Minutes of Meeting

Alabama Medicaid Agency
Pharmacy and Therapeutics Committee

August 12, 2009

Members Present: Chairman Ben Main, Dr. Lucy Culpepper, Dr. Gerard J. Ferris, Dr. Kelli Littlejohn, Dr. Robert Moon, Ms. Latonage Porter,

Members Present via web conferencing: Dr. Michelle Freeman, Ms. Vicki Little Faulk, Dr. Joseph Thomas and Dr. Chivers R. Woodruff

Members Absent: Dr. Nancy Sawyer

Presenters: Dr. Laureen Biczak and Dr. Tina Hisel

1. OPENING REMARKS

Chairman Main called the Pharmacy and Therapeutics (P&T) Committee Meeting to order at 9:07 a.m.

2. APPROVAL OF MINUTES

Chairman Main asked if there were any corrections to the minutes from the May 13, 2009 P&T Committee Meeting.

There were no objections. Dr. Thomas made a motion to approve the minutes as presented and Dr. Culpepper seconded to approve the minutes. The minutes were unanimously approved.

3. PHARMACY PROGRAM UPDATE

Dr. Littlejohn noted that a routine Preferred Drug List quarterly update was completed on July 1, 2009.

An alert specific to Synagis® was posted on the Alabama Medicaid website on July 15, 2009. A statewide web conference will be held on August 14, 2009 for all providers. The web conference will provide a public forum for a review of Synagis® use, including clinical criteria and prior authorization forms. Additional information is available on the Medicaid website (www.medicaid.alabama.gov).

An abbreviated verbal review process will be introduced for AHFS classes in which there have been no changes since the last formal review. Complete clinical data will continue to be included

in the clinical packet and will be posted on the Medicaid website. The first abbreviated verbal review will occur with the chloramphenicol class during today's meeting. This new process will take place for all applicable classes beginning with the November 18, 2009 meeting. Members are encouraged to provide feedback on the new process to Dr. Littlejohn.

Correspondence with Committee members and manufacturers will occur via e-mail for all future P&T meetings. Manufacturers are asked to update their e-mail address using the Manufacturer Contact Form found on the Medicaid website. Oral and written manufacturer comment submissions will only be accepted electronically. The updated policy is available on the Medicaid website.

In preparation for the risk of a possible outbreak of H_1N_1 influenza due to the start of the school year, the Agency will continue to maintain Relenza® and Tamiflu® as preferred agents.

Mr. Main was recognized for his year of service as the P&T Committee Chairman. Dr. Littlejohn thanked Mr. Main on behalf of the State of Alabama, providers and Medicaid recipients. Dr. Culpepper will become the Committee's Chair beginning in November 2009. Ms. Faulk will be leaving the Committee, which leaves an opening for a long-term care pharmacist.

4. ORAL PRESENTATIONS BY MANUFACTURERS/MANUFACTURERS' REPRESENTATIVES

Five-minute verbal presentations were made on behalf of some pharmaceutical manufacturers. The process and timing system for the manufacturers' oral presentations were explained. The drugs and corresponding manufacturers are listed below with the appropriate therapeutic class. There were a total of two manufacturer verbal presentations at the meeting.

5. PHARMACOTHERAPY CLASS REVIEWS (Please refer to the website for full text reviews.)

The pharmacotherapy reviews began at approximately 9:20 a.m. The anti-infective classes were last reviewed in May 2007.

Anthelmintics: American Hospital Formulary Service (AHFS) 080800
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the anthelmintics that are included in this review are listed in Table 1. Mebendazole is the only product available in a generic formulation and pyrantel pamoate is available over-the-counter. Pyrantel pamoate is currently not covered by Alabama Medicaid.

The anthelmintics have been shown to be active against the strains of microorganisms listed in Table 2. This activity has been demonstrated in clinical infections and is represented by the Food

and Drug Administration (FDA)-approved indications. A similar table is included in each anti-infective class review throughout the clinical packet.

Current treatment guidelines that incorporate the use of the anthelmintics are summarized in Table 3. There are very few national or international guidelines that discuss the role of the agents in the treatment of parasitic diseases. The recommendations from the 2009 Sanford Guide to Antimicrobial Therapy and the 2006 American Academy of Pediatrics Redbook have been included in this review. The recommendations are dependent upon the infectious organism being treated and the spectrum of activity of the anthelmintic agent. Mebendazole is recommended as a primary treatment option for nematode infections, including ascariasis, hookworms, pinworms and whipworms. Pyrantel pamoate is recommended as either a primary or an alternative treatment option for pinworms, depending on the guideline. Albendazole is recommended as an initial treatment option for the management of cystic hydatid disease and parenchymal neurocysticercosis. Although albendazole has limited FDA-approved indications, this agent is also considered an initial treatment option for ascariasis, hookworms, pinworms and whipworms. Ivermectin is recommended as an initial treatment option for onchocerciasis and strongyloidiasis. Praziquantel is recommended as the primary treatment option for trematode infections.

The FDA-approved indications for the anthelmintics are noted in Table 4. In general, the approved indications do not overlap among the various agents, with the exception of mebendazole and pyrantel pamoate. Both agents are indicated for the treatment of pinworms. The pharmacokinetics, drug interactions, adverse events, as well as dosing and administration sections have been updated as necessary.

Clinical trials evaluating the safety and efficacy of the anthelmintics are summarized in Table 9. Studies have demonstrated successful treatment of helminthic infections with the agents in this class; however, there are very few comparative trials. Two trials demonstrated comparable efficacy with albendazole and mebendazole for the treatment of ascariasis. Three studies demonstrated that albendazole was more effective than mebendazole for treating hookworm infections, while two other studies found that mebendazole was more effective than albendazole for treating whipworm. There were no published studies found which directly compared mebendazole and pyrantel pamoate for the treatment of pinworms.

Dr. Hisel concluded that there are very few guidelines that define the appropriate place in therapy for the anthelmintics. The specific agent that is recommended is dependent upon the infectious organism being treated and the spectrum of activity of the anthelmintic agent. Mebendazole is the only anthelmintic available in a generic formulation and pyrantel pamoate is available over-the-counter. Albendazole, ivermectin, and praziquantel are considered first-line therapy for some parasitic diseases that are not commonly seen in the U.S. Therefore, patients with a diagnosis of one of these uncommon helminthic infections should be allowed approval for a brand anthelmintic through the medical justification portion of the prior authorization process.

Therefore, all brand anthelmintics within the class reviewed are comparable to each other and to the generics and OTC products in the class and offer no significant clinical advantage over other alternatives in general use. Currently, Alabama Medicaid does not cover pyrantel pamoate. This

product is available over-the-counter and there is insufficient evidence to demonstrate that the agent poses a significant safety risk over other currently covered anthelmintics.

No brand anthelmintic is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands. Alabama Medicaid should consider covering pyrantel pamoate.

Dr. Ferris asked about the need for a neuromuscular blocking agent prior to the use of albendazole or mebendazole due to concerns about large ascarids causing damage to the intestine when exposed to albendazole or mebendazole. Dr. Biczak replied that there was no evidence available that suggested the need for this and that the guidelines currently available recommend only single agent therapy. Dr. Ferris also asked about preferred agents and whether treatment with albendazole requires prior authorization. Dr. Littlejohn replied that since tapeworm infections are uncommon, the medical justification process is necessary to access the drugs in this class other than mebendazole.

There was no further discussion on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Aminoglycosides: AHFS 081202
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the aminoglycosides that are included in this review are listed in Table 1. All of the agents are available in an injectable formulation, with the exception of neomycin, which is only available in an oral formulation. Tobramycin is also available in an inhalation solution. All of the aminoglycosides are available generically with the exception of TOBI®.

The current treatment guidelines that incorporate the use of the aminoglycosides are summarized in Table 3. The Cystic Fibrosis Pulmonary Guidelines have been updated since this class was last reviewed. The chronic use of tobramycin inhalation solution is recommended for patients 6 years of age and older with cystic fibrosis and the persistent presence of *P. aeruginosa* in cultures of the airways regardless of the severity of lung disease. The other guidelines have remained unchanged since this class was last reviewed. In general, the parenteral aminoglycosides are recommended as an initial empiric treatment option for serious infections, including acute pyelonephritis, community-acquired and nosocomial pneumonia, and febrile neutropenia. They are also recommended as specific therapy for the treatment of susceptible pathogens causing meningitis, endocarditis, and plague. Neomycin is recommended as prophylaxis for colorectal operations in combination with erythromycin or metronidazole and a mechanical bowel preparation.

Dr. Woodruff asked whether ophthalmological solutions would be included in the review. Dr. Hisel replied that the EENT antibacterials are a new PDL class and will be reviewed separately during the November 2009 meeting.

The FDA-approved indications for the aminoglycosides are noted in Table 4. The pharmacokinetics, drug interactions, as well as dosing and administration sections have been

updated as necessary. The most common adverse drug events reported with the aminoglycosides are listed in Table 7. Ototoxicity and nephrotoxicity are the most serious adverse events associated with these agents. The boxed warning for the parenteral aminoglycosides is listed in Table 8 and the boxed warning for oral neomycin is listed in Table 9. Close monitoring is recommended for all patients receiving aminoglycosides due to the potential ototoxicity and nephrotoxicity associated with their use.

Clinical trials evaluating the safety and efficacy of the aminoglycosides are summarized in Table 11. Several studies have demonstrated similar efficacy when the oral and parenteral aminoglycosides have been compared to each other and to antibacterial agents in other classes. Treatment with tobramycin inhalation solution in patients with cystic fibrosis has been associated with improvements in pulmonary function, improved quality of life, decreased requirement for intravenous anti-pseudomonal antibiotics, and a decrease in hospitalizations compared to placebo. Open-label studies following patients for up to 2 years have also demonstrated continued benefit over time.

Therefore, all brand aminoglycosides within the class reviewed are comparable to each other and to the generics in the class and offer no significant clinical advantage over other alternatives in general use. For patients with cystic fibrosis with *P. aeruginosa* persistently present in cultures of the airways, the chronic use of tobramycin inhalation solution is recommended to improve lung function and reduce exacerbations. Therefore, patients with cystic fibrosis should be allowed approval for tobramycin inhalation solution through the medical justification portion of the prior authorization process.

No brand aminoglycoside is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There was no further discussion on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Cephalosporins: AHFS 081206
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the cephalosporins that are included in this review are listed in Table 1. Cefdinir and cefepime have become available in a generic formulation since this class was last reviewed. The cephalosporins are grouped into generations according to their spectrum of activity. There is at least one oral and one injectable agent available in a generic formulation within each cephalosporin generation, with the exception of cefepime (no oral formulations available). All of the injectable cephalosporins are now available in a generic formulation.

Current treatment guidelines that incorporate the use of the cephalosporins are summarized in Table 3. The American College of Obstetricians and Gynecologists (ACOG) guidelines for the treatment of urinary tract infections in nonpregnant women published in 2008 have been added to this class review. The GOLD guidelines for the diagnosis, management and prevention of COPD

have been updated since this class was last reviewed. The cephalosporins are recommended as initial therapy for the treatment of meningitis, skin and soft-tissue infections, sexually transmitted diseases, nosocomial pneumonia, febrile neutropenia, endocarditis, intra-abdominal infections, early Lyme disease, and as antimicrobial prophylaxis for surgery. These guidelines do not give preference to one cephalosporin agent over another within a specific generation.

The FDA-approved indications for the cephalosporins are noted in Table 4. The indications vary based on the particular agent and antimicrobial properties. The pharmacokinetics, drug interactions, adverse events, as well as dosing and administration sections have been updated as necessary.

Clinical trials evaluating the safety and efficacy of the cephalosporins are summarized in Table 9. Numerous studies have demonstrated comparable efficacy among the cephalosporins for the treatment of skin and skin-structure infections, urinary tract infections, respiratory tract infections, febrile neutropenia, and for surgical prophylaxis. There are relatively few studies which demonstrate greater clinical cure or microbiological eradication rates with one cephalosporin over another. Clinical data from published studies supports similar safety profiles among the cephalosporins, particularly within each generation.

Therefore, all brand cephalosporins within the class reviewed are comparable to each other and to the generics, within each cephalosporin generation, and offer no significant clinical advantage over other alternatives in general use.

No brand cephalosporin is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Dr Ferris asked about the relationship of allergic reactions between patients allergic to penicillins and cephalosporins. Dr. Biczak stated that the generally accepted incidence of cross reaction to cephalosporins for penicillin-allergic patients is 1-3%. The data for reaction to penicillin for cephalosporin allergic patients is less clear, but may be higher. Dr Ferris also asked if the patient is likely to have the same reaction. Dr. Biczak replied that once a patient has had a rash, they will likely have a rash again, but it may be more severe, including Steven's Johnson syndrome. Re-challenge is not recommended, although it is acceptable to treat a penicillin-allergic patient with a cephalosporin due to the low rate of cross reactivity. Dr. Biczak stated that she was not aware of any data that suggested a change in the allergic response over time, and that due to the immunologic nature of allergic reactions, severe reactions may occur despite many years between exposures.

Dr. Woodruff asked if a relationship could be drawn between the severity of the reaction and the time between the first and the second reaction. Dr. Biczak stated that she has not seen any clinical studies to support this theory.

There was no further discussion on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Miscellaneous β-Lactams: AHFS 081207
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the miscellaneous β-lactams that are included in this review are listed in Table 1. These agents are only available in an injectable formulation and are primarily administered in the inpatient setting. Doripenem is a new product that has become available since this class was last reviewed. Cefotetan and cefoxitin are the only agents available in a generic formulation.

Current treatment guidelines that incorporate the use of the miscellaneous β-lactams are summarized in Table 3. The ACOG and GOLD guidelines have been updated as described previously. Other treatment guidelines have not changed since this class was last reviewed. The miscellaneous β-lactams are recommended as one of several options for the initial treatment of skin and soft-tissue infections, pelvic inflammatory disease, nosocomial pneumonia, intra-abdominal infections, and for surgical prophylaxis.

The FDA-approved indications for the miscellaneous β-lactams are noted in Table 4. The pharmacokinetics, drug interactions, adverse events, as well as dosing and administration sections have been updated as necessary.

Clinical trials evaluating the safety and efficacy of the miscellaneous β-lactams are summarized in Table 9. Studies have demonstrated comparable efficacy among these agents for the treatment of skin and soft-tissue infections, urinary tract infections, endometritis, pneumonia, intra-abdominal infections, and for surgical prophylaxis. Few studies have demonstrated greater efficacy with one miscellaneous β-lactam over another. These agents have also been shown to be comparable to antibiotics in other classes. Clinical data from published studies demonstrates similar safety profiles among the miscellaneous β-lactams.

There is insufficient evidence to support that one brand miscellaneous β-lactam is safer or more efficacious than another within its given indication. Since these agents are not indicated as first-line therapy for the management of common infectious diseases that would be seen in general use and due to concerns for the development of resistance, these agents should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand miscellaneous β-lactams within the class reviewed are comparable to each other and to the generics in the class and offer no significant clinical advantage over other alternatives in general use.

No brand miscellaneous β-lactam is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There was no further discussion on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Chloramphenicol: AHFS 081208
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that there have been no major changes in the prescribing information, treatment guidelines or clinical studies since the chloramphenicol class was last reviewed.

Therefore, all brand chloramphenicol products within the class reviewed are comparable to each other and to the generics in the class and offer no significant clinical advantage over other alternatives in general use.

No brand chloramphenicol product is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There was no further discussion on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Macrolides: AHFS 081212
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the macrolides that are included in this review are listed in Table 1. All of the macrolides are available in a generic formulation with the exception of erythromycin lactobionate, erythromycin stearate and telithromycin.

Current treatment guidelines that incorporate the use of the macrolides are summarized in Table 3. The GOLD guidelines and the joint NIH/CDC/IDSA guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents have been updated since this class was last reviewed. In general, the macrolides are recommended as initial therapy for the treatment of skin and soft-tissue infections, *Helicobacter pylori* infections, sexually transmitted diseases, community-acquired pneumonia, pertussis, and prophylaxis/treatment of disseminated *Mycobacterium avium* disease in patients with HIV infection.

The FDA-approved indications for the macrolides are noted in Table 4. The pharmacokinetics, drug interactions, as well as dosing and administration sections have been updated as necessary. The most common adverse drug events reported with the macrolides are listed in Table 7. Acute hepatic failure and severe liver injury (in some cases fatal) have been reported in patients treated with telithromycin. Visual disturbances and loss of consciousness have also been associated with the use of telithromycin. In February 2007, FDA concluded that the risks associated with telithromycin outweigh its benefits for minor illnesses and the indications for the treatment of sinusitis and bronchitis were removed from the prescribing information. A boxed warning was added to the label stating that telithromycin should not be used in patients with myasthenia gravis, which is listed in Table 8.

Clinical trials evaluating the safety and efficacy of the macrolides are summarized in Table 10. Studies have demonstrated comparable efficacy among the macrolides for the treatment of genital ulcers, respiratory tract infections, and disseminated *Mycobacterium avium* disease. The macrolides have also been shown to be comparable in efficacy to antibacterial agents in other classes. A few studies have demonstrated better adherence with the use of macrolides that are dosed once or twice daily; however, there was no significant difference in clinical outcomes. There is a lack of data demonstrating clinical advantages with telithromycin over other macrolides.

Therefore, all brand macrolides within the class reviewed, with the exception of telithromycin, are comparable to each other and to the generics in the class and offer no significant clinical advantage over other alternatives in general use. Telithromycin possesses an extensive adverse effect profile compared to the other brands and generics in the class and should be managed through the existing medical justification portion of the prior authorization process.

No brand macrolide is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands. No brand telithromycin product is recommended for preferred status, regardless of cost.

There was no further discussion on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Penicillins: AHFS 081216
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the penicillins that are included in this review are listed in Table 1. The majority of the penicillins are available in a generic formulation, with the exception of penicillin G benzathine (with or without penicillin G procaine), piperacillin/tazobactam, ticarcillin and ticarcillin/clavulanate.

Current treatment guidelines that incorporate the use of the penicillins are summarized in Table 3. The GOLD guidelines and the ACOG guidelines have been updated since this class was last reviewed. The penicillins are recommended for the initial treatment of meningitis, skin and soft-tissue infections, *Helicobacter pylori* infections, syphilis, pyelonephritis, otitis media, sinusitis, pharyngitis, infectious exacerbations of COPD, community-acquired and nosocomial pneumonia, endocarditis, intra-abdominal infections, early Lyme disease, and as prophylaxis for rheumatic fever.

The FDA-approved indications for the penicillins are noted in Table 5 and Table 6. The pharmacokinetics, drug interactions, adverse drug events, as well as dosing and administration sections have been updated as necessary. The boxed warning for penicillin G benzathine is listed in Table 11. The warning states that this agent is not for intravenous use, and administration in this manner may result in cardiorespiratory arrest and death.

Clinical trials have demonstrated comparable efficacy among the penicillins for the treatment of skin and soft-tissue infections, genitourinary infections, upper/lower respiratory tract infections, as well as several miscellaneous infections. The penicillins have also been shown to be comparable in efficacy to antibacterial agents in other classes. Clinical data from published studies supports similar safety profiles among the penicillins.

There is insufficient evidence to support that one brand penicillin is safer or more efficacious than another. Since the injectable penicillins are not indicated for the management of common infectious diseases that would be seen in general use and due to concerns for the development of resistance, these agents should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand penicillins within the class reviewed are comparable to each other and to the generics in the class and offer no significant clinical advantage over other alternatives in general use.

No brand penicillin is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Dr. Ferris asked why penicillin benzathine was not available in a generic formulation despite being produced for many years. Dr. Biczak stated that she is not aware of the reason, but that the drug is not used that commonly and that may play a role.

There was no further discussion on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

At 10:00 am, Chairman Main called for a 10-minute break. The meeting resumed at 10:10 a.m.

Quinolones: AHFS 081218

Manufacturer comments on behalf of these products:

Avelox® (moxifloxacin) – Schering-Plough

Dr. Hisel commented that the quinolones that are included in this review are listed in Table 1. An extended-release ciprofloxacin product is now available in a generic formulation. Therefore, all ciprofloxacin formulations (immediate-release tablets, extended-release tablets, and intravenous formulations) as well as ofloxacin tablets are available generically.

Current treatment guidelines that incorporate the use of the quinolones are summarized in Table 3. The GOLD guidelines and the ACOG guidelines have been updated since this class was last reviewed. The quinolones are recommended for the initial treatment of infectious diarrhea, chancroid, urinary tract infections, community-acquired and nosocomial pneumonia, febrile neutropenia, anthrax, and intra-abdominal infections. The IDSA guidelines on the management of community-acquired pneumonia were recently updated in 2007. The guidelines recommend treatment with either a macrolide or doxycycline for the outpatient treatment of previously healthy individuals with no risk factors for drug-resistant *S. pneumoniae*. If comorbidities are present (i.e., chronic heart, lung, liver, or renal disease; diabetes; alcoholism; malignancies; asplenia;

immunosuppressing conditions or drugs; use of antimicrobials within the previous 3 months), if risk factors for drug-resistant *S. pneumoniae* infection are present, or if inpatient treatment is required, the guidelines recommend either a respiratory fluoroquinolone a β-lactam plus a macrolide. The respiratory fluoroquinolones include gemifloxacin, levofloxacin and moxifloxacin.

The FDA-approved indications for the quinolones are noted in Table 4. The pharmacokinetics, drug interactions, as well as dosing and administration and adverse event sections have been updated as necessary. The boxed warning for the quinolones is summarized in Table 8. The boxed warning states that treatment with the quinolones has been associated with an increased risk of tendonitis and tendon rupture in all age groups. This risk is further increased in older patients usually older than 60 years of age, in patients taking corticosteroids, and in patients with kidney, heart, or lung transplants. Because of this risk, the use of the quinolones has been limited in the pediatric population. Ciprofloxacin and levofloxacin are the only quinolones approved for use in pediatric patients.

Clinical studies evaluating the safety and efficacy of the quinolones are summarized in Table 10. Numerous clinical trials have demonstrated comparable efficacy among the quinolones for the treatment of skin and soft-tissue infections, genitourinary infections and respiratory tract infections. Data from published studies supports similar safety profiles among the quinolones.

Although there are many head-to-head trials that have been conducted with the quinolones, there is insufficient evidence to support that one brand quinolone is safer or more efficacious than another within its given indication. If a respiratory fluoroquinolone (gemifloxacin, levofloxacin or moxifloxacin) is necessary for the treatment of community-acquired pneumonia, these agents should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand quinolones within the class reviewed are comparable to each other and to the generics in the class and offer no significant clinical advantage over other alternatives in general use.

No brand quinolone is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There was no further discussion on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Sulfonamides: AHFS 081220

Manufacturer comments on behalf of these products:

None

Dr. Hisel commented that the sulfonamide class includes four different agents, which are listed in Table 1. Sulfadiazine, sulfamethoxazole/trimethoprim and sulfisoxazole are used to treat a variety of infections and sulfasalazine is indicated for the treatment of ulcerative colitis and rheumatoid arthritis. All of the sulfonamides are available in a generic formulation, with the exception of sulfisoxazole.

Current treatment guidelines that incorporate the use of the sulfonamides are summarized in Table 3. The ACOG guidelines, GOLD guidelines and the joint NIH/CDC/IDSA guidelines have been updated since this class was last reviewed. The 2008 American College of Rheumatology guidelines for the use of nonbiologic and biologic disease-modifying antirheumatic drugs have been added to the packet. Sulfadiazine is recommended as initial therapy for the treatment of *Toxoplasma* encephalitis (as part of a three-drug regimen) and for the secondary prophylaxis of rheumatic fever. Sulfamethoxazole/trimethoprim is recommended as initial therapy for the treatment of urinary tract infections, infectious exacerbations of COPD, prophylaxis and treatment of PCP, and for the prophylaxis of *Toxoplasma* encephalitis. Due to widespread drug resistance, it is no longer useful for the prevention or treatment of traveler's diarrhea. Sulfasalazine is recommended as one of several initial treatment options for ulcerative colitis and rheumatoid arthritis. There is no specific mention of sulfisoxazole in any of the available treatment guidelines.

The FDA-approved indications for the sulfonamides are noted in Table 4. The pharmacokinetics, drug interactions, as well as dosing and administration sections have been updated as necessary. The most common adverse drug events are listed in Table 7. Stevens-Johnson syndrome, fulminant hepatic necrosis, agranulocytosis, aplastic anemia and other blood dyscrasias are rare but serious side effects reported with the sulfonamides.

Clinical studies evaluating the safety and efficacy of the sulfonamides are summarized in Table 9. There are very few clinical studies that directly compare the efficacy and safety of the sulfonamides. However, several studies and meta-analyses have demonstrated similar efficacy with the sulfonamides when compared to agents in other classes.

Therefore, all brand sulfonamides within the class reviewed are comparable to each other and to the generics in the class and offer no significant clinical advantage over other alternatives in general use.

No brand sulfonamide is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There was no further discussion on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Tetracyclines: AHFS 081224

Manufacturer comments on behalf of these products:

None

Dr. Hisel commented that the tetracyclines that are included in this review are listed in Table 1. Demeclocycline, doxycycline, minocycline and tetracycline are all available in a generic formulation.

Current treatment guidelines that incorporate the use of the tetracyclines are summarized in Table 3. The tetracyclines are recommended for the initial treatment of *Helicobacter pylori* infections, sexually transmitted diseases, infectious exacerbations of COPD, community-acquired pneumonia,

plague, anthrax, and early Lyme disease. Tigecycline is a newer agent approved by the FDA in 2005. None of the available guidelines specifically address the place in therapy for tigecycline.

The FDA-approved indications for the tetracyclines are noted in Table 4. The pharmacokinetics, drug interactions, as well as dosing and administration sections have been updated as necessary. The most common adverse drug events are listed in Table 7. The use of tetracyclines during the period of tooth development may cause permanent discoloration of teeth. Due to the risk of this discoloration, the tetracyclines should not be used in children under eight years of age, unless other drugs are not likely to be effective or are contraindicated.

Clinical studies evaluating the safety and efficacy of the tetracyclines are summarized in Table 9. There are few published studies that directly compare the tetracyclines. Doxycycline and minocycline have demonstrated similar efficacy and safety when used for the treatment of genitourinary and respiratory infections. The tetracyclines have also been found to be comparable in efficacy to antibiotics in other classes. Tigecycline has been evaluated in several clinical trials for the treatment of skin and soft-tissue infections, community-acquired pneumonia, and intra-abdominal infections. Clinical response rates were found to be similar with tigecycline as compared to aztreonam, vancomycin, levofloxacin and imipenem/cilastatin.

There is insufficient evidence to support that one brand tetracycline is safer or more efficacious than another. Therefore, all brand tetracyclines within the class reviewed are comparable to each other and to the generics in the class and offer no significant clinical advantage over other alternatives in general use.

No brand tetracycline is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There was no further discussion on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Antibacterials, Miscellaneous: AHFS 081228
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the miscellaneous antibacterials include a diverse group of products which are used to treat many different types of infections. The FDA-approved indications and mechanism of action vary depending on the particular agent and antimicrobial properties. The miscellaneous antibacterials that are included in this review are listed in Table 1. Bacitracin, clindamycin, colistimethate, polymyxin B sulfate and vancomycin are available in a generic formulation. There are two combination products containing bismuth, metronidazole and tetracycline that are included in this review (Helidac® and Pylera®). Pylera® is a new product that has been approved since this class was last reviewed. Both products are used to eradicate *Helicobacter pylori* in patients with duodenal ulcer disease. Helidac® is supplied in a 14-day blister card which contains each of the three antibacterial components as separate dosage forms. Pylera® contains all three of the antibacterial components in a single capsule.

Due to the diverse nature of the products included in this review, Dr. Hisel summarized the available information for each drug.

The use of bacitracin is limited to the treatment of infants with pneumonia and empyema caused by susceptible strains of staphylococci. Treatment may cause renal failure due to tubular and glomerular necrosis. Polymyxin B sulfate and colistimethate are indicated for the treatment of serious infections caused by susceptible gram-negative bacteria when less toxic drugs are ineffective or contraindicated. The use of these agents has resulted in nephrotoxicity and neurotoxicity. Guidelines do not discuss the use of bacitracin, polymyxin B sulfate or colistimethate and published clinical trials are limited.

The lincosamide antibacterials include clindamycin and lincomycin. Guidelines recommend the use of clindamycin for the treatment of skin and soft-tissue infections and pelvic inflammatory disease. Lincomycin is not discussed in the available guidelines and has no therapeutic advantage over clindamycin. There are many FDA-approved indications for clindamycin; however, the increased risk of pseudomembranous colitis, which may end fatally, limits the use of this agent. The lincosamides should be reserved for the treatment of serious infections for which less toxic antimicrobial agents are inappropriate.

Daptomycin is approved for the treatment of complicated skin and skin-structure infections, *Staphylococcus aureus* bacteremia, and right-sided infective endocarditis. The spectrum of activity with daptomycin is similar to that of vancomycin. Guidelines recommend daptomycin as one of several options for the initial treatment of soft-tissue infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA). Published studies have demonstrated similar clinical response rates when daptomycin was compared to treatment with vancomycin or penicillinase-resistant penicillins.

Linezolid is approved for the treatment of skin and skin-structure infections, pneumonia and vancomycin-resistant *Enterococcus faecium* (VRE) infections. Guidelines recommend the use of linezolid as an initial treatment option for meningitis (due to VRE), skin and soft-tissue infections, community-acquired and nosocomial pneumonia (due to MRSA), and endocarditis (due to VRE). Several trials have demonstrated similar clinical response rates when linezolid was compared to vancomycin. Linezolid can be administered either orally or parenterally when treating serious infections. Vancomycin is also available in an oral and injectable formulation; however, oral vancomycin has only been shown to be effective for the treatment of enterocolitis and pseudomembranous colitis. The intravenous formulation must be used for the treatment of serious infections. Several studies have demonstrated a shorter length of hospital stay and duration of intravenous therapy with the use of linezolid compared to vancomycin. Myelosuppression has been reported in patients receiving linezolid.

Quinupristin/dalfopristin is indicated for the treatment of patients with serious or life-threatening infections associated with VRE bacteremia and complicated skin and skin-structure infections caused by *Staphylococcus aureus* or *Streptococcus pyogenes*. Guidelines recommend the use of quinupristin/dalfopristin as an initial treatment option for skin and soft-tissue infections (due to MRSA) and endocarditis (due to VRE). Several studies have demonstrated similar clinical

response rates when quinupristin/dalfopristin was compared to cefazolin, linezolid, oxacillin and vancomycin.

Intravenous vancomycin is indicated for the treatment of a variety of serious infections caused by susceptible strains of methicillin-resistant staphylococci, for penicillin-allergic patients, for patients who cannot receive or who have failed to respond to other drugs, and for infections caused by vancomycin-susceptible organisms that are resistant to other antimicrobial agents. Several studies have demonstrated similar clinical response rates when vancomycin was compared to daptomycin, linezolid, and quinupristin/dalfopristin. Ototoxicity and nephrotoxicity have been reported with the use of intravenous vancomycin.

Rifaximin is approved for the treatment of travelers' diarrhea caused by noninvasive strains of *Escherichia coli* and guidelines recommend the use of this agent as one of several initial treatment options. Clinical trials have demonstrated similar efficacy when rifaximin was compared to sulfamethoxazole/trimethoprim and ciprofloxacin.

There are two combination products containing bismuth, metronidazole and tetracycline that are included in this review (Helidac® and Pylera®). Both products are used to eradicate *Helicobacter pylori* in patients with duodenal ulcer disease. Guidelines recommend either proton-pump inhibitor (PPI)-based triple therapy or quadruple therapy with a PPI or H_2-receptor antagonist, bismuth, tetracycline, and metronidazole for the eradication of *H. pylori*. Clinical trials comparing quadruple therapy to triple therapy have demonstrated comparable efficacy. There were no published studies found that directly compared Helidac® or Pylera® combination products with bismuth, metronidazole and tetracycline administered as separate formulations.

There is insufficient evidence to support that one brand miscellaneous antibacterial is safer or more efficacious than another within its given indication. Since the majority of these agents are not indicated as first-line therapy for the management of common infectious diseases that would be seen in general use and due to concerns for the development of resistance, these agents should be managed through the medical justification portion of the prior authorization process.

Therefore, all brand miscellaneous antibacterials within the class reviewed are comparable to each other and to the generics in the class and offer no significant clinical advantage over other alternatives in general use.

No brand miscellaneous antibacterial is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There was no further discussion on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

6. NEW DRUG REVIEW

Trilipix® (fenofibric acid) AHFS Class 240606 – Fibric Acid Derivatives
Manufacturer comments on behalf of these products:

Trilipix® (fenofibric acid) – Abbott

Dr. Hisel commented that the fibric acid derivatives class was last reviewed in May 2008. Currently, generic fenofibrate and gemfibrozil are preferred agents. Niacor and Niaspan are also preferred miscellaneous antilipemic agents. Fenofibric acid was approved by the FDA in December 2008 as a lipid regulating agent and is available as a delayed-release capsule for oral administration. Fenofibric acid is the active metabolite of fenofibrate. Several fenofibrate products are currently available, including non-micronized and micronized formulations. There are no generic fenofibric acid products available.

Current treatment guidelines that incorporate the use of the fibric acid derivatives are summarized in Table 2. These guidelines have not changed since the fibric acid derivatives were last reviewed. Guidelines for the treatment of lipid disorders identify LDL-C as the primary target of cholesterol lowering therapy and HMG-CoA reductase inhibitors are generally considered first-line therapy. Fibric acid derivatives have an adjunctive role in the treatment of patients with high triglycerides and low HDL-C, especially in combination with an HMG-CoA reductase inhibitor. For patients with very high triglycerides ($\geq$500 mg/dL), treatment with fibric acid derivatives or niacin should be implemented before LDL-lowering therapy to prevent pancreatitis.

Fenofibric acid is FDA-approved for the treatment of mixed dyslipidemia in combination with an HMG-CoA reductase inhibitor, as well as monotherapy for the treatment of hyperlipidemia, mixed dyslipidemia and hypertriglyceridemia. It is administered once daily and the dose varies depending on the lipid disorder being treated. The safety and effectiveness in pediatric patients has not been established.

Fenofibric acid derivatives and HMG-CoA reductase inhibitors increase the risk of myositis or myopathy, and have been associated with rhabdomyolysis. Data from observational studies suggest that the risk for rhabdomyolysis is increased when fibric acid derivatives are co-administered with HMG-CoA reductase inhibitors. The risk for serious muscle toxicity appears to be increased in elderly patients and in patients with diabetes, renal failure or hypothyroidism.

Three published clinical trials were found in the medical literature evaluating the efficacy and safety of fenofibric acid, which can be found beginning on page 556. The studies were similarly designed and evaluated fenofibric acid in combination with a statin (atorvastatin, rosuvastatin and simvastatin) as compared to monotherapy with either fenofibric acid or a statin. The results from all three studies demonstrated greater improvements in HDL-C, triglycerides and LDL-C with combination therapy compared to monotherapy. A pooled analysis of these 3 trials, as well as a 52 week open-label extension trial, have also been published. The results from these two analyses are consistent with the results from the primary randomized controlled trials. According to the prescribing information, no incremental benefit of fenofibric acid on cardiovascular morbidity and mortality over and above that demonstrated for statin monotherapy has been established. Fenofibrate at a dose equivalent to 135 mg of fenofibric acid was not shown to reduce coronary heart disease morbidity and mortality in the FIELD trial, a randomized controlled trial of patients with type 2 diabetes mellitus.

Dr. Hisel concluded that fenofibric acid is indicated in combination with an HMG-CoA reductase inhibitor as well as monotherapy for the treatment of hyperlipidemia, mixed dyslipidemia and hypertriglyceridemia. Guidelines identify LDL-C as the primary target and the fibric acid derivatives have an adjunctive role in the treatment of patients with high triglycerides and low HDL-C, especially in combination with an HMG-CoA reductase inhibitor, and for patients with very high triglycerides ($\geq$500 mg/dL). Guidelines do not give preference to one fibric acid derivative over another. Three clinical trials have demonstrated greater improvements in HDL-C, triglycerides and LDL-C with the combination of fenofibric acid and a statin as compared to monotherapy. There were no published studies directly comparing the efficacy and safety of fenofibric acid to other fibric acid derivatives. There is also no data to support that adding fenofibric acid to a statin is safer or more effective than adding any other fibric acid derivative to a statin. No incremental benefit of fenofibric acid on cardiovascular morbidity and mortality over and above that demonstrated for statin monotherapy has been established.

At this time, there is insufficient evidence to conclude that fenofibric acid is safer or more efficacious than other brand or generic products within the class reviewed, and that it offers a significant clinical advantage over other alternatives in general use.

No brand fenofibric acid product is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There was no further discussion on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

7. RESULTS OF VOTING ANNOUNCED

The results of voting for each of the therapeutic classes were announced; all classes were approved as recommended. Results of voting are described in the Appendix to the minutes.

8. NEW BUSINESS

It was announced that it was Mr. Main's last meeting as Chairman and that a vote would be made for a new Vice-Chair. The new Vice-Chair will be announced to the P&T Committee upon tallying the votes. Mr. Main and Ms. Faulk were recognized for their service to the P&T Committee.

9. NEXT MEETING DATE

The next P&T Committee Meeting is scheduled for November 18, 2009 at the Medicaid Building. February 10, 2010 is the first meeting date for 2010.

10. ADJOURN

There being no further business, Dr. Culpepper moved to adjourn, and Dr. Ferris seconded.

The meeting was adjourned at 10:46 a.m.

Appendix

RESULTS OF THE BALLOTING
Alabama Medicaid Agency
Pharmacy and Therapeutics Committee
August 12, 2009

A. **Recommendation:** No brand anthelmintic is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands. Alabama Medicaid should consider covering pyrantel pamoate.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Hall — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

Carol Hood — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

B. **Recommendation:** No brand aminoglycoside is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Hall — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

Carol Hood — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

C. **Recommendation:** No brand cephalosporin is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Kell ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

D. **Recommendation:** No brand miscellaneous β-lactam is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Kell ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

E. **Recommendation:** No brand chloramphenicol product is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

F Moore MD ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Hall ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

F. **Recommendation:** No brand macrolide is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands. No brand telithromycin product is recommended for preferred status, regardless of cost.

Amendment: None

Vote: Unanimous to approve as recommended

F Moore MD ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Hall ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

G. **Recommendation:** No brand penicillin is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Kell ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

H. **Recommendation:** No brand quinolone is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Kell ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

I. **Recommendation:** No brand sulfonamide is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Kelly ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

J. **Recommendation:** No brand tetracycline is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Kelly ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

K. **Recommendation:** No brand miscellaneous antibacterial is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Medical Director	☑ Approve	☐ Approve as amended	☐ Disapprove	☐ No action
Deputy Commissioner	☑ Approve	☐ Approve as amended	☐ Disapprove	☐ No action
Commissioner	☑ Approve	☐ Approve as amended	☐ Disapprove	☐ No action

L. **Recommendation:** No brand fenofibric acid is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

Medical Director	☑ Approve	☐ Approve as amended	☐ Disapprove	☐ No action
Deputy Commissioner	☑ Approve	☐ Approve as amended	☐ Disapprove	☐ No action
Commissioner	☑ Approve	☐ Approve as amended	☐ Disapprove	☐ No action

Respectfully submitted,

Tina Hisel, Pharm.D., BCPS

August 12, 2009
Date