Mo. 2005.
7. Minocycline Monograph. APhA Drug Information Handbook. Lexi-Comp, Inc. Hudson Ohio. 2003-2004.

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Amikacin

(Amikin®, various)

Classification: Infectious Disease Agents; Antibiotics; Aminoglycosides

Pharmacology: A semi-synthetic aminoglycoside antibiotic derived from kanamycin. It is bactericidal and interferes with protein synthesis by binding to the 30S ribosomal subunits of susceptible organisms. Its activity spectrum covers gram-negative bacilli and some gram-positive organisms.

Pharmacokinetics:

Absorption: IM absoption may be delayed in bedridden patients.
Distribution: Penetrates the blood brain barrier when meninges inflamed; crosses placenta
Elimination: Excreted in the urine; determined by age and renal function status.

Therapeutic peak level: 15 to 30 mcg/mL depending on the severity of the infection.
Trough levels: 1 to 8 mcg/mL
Toxic levels: peak >35 mcg/mL, trough >10 mcg/mL

Indications: Short-term treatment of serious infections due to organisms resistant to Gentamycin and Tobramycin including Pseudomonas, Serratia, Proteus and other gram-positive bacilli.

Dosage: Individualization of dose based on ideal body weight (IBW) is critical because of the low therapeutic index.

- In morbidly obese patients, dosage requirement may best be estimated using a dosing weight of IBW + 0.4 (TBW – IBW)
- Dose is 5 – 7.5 mg/kg/dose IM or IV every 8 hours. Administer IM dose in a large muscle mass.
- Alternate dosing in patients with normal renal function: 15 – 20 mg/kg per day. Some clinicians suggest that this daily dose is at least as efficacious but less toxic than the conventional dosing regimen.
- The dosing interval should be extended in patients with impaired renal function
  $Cl_{Cr} \geq 60$ mL/minute – administer every 8 hours
  Cl_{Cr} 40-60 mL/minute – administer every 12 hours
  Cl_{Cr} 20-40 mL/minute – administer every 24 hours
  $Cl_{Cr} < 20$ mL/minute – administer loading dose, then monitor levels
- Hemodialysis: dialyzable (50% to 100%) administer dose postdialysis or administer 2/3 normal dose as a supplemental dose post dialysis and follow levels.

Contraindications and Precautions:

- Pregnancy category C
- Hypersensitivity to aminoglycoside antibiotics
- Modify dose in renal impairment
- Boxed warning regarding the increased risk of ototoxicity and nephrotocity with intravenous administration.
- Discontinue immediately if signs of ototoxicity, nephrotoxicity or hypersensitivity occur
- May contain sulfites, use with caution in patients with asthma.

Interactions:

Amikacin may increase or prolong the effect of neuromuscular blocking agents. Concurrent use of amphotericin (or other nephrotoxic agents) may increase the risk of Amikacin-induced nephrotoxicity. The risk of ototoxicity may be increased with the use of other ototoxic agents.

Adverse Reactions:

Most common include neurotoxicity, ototoxicty and nephrotoxicity. Rare but significant ADRs include allergic reaction, dyspnea or eosinophilia.

Costs and Monitoring:

Monitoring include urinalysis, BUN, serum creatinine, peak & trough levels, vital signs, temperature, weight, I & Os and hearing parameters.

Cost is determined by the dose required to treat the infection and the size of the individual. The mythical 70 kg individual utilizing the 15 – 20 mg/kg/day dose would cost approximately $10/day.

Product Identification:

Injection: 50mg/mL, 250mg/mL

Conclusions: Amikacin is efficacious in the treatment of serious infections due to organisms resistant to gentacmycin and tobramycin including Pseudomonas, Proteus, Serratia and other gram-negative bacilli including bone infections, respiratory tract infections, endocarditis, and septicemia

Recommendation: Add to formulary

References:

8. Amikacin Monograph. APhA Drug Information Handbook. Lexi-Comp, Inc. Hudson Ohio. 2003-2004.

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Terbinafine

(Lamisil®, Novartis Pharmaceuticals)

Classification: Infectious Disease Agents; Antifungals

Pharmacology: Terbinafine is a synthetic allylamine derivative. Terbinafine is hypothesized to act by inhibiting squalene epoxidase, thus blocking the biosynthesis of ergosterol, an essential component of fungal cell membranes. Terbinafine has been shown to be active against most strains of *Trichophyton mentagrophytes* and*Trichophyton rubrum*

Pharmacokinetics:

Absorption: Well absorbed from the GI tract with an absolute bioavailability of only 40% due to extensive first pass metabolism

Distribution: Highly protein bound and distributed to the sebum and skin

Metabolism: extensively metabolized in the liver

Elimination: The parent drug and metabolites are primarily excreted in the urine

Indications: Terbinafine HCl tablets are indicated for the treatment of onychomycosis of the toenail or fingernail due to dermatophytes (tinea unguium)

Dosage: Terbinafine 250 mg once daily for 6 weeks for fingernail onychomycosis. Terbinafine 250 mg once daily for 12 weeks for toenail onychomycosis.

Contraindications and Precautions:

- Pregnancy category B
- Contraindicated in patients with a known hypersensitivity to terbenafine
- Rare cases of liver failure, some leading to death or liver transplant, have occurred with the use of Terbinafine. Liver function should be assessed prior to initiation of treatment.
- There have been isolated reports of serious skin reactions (*e.g.,* Stevens-Johnson Syndrome and toxic epidermal necrolysis)

Interactions:

In vitro studies have also shown that terbinafine inhibits CYP2D6- mediated metabolism. This may be of clinical relevance for compounds predominantly metabolized by this enzyme, such as tricyclic antidepressants, β- blockers, selective serotonin reuptake inhibitors (SSRIs), and monoamine oxidase inhibitors.

Terbinafine clearance is increased 100% by rifampin, a CyP450 enzyme inducer, and decreased 33% by cimetidine, a CyP450 enzyme inhibitor.

Adverse Reactions:

The most common adverse reactions (1% to 10%) include: headache, dizziness, vertigo, rash, Pruritus, alopecia, nausea, diarrhea, dyspepsia, abdominal pain, appetite decrease, taste disturbance, lymphocytopenia, liver enzyme elevations, visual distrubace and allergic reaction.

Costs and Monitoring:

Prior to initiating treatment, appropriate nail specimens for laboratory testing (KOH preparation, fungal culture, or nail biopsy) should be obtained to confirm the diagnosis of onychomycosis. A CBC and liver function should be assessed prior to the initiation of treatment and repeated if treatment exceeds 6 weeks.

Cost of therapy is $ 9.07 per day.

Product Identification:

Tablet: 250 mg

Efficacy: The efficacy of terbinafine in the treatment of onychomycosis is illustrated by the response of patients with toenail and/ or fingernail infections who participated several placebo- controlled clinical trials. Demonstrated mycological cure, defined as simultaneous occurrence of negative KOH plus negative culture was demonstrated in up to 79% of patients. Up to 75% of patients experienced effective treatment (mycological cure plus 0% nail involvement or >5 mm of new unaffected nail growth) and up to 59% of patients demonstrated mycological cure plus clinical cure (0% nail involvement). Patients with involvement of the fingernails showed greater improvements than those with toenail involvement. Following treatment, the clinical relapse rate was approximately 15%.

The optimal clinical effect is seen some months after mycological cure and cessation of treatment. This is related to the period required for outgrowth of healthy nail.

Recommendation: Add to formulary

References:

9. Terbenafine Monograph. Mosby's Drug Consult. Mosby's Inc., St. Louis Mo. 2005.

10. Terbenafine Monograph. APhA Drug Information Handbook. Lexi-Comp, Inc. Hudson Ohio. 2003-2004.

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Rifabutin

(Mycobutin®, Pfizer U.S. Pharmaceuticals Group)

Classification: Infectious Disease Agents; Antituberculars

Pharmacology: Rifabutin is a semisynthetic ansamycin antibiotic derived from rifamycin S. Rifabutin inhibits DNA- dependent RNA polymerase which precents chain initiation.

Pharmacokinetics:

Absorption: readily absorbed from the gastrointestinal tract with an absolute bioavailability of 53%

Distribution: Rifabutin, due to its high lipophilicity, demonstrates a high propensity for distribution and intracellular tissue uptake. 85% of the drug is bound in a concentration- independent manner to plasma proteins

Metabolism: to both active and inactive metabolites

Elimination: Both the parent and active metabolites are eliminated in the urine and feces

Indications: Rifabutin is indicated for the prevention of disseminated *Mycobacterium avium* complex (MAC) disease in patients with advanced HIV infection.

Dosage: It is recommended that 300 mg of rifabutin be administered once daily. For those patients with propensity to nausea, vomiting, or other gastrointestinal upset, administration of rifabutin at doses of 150 mg twice daily taken with food may be useful. For patients with a ClCr <30 mL/minute, reduce dose by 50%.

Contraindications and Precautions:

- Pregnancy category B
- must not be administered for MAC prophylaxis to patients with <u>active</u> tuberculosis
- Because treatment with rifabutin may be associated with neutropenia, and more rarely thrombocytopenia, physicians should consider obtaining hematologic studies periodically in patients receiving rifabutin prophylaxis
- Contraindicated in patients with a WBC <1000/mm^3 or a platelet count <50,000/mm^3

Interactions:

Rifabutin is a CYP 3A3/4 enzyme inducer.

Increased effect/toxicity: Rifabutin is increased by Indinavir and Ritonavir. Fluconazole increases Rifabutin concentrations.

Decreased effect: Rifabutin may decrease plasma concentrations of Verapamil, methadone, digoxin, cyclosporine, corticosteroids, oral anticoagulants, Theophylline, barbiturates, chloramphenicol, itraconazole, Ketoconazole, oral contraceptives, Quinidine, protease inhibitors (Indinavir, Nelfinavir, Ritonavir, Saquinavir) and non-nucleoside reverse transcrptase inhibitors and clarithromycin.

Adverse Reactions:

The most common adverse reactions (>10%) include: rash, discolored urine, neutropenia, and leukopenia. Less common adverse reactions (1% to 10%) include: headache, nausea, vomiting, diarrhea, abdominal pain, anorexia, flatulence, anemia, thrombocytopenia, increased AST/ALT and myalgia.

Costs and Monitoring:

Monitoring includes periodic liver function tests and CBC with differential.

Cost of therapy is $ 11.62 per day.

Product Identification:

Capsule: 150 mg

Recommendation: Add to formulary.

References:

11. Rifabutin Monograph. Mosby's Drug Consult. Mosby's Inc., St. Louis Mo. 2003.
12. Rifabutin Monograph. APhA Drug Information Handbook. Lexi-Comp, Inc. Hudson Ohio. 2002-2003.

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Oseltamivir

(Tamiflu, Roche Laboratories)

Classification: Infectious Disease Agents; Antivirals

Pharmacology: Oseltamivir is a prodrug. Once hydrolyzed to the active drug, Oseltamivir carboxylate, it is thought to inhibit influenza virus neuraminidase, with the possibility of alteration of virus particle aggregation and release.

Pharmacokinetics:

Absorption: Well absorbed with an absolute bioavailability of 75%

Metabolism: Metabolized by esterases predominately found in the liver to the active drug. Neither the parent drug nor the active drug has any effect on the cytochrome P450 system.

Elimination: Oseltamivir carboxylate is not further metabolized and is eliminated in the urine

Indications: Used in the treatment of uncomplicated acute illness due to influenza (A or B) infection in adults and children >1 year of age who have been symptomatic for no more than 2 days or for prophylaxis against influenza (A or B) infection.

Dosage:

For the treatment of Influenza: 75 mg twice daily for 5 days. Treatment should begin within 2 days of onset of symptoms of influenza.

Prophylaxis of Influenza: 75 mg once daily for at least 7 days. Therapy should begin within 2 days of exposure. The duration of protection lasts for as long as dosing is continued.

For patients with a creatinine clearance between 10 and 30 ml/ min, the dosing interval should be doubled – 75mg daily for treatment and 75 mg every other day for prophylaxis.

Contraindications and Precautions:

- Pregnancy category C
- Hypersensitivity to Oseltamivir
- Oseltamivir is not a substitute for the flu vaccination
- There is no evidence for efficacy of oseltamivir phosphate in any illness caused

by agents other than influenza viruses Types A and B.

Interactions:

Probenecid increased serum concentration of Oseltamivir.

Information derived from pharmacology and pharmacokinetic studies of oseltamivir suggests that clinically significant drug interactions are unlikely. Neither the parent drug nor the active drug has any effect on the cytochrome P450 system.

Adverse Reactions:

When used prophylactically, the most common adverse reactions include: headache, fatigue and diarrhea.

Costs and Monitoring:

Cost ranges from $ 41.58 for prophylaxis to $ 59.40 for a treatment course.

Product Identification:

Capsule: 75 mg

Efficacy:

Efficacy of Oseltamivir has been evaluated in double-blind, placebo- controlled trials were conducted in febrile patients and at least one respiratory symptom (cough, nasal symptoms, or sore throat) and at least one systemic symptom (myalgia, chills/ sweats, malaise, fatigue, or headache) and known influenza virus circulating in the community. Of 1355 patients enrolled, 849 (63%) patients were influenza- infected (age range 18- 65 years; median age 34 years; 52% male; 90% Caucasian; 31% smokers). Of the 849 influenza- infected patients, 95% were infected with influenza A, 3% with influenza B, and 2% with influenza of unknown type.

Oseltamivir 75 mg twice daily for 5 days was started within 40 hours of onset of symptoms. Subjects participating in the trials were required to self- assess the influenza- associated symptoms as "none", "mild", "moderate" or "severe". Time to improvement was calculated from the time of treatment initiation to the time when all symptoms (nasal congestion, sore throat, cough, aches, fatigue, headaches, and chills/ sweats) were assessed as "none" or "mild". There was a 1.3 day reduction in the median time to improvement in the treatment group compared the placebo group.

In a pooled analysis of 2 seasonal prophylaxis studies in healthy unvaccinated adults (aged 13- 65 years), oseltamivir phosphate 75 mg once daily taken for 42 days during a community outbreak reduced the incidence of laboratory confirmed clinical influenza from 4.8% (25/ 519) for the placebo group to 1.2% (6/ 520) for the

oseltamivir phosphate group.

Conclusions: Oseltamivir is an effective way to treat or prevent Influenza. This is especially desirable in the closed population of the schools where Influenza can be fatal in the medically fragile.

Recommendation: Add to formulary.

References:

13. Oseltamivir Monograph. Mosby's Drug Consult. Mosby's Inc., St. Louis Mo. 2005.
14. Oseltamivir Monograph. APhA Drug Information Handbook. Lexi-Comp, Inc. Hudson Ohio. 2003-2004.

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Zanamivir

(Relenza®, GlaxoSmithKline)

Classification: Infectious Disease Agents; Antivirals

Description: For Oral Inhalation Only. For Use With the Diskhaler Inhalation Device.

Relenza is for administration to the respiratory tract by oral inhalation only. Each Relenza Rotadisk contains 4 regularly spaced double- foil blisters with each blister containing a powder mixture of 5 mg of zanamivir and 20 mg of lactose (which contains milk proteins). The contents of each blister are inhaled using a specially designed breath- activated plastic device for inhaling powder called the Diskhaler. After a Relenza Rotadisk is loaded into the Diskhaler, a blister that contains medication is pierced and the zanamivir is dispersed into the air stream created when the patient inhales through the mouthpiece. The amount of drug delivered to the respiratory tract will depend on patient factors such as inspiratory flow.

Pharmacology: The proposed mechanism of action of zanamivir is via inhibition of influenza virus neuraminidase with the possibility of alteration of virus particle aggregation and release. No studies have been performed to assess risk of emergence of cross resistance during clinical use.

Pharmacokinetics:

Absorption: orally inhaled zanamivir indicate that approximately 4- 17% of the inhaled dose is systemically absorbed

Metabolism: none

Elimination: renally excreted as the unchanged drug

Indications: Zanamivir is indicated for treatment of uncomplicated acute illness due to influenza A and B virus in adults and pediatric patients 7 years and older who have been symptomatic for no more than 2 days. Zanamivir is not recommended for treatment of patients with underlying airways disease (such as asthma or chronic obstructive pulmonary disease).

Dosage:

- Zanamivir is for administration to the respiratory tract by oral inhalation only, using the inhalation device provided. **Patients should be instructed in the use of the delivery system. Instructions should include a demonstration whenever possible.**

- The recommended dose of zanamivir for treatment of influenza in adult and pediatric patients ages 7 years and older is 2 inhalations (one 5 mg blister per inhalation for a total dose of 10 mg) twice daily (approximately 12 hours apart) for 5 days.
- Two doses should be taken on the first day of treatment whenever possible provided there is at least 2 hours between doses. On subsequent days, doses should be about 12 hours apart

Contraindications and Precautions:

- Pregnancy category C
- Contraindicated in patients with a known hypersensitivity to zanzmivir
- If treatment with zanamivir is considered for a patient with underlying airways disease, the potential risks and benefits should be carefully weighed.
- Allergic- like reactions, including oropharyngeal edema and serious skin rashes, have been reported in postmarketing experience with zanamivir.

Interactions:

No clinically significant pharmacokinetic drug interactions are predicted based on data from *in vitro* studies.

Adverse Reactions:

Most adverse reactions occurred at a frequency which was equal to the control (lactose vehicle). The most common adverse reactions (1.5) include: headache, dizziness, nausea, diarrhea, vomiting, sinusitis, bronchitis and cough.

Costs and Monitoring:

Cost of and entire course of therapy is $ 51.59

Product Identification:

Powder for inhalation: 5 mg

Efficacy:

The efficacy of zanamivir 10 mg inhaled twice daily for 5 days in the treatment of influenza has been evaluated in placebo- controlled studies conducted in North America, the Southern Hemisphere, and Europe during their respective influenza seasons. The magnitude of treatment effect varied between studies, with possible relationships to population- related factors including amount of symptomatic relief medication used.

The effectiveness of Relenza was inconsistent across the three trials, with the largest of the three, the North American trial, demonstrating no treatment effect. Both of the foreign trials demonstrated a modest treatment effect (2.5 days in the European trial and 1.5 days in the Southern Hemisphere trial according to GlaxoWellcome; 1.8 days and 1.1 days, respectively, according to the FDA statistician).

Recommendation: Add to formulary

References:

15. Zanamivir Monograph. Mosby's Drug Consult. Mosby's Inc., St. Louis Mo. 2005.

16. Zanamivir Monograph. APhA Drug Information Handbook. Lexi-Comp, Inc. Hudson Ohio. 2003-2004.

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Valacyclovir

(Valtrex®, GlaxoSmithKline)

Classification: Infectious Disease Agents; Antivirals

Pharmacology: Valacyclovir is the hydrochloride salt of *L* - valyl ester of the antiviral drug acyclovir. Valacyclovir is rapidly converted to acyclovir which has demonstrated antiviral activity against herpes simplex virus types 1 (HSV- 1) and 2 (HSV- 2) and varicella- zoster virus (VZV) both *in vitro* and *in vivo.* The inhibitory activity of acyclovir is highly selective due to its affinity for the enzyme thymidine kinase (TK) encoded by HSV and VZV. This viral enzyme converts acyclovir into acyclovir monophosphate, a nucleotide analogue. The monophosphate is further converted into diphosphate by cellular guanylate kinase and into triphosphate by a number of cellular enzymes. *In vitro,* acyclovir triphosphate stops replication of herpes viral DNA. This is accomplished in 3 ways: (1) competitive inhibition of viral DNA polymerase, (2) incorporation and termination of the growing viral DNA chain, and (3) inactivation of the viral DNA polymerase. The greater antiviral activity of acyclovir against HSV compared to VZV is due to its more efficient phosphorylation by the viral TK.

Pharmacokinetics:

Absorption: well absorbed from the GI tract with absolute bioavailability of acyclovir after administration of valacyclovir is 55 %

Metabolism: Valacyclovir is converted to acyclovir and *L* - valine by first- pass intestinal and/ or hepatic metabolism. Acyclovir is converted to a small extent to inactive metabolites by aldehyde oxidase and by alcohol and aldehyde dehydrogenase. Neither valacyclovir nor acyclovir is metabolized by cytochrome P450 enzymes.

Elimination: Eliminated in the urine (45%) and the feces (47%)

Indications: Valacyclovir is indicated for the treatment of herpes zoster (shingles), for the treatment or suppression of genital herpes in immunocompetent individuals and for the suppression of recurrent genital herpes in HIV- infected individuals and for the treatment of cold sores (herpes labialis).

Dosage:

- Herpes Zoster: 1 g orally 3 times daily for 7 days. Therapy should be initiated at the earliest sign or symptom of herpes zoster and is most effective when started within 48 hours of the onset of zoster rash.

- Genital herpes:
    - initial episode: 1 g twice daily for 10 days. Therapy was most effective when administered within 48 hours of the onset of signs and symptoms.
    - recurrent episodes: 500 mg twice daily for 3 days.
    - suppressive therapy: 1 g once daily in patients with normal immune function. In patients with a history of 9 or fewer recurrences/ year, an alternative dose is 500 mg once daily. In HIV- infected patients with CD4 cell count ≥100 cells/ mm^3, the recommended dosage of valacyclovir HCl for chronic suppressive therapy of recurrent genital herpes is 500 mg twice daily.
- Cold Sores (herpes labialis): 2 g twice daily for 1 day taken about 12 hours apart. Therapy should be initiated at the earliest symptom of a cold sore (*e.g.,* tingling, itching, or burning).
- Dose adjustments are required in renal dysfunction.

Dosages for Patients With Renal Impairment

	Normal Dosage Regimen **Creatinine Clearance (ml/ min)**
Indications	**(Creatinine Clearance ≥50)**
	30- 49
	10- 29
	<10
Herpes Zoster	
	1 g q8h
	1 g q12h
	1 g q24h
	500 mg q24h
Genital Herpes	
Initial treatment	
	1 g q12h
	no reduction
	1 g q24h

	500 mg q24h
Recurrent episodes	
	500 mg q12h
	no reduction
	500 mg q24h
	500 mg q24h
Suppressive therapy	
	1 g q24h
	no reduction
	500 mg q24h
	500 mg q24h
Suppressive therapy	
	500 mg q24h
	no reduction
	500 mg q48h
	500 mg q48h
Suppressive therapy in HIV- infected patients	
	500 mg q12h
	no reduction
	500 mg q24h
	500 mg q24h
Herpes Labialis (Cold Sores) *	
	Two 2 g doses†
	Two 1 g doses†
	Two 500 mg doses†
	500 mg single dose

*
Do not exceed 1 day of treatment.
†
Taken about 12 hours apart.

Contraindications and Precautions:

- Pregnancy category B
- Contraindicated in patients with a known sensitivity to valacyclovir or acyclovir
- **Thrombotic thrombocytopenic purpura/ hemolytic uremic syndrome (TTP/**

HUS), in some cases resulting in death, has occurred in some immunocompromised **patients**

- **Dosage reduction is recommended when administering to patients with renal impairment**

Interactions:

Increased effect/toxicity: increased CNS toxicity is seen when valacyclovir is given with Zidovudine and Probenecid.

Decreased effect: Cimetidine or Probenecid has decreased the rate but not the extent of valacyclovir conversion to acyclovir leading to decreased effectiveness of valacyclovir.

Adverse Reactions:

The most common adverse reactions (>10%) include: headache and nausea. Less common adverse reactions (1% to 10%) include: dizziness, depression, dysmenorrheal, abdominal pain, vomiting, leucopenia, thrombocytopenia, AST increase and arthralgia.

Costs and Monitoring:

Monitoring should include: urinalysis, BUN, serum creatinine, liver enzymes and CBC.

Cost of therapy range varies by treatment indication. Herpes labialis - $ 14.78, Herpes zoster - $ 22.17 and genital herpes, initial - $ 14.78, suppressive - $ 7.39 and recurrent - $ 8.46

Product Identification:

Caplets: 500 mg, 1 g

Efficacy:

Herpes Zoster: Efficacy has been demonstrated in immunocompetent adults with localized herpes zoster. The median time to cessation of new lesion formation was 2 days for those treated with valacyclovir compared to 3 days for those treated with placebo. There was no difference with respect to the duration of pain after healing (post- herpetic neuralgia) between the recipients of valacyclovir and placebo.
Genital Herpes Infections: Valacyclovir (1 g bid) has been shown to be as efficacious as Acyclovir (200 mg 5Xday) in immunocompetent adults with first episode genital herpes. When therapy is initiated within 72 hours of symptom onset, the median time to lesion healing was 9 days, the median time to cessation of pain was 5 days and the median time to cessation of viral shedding was 3 days.

Placebo controlled trials in immunocopetent adults with recurrent genital herpes have demonstrated that valacyclovir (500 mg bid X 5 days) shortens the median time to lesion healing (4 days v. 6 days), the median time to cessation of viral shedding (2 days v. 4 days) and the median time to cessation of pain (3 days v. 4 days).

Controlled trials in immunocompetent adults and HIV-infected adults have been conducted to assess the efficacy of valacyclovir in the suppression of genital herpes recurrence. Valacyclovir (1 g bid) is as effective as Acyclovir (400 mg bid) at both 6 months and 12 months. Both were significantly more effective than placebo.

Cold Sores (herpes labialis): Valacyclovir has been demonstrated to shorten the duration of cold sore episodes was about 1 day shorter in treated subjects as compared to placebo. There was no significant difference observed between subjects receiving valacyclovir or placebo in the prevention of progression of cold sore lesions beyond the papular stage.

Recommendation: Add to formulary

References:

1. Valacyclovir Monograph. Mosby's Drug Consult. Mosby's Inc., St. Louis Mo. 2005.

2. Valacyclovir Monograph. APhA Drug Information Handbook. Lexi-Comp, Inc. Hudson Ohio. 2003-2004.

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18 October 2005

Ivermectin

(Stromectol®, Merck)

Classification: Infectious Disease Agents; Antihelmintics

Pharmacology: Ivermectin is a semisynthetic antihelminthic agent that binds selectively to glutamate-gated chloride iron channels which occur in invertebrate nerve and muscle cells. This leads to increased permeability of cell membranes to chloride ions leading to hyperpolarization of the nerve and muscle cell which results in the parasites death.

Pharmacokinetics:

Absorption: Well absorbed from the GI tract
Distribution: Does not cross the blood brain barrier
Metabolism: Substrate for CYP 450 3A4
Elimination: Less than 1% is eliminated in the urine; remainder in the feces over the next 12 days

Indications: Use in the treatment of infections due to Strongyloides stercoralis, Onchocerca volvulus. Ivermectin has been used for other parasitic infections including Ascaris lumbicoides, Bancroftian filariasis, Brugia malayi, scabies, Enterobius vermicularis, Mansonella ozzardi, and Trichuris trichiura.

Dosage:

- Ivermectin should be taken as a single oral dose on an empty stomach with water.

Body Weight (kg)	Number of 3- mg Tablets
15- 24	1 tablet
25- 35	2 tablets
36- 50	3 tablets
51- 65	4 tablets
66- 79	5 tablets
≥80	200 µg/ kg

Contraindications and Precautions:

- Pregnancy category C
- Hypersensitivity to Ivermectin

Interactions: none have been identified

Adverse Reactions:

The most common reactions include dizziness and Pruritus (2.8%). Less common reactions include: asthenia/fatigue, abdominal pain, anorexia, constipation, diarrhea, nausea, vomiting, somnolence, vertigo, tremor, rash and urticaria.

Costs and Monitoring:

Monitoring: skin and eye microfilarial counts and periodic ophthalmologic exams

Each 3 mg tablet costs $ 4.22. Therapy should range from $ 4.22 to $ 21.10

Product Identification:

Tablet: 3 mg

Efficacy: Efficacy, as measured by cure rate, was defined as the absence of larvae in at least two follow- up stool examinations 3- 4 weeks posttherapy. Based on this criterion, efficacy was significantly greater for ivermectin (a single dose of 170- 200 µg/ kg) than for albendazole (200 mg bid for 3 days). Ivermectin administered as a single dose of 200 µg/ kg for 1 day was as efficacious as thiabendazole administered at 25 mg/ kg bid for 3 days.

Cure Rate* (%)

	Ivermectin	**Comparative Agent**
Albendazole Comparative		
International Study	24/ 26 (92%)	12/ 22 (55%)
WHO Study	126/ 152 (83%)	67/ 149 (45%)
Thiabendazole Comparative		
International Study	9/ 14 (64%)	13/ 15 (87%)
US Studies	14/ 14 (100%)	16/ 17 (94%)

Recommendation: Add to formulary

References:

17. Ivermectin Monograph. Mosby's Drug Consult. Mosby's Inc., St. Louis Mo. 2003.
18. Ivermectin Monograph. APhA Drug Information Handbook. Lexi-Comp, Inc. Hudson Ohio. 2003-2004.

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