

Medication Safety Update

CLINICAL PRESENTATION AND TREATMENT FOR HIT

Unfractionated heparin and low-molecular-weight heparins (LMWHs) are routinely used for thromboprophylaxis and treatment. Despite heparin therapy, patients sometimes

develop new or recurrent thrombosis if anticoagulation fails or heparin-induced thrombocytopenia (HIT) occurs. HIT should be suspected if venous

thromboembolism (VTE) develops during or soon after unfractionated heparin use. In 70% of HIT occurrences, platelet counts begin to fall 5 to 10 days after starting heparin

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Therapy Update

ANTIBIOTIC SUSCEPTIBILITY TRENDS (2006 CUMULATIVE DATA)

Recent trends in antibiotic susceptibilities at TMC are noted from the 2006 cumulative data. Gram negative Enterobacteriaceae have reduced susceptibilities to multiple classes of antibiotics. Acinetobacter continues to

express increased resistance to imipenem requiring the addition of colistin. *S. maltophilia* remains 96% susceptible to trimethoprim-sulfamethoxazole. 97% of *E. coli* from urinary sources were susceptible to nitrofurantoin. The incidence of

MRSA is relatively unchanged at 71%. There has been an increase in vancomycin resistant Enterococci and multi-drug resistant *S. pneumoniae*. See the cumulative antibiogram data on Page 3.

Suspect HIT if Venous Thromboembolism Develops During or Soon After Unfractionated Heparin Use

FDA Fast Facts

BIRD FLU VACCINE

A vaccine for humans against the H5N1 influenza virus, commonly known as avian or bird flu, has been approved. The vaccine could be used in the event the current H5N1 avian virus was to develop the capability of spreading by direct human to human contact. Unlike seasonal influenza virus, the disease caused by H5N1 is far more severe and progresses more rapidly. The manufacturer, Sanofi Pasteur Inc., is not making the vaccine available commercially. Instead, the vaccine has been purchased by the federal government for inclusion within the U.S. Strategic National Stockpile for distribution by public health officials if needed.

ZELNORM DISCONTINUED

Novartis Pharmaceuticals has agreed to comply with the FDA's request to voluntarily discontinue the marketing of tegaserod (Zelnorm®) based upon recent findings for the increased risk of serious cardiovascular adverse events. The FDA concluded that the benefit of this drug no longer outweighed the risks after reviewing the results of a new analysis of 29 randomized, controlled clinical trials of tegaserod. The FDA will work with Novartis to allow access to tegaserod as an investigational drug for patients with no other treatment options where the benefits may outweigh the risks.

PERGOLIDE WITHDRAWN

The FDA has announced that the manufacturers of pergolide drug products for Parkinson's disease will voluntarily remove these agents from the market. This move comes after recent findings that confirm an association between pergolide and increased risk of mitral, tricuspid, and aortic valve regurgitation. The FDA is working with the manufacturers of pergolide to determine if it might be possible to make the product available under an Investigational New Drug Application (IND) for patients who are currently receiving pergolide and can not be successfully converted to alternative therapies.

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Therapy Update

ANTIEMETIC GUIDELINES UPDATED

Nausea and vomiting are the most feared side effects of cancer treatment. About 70% to 80% of people treated for cancer experience these side effects. These adverse effects may lead to dehydration, fatigue, difficulty concentrating, slow wound healing, and loss of appetite. The National Comprehensive Cancer Network (NCCN) has developed guidelines for the treatment and prevention of cancer therapy related nausea and vomiting. These published guidelines have recently been updated, and Columbus Regional has updated our institution specific guidelines based upon the NCCN recommendations (See Insert).

Nausea and vomiting in the cancer patient can be exacerbated by several factors that include medication therapy, radiation therapy, the cancer itself, and anxiety. Chemotherapy stimulates the vomiting center in the brain and certain parts of the esophagus, stomach, small intestine, and large intestine. Chemotherapy-related nausea and vomiting is divided into several categories. Acute nausea and vomiting typically occurs a few minutes to several hours after chemotherapy, and resolves within the first 24 hours. Delayed nausea and vomiting develops more than 24 hours after chemotherapy, and can last for several

days. Anticipatory nausea and vomiting occurs as a result of a previous episode of nausea and vomiting from chemotherapy. Breakthrough vomiting occurs despite treatment to prevent it. Refractory nausea and vomiting can occur after one, few, or several chemotherapy treatments because the patient is no longer responding to the anti-emetic therapy.

When the area of the body irradiated includes a large part of the abdomen, there is approximately a 50% risk of developing nausea and vomiting. Between 60% to 90% of patients receiving total body radiation therapy will develop nausea and vomiting. Those who receive one large dose of radiation are more likely to develop nausea and vomiting than those who receive the radiation therapy in smaller doses. Additionally, the risk is increased when both radiation and chemotherapy are used in combination.

Prevention of nausea and vomiting in patients with cancer is the goal. The guidelines recommend certain anti-emetic regimens depending upon the dose and specific agent's likelihood of inducing gastrointestinal side effects (see insert). If the patient experiences nausea and vomiting after being treated according to

the guidelines, treatment should be escalated according to the next highest risk level.

Anti-emetic drug therapies are the main treatments for chemotherapy induced nausea and vomiting, but there are some non-drug treatment options that are also employed. These techniques promote relaxation, distract individual's attention, enhance feelings of control, and reduce feelings of helplessness. Self-hypnosis, progressive muscle relaxation, and biofeedback are a few examples of non-pharmacologic measures that can be employed along with pharmacologic treatments in the prevention and treatment of nausea and vomiting.

The use of anti-emetic therapy is necessary for preventing or decreasing nausea and vomiting in those patients receiving chemotherapy. By using the appropriate pharmacological and non-pharmacological therapies, patients may better tolerate their chemotherapy regimens with improved quality of life and optimal therapy outcomes.

Brad Brown, PharmD candidate
Auburn University
Harrison School of Pharmacy

Policy Update

FORMULARY CHANGES

Oxandrolone (Oxandrin[®]) has been added to the formulary for the treatment of wasting syndrome due to its effects on lean body mass.

Repaglinide (Prandin[®]) is an insulin secretagogue that has been added to the formulary for the treatment of Type 2 diabetes mellitus. Repaglinide has a rapid onset and short duration of action.

Amylase-lipase-protease 25,000-4,000-25,000 units (Pancrecarb MS-4) as been added to the formulary for pancreatic enzyme insufficiency. Pancreatic enzyme products are not considered bioequivalent by the FDA at this time; therefore, they should not be used interchangeably.

Aztreonam (Azactam[®]) has been added to the formulary for the treatment of infectious diseases caused by aerobic gram-negative bacteria in penicillin allergic patients not allergic to ceftazidime and for patients where multidrug resistant-organisms are suspected/confirmed. Aztreonam should not be used with broad

spectrum antimicrobics (e.g., piperacillin/tazobactam; carbapenems).

Atorvastatin (Lipitor[®]) and fluvastatin (Lescol[®] and Lescol XL[®]) have been removed from the formulary (see table 1). When atorvastatin is ordered, simvastatin or rosuvastatin will be dispensed. Also, when Lescol XL[®] is ordered, pravastatin will be dispensed.

TABLE 1: HMG-Co-A REDUCTASE INHIBITOR FORMULARY CHANGES

When Ordered*	Pharmacy Will Dispense
Atorvastatin (Lipitor [®]) 80mg	Rosuvastatin (Crestor [®]) 40mg
Fluvastatin (Lescol [®]) 20mg	Pravastatin (Pravachol [®]) 10 mg
Fluvastatin (Lescol [®]) 40mg	Pravastatin (Pravachol [®]) 20 mg
Fluvastatin (Lescol [®]) 80mg	Pravastatin (Pravachol [®]) 40 mg
Fluvastatin (Lescol XL [®]) 80mg	Pravastatin (Pravachol [®]) 40 mg

*Non-formulary medication

2006 CUMULATIVE ANTIBIOGRAM

Light Teal = decreasing susceptibility, and Gray = increasing susceptibility

Strains were isolated from patient clinical specimens at The Medical Center, Columbus, Georgia :
Prepared by Deanne Tabb Pharm.D., MT with the assistance of Dan Cullison, Dept. of Microbiology.

Antibiotic Ψ	Organism	Gram Negative Rods											Gram Positive Cocci					
		125	20	31	72	601	20	178	25	107	218	52	11	1242	227	334	79	46
		Acinetobacter baumannii	Citrobacter freundii	Enterobacter aerogenes	Enterobacter cloacae	Escherichia coli	Klebsiella oxytoca	Klebsiella pneumoniae	Morganella morganii	Proteus mirabilis	Pseudomonas aeruginosa	Serratia marcescens	Providencia stuartii	Staphylococcus aureus	Staphylococcus epidermidis	Enterococcus faecalis	Enterococcus faecium	Streptococcus pneumoniae
Amikacin		96	100	100	100	99	100	96	96	99	92	100	100					
Amoxicillin/Clav			30			92	80	92		94				29	13			74
Ampicillin			40			47				90						99 ^γ	10	
Ampicillin/Sulb			70	42		51	70	78		95				29	13			
Aztreonam			80	81	72	99	85	90	88	95	62	96	91					
Cefazolin			20			92	65	87		96				29	13			
Cefepime		22	100	97	92	99	100	92	100	100	80	96	100					80
Cefotaxime		17	80	71	69	99	95	92	96	99		92	82					83
Cefotetan			85	68	60	99	90	99	100	98		87	91					
Ceftazidime		22	70	68	68	99	90	90	88	99	86	94	91					
Ceftriaxone		18	80	74	68	99	85	91	100	98		96	91					80
Cephalothin						59	60	79		95				29	13			
Ciprofloxacin		19	100	84	88	74	85	88	60	79	68	83	45	43	43			
Clindamycin														84*	57			
Erythromycin														24	22			53
Gentamicin		49	100	97	92	90	95	93	84	93	72	100	45	98 [†]				
Imipenem		46	95	94	100	100	95	100	100	100	88	96	100	29	13			
Levofloxacin		22	100	90	89	74	85	88	64	80	68	96	45	46	43	62 [‡]	8	98
Oxacillin														29	13			
Penicillin																99	10	50
Piperacillin		18	75	65	68	51	70	71	80	93	87	96	82					
Pipercillin/Tazo			100	74	72	98	85	94	100	99	89	96	91					
Tetracycline		22	85	84	82	75	85	80	40					94	89	30	87	63
Ticarcillin/Clav		24	65	65	61	89	80	89	92	100	78	90	100					
Tobramycin		94	100	100	94	92	90	90	84	94	86	94	36					
Trimethoprim/ Sulfamethoxazole		22	100	94	90	73	85	87	80	83		96		97	64			56
Vancomycin														100	100	92	19	100

Ψ Blank areas are not tested or are not susceptible (<10%)

* This figure underestimates clindamycin resistance due to inducible mechanisms; confirmatory tests for inducible resistance began in mid 2004.

γ Amox, amp/sulb, amox/clav, pip/tazo, and imipenem are active against ampicillin susceptible Enterococcus faecalis species however not against E. faecium.

‡ Only Suitable for uncomplicated cystitis.

† Never use as monotherapy. Use only with another antibiotic for synergy.



Drug Information Center
Columbus Regional Healthcare System
710 Center Street
Columbus, Georgia 31902

Phone: (706) 571-1934
Fax: (706) 571-1625

Editor, Pharmacy Bulletin
Coordinator, Drug Information
Lisa Boothby, PharmD, BCPS

Director, Department of Pharmacy Services
Burnis D. Breland, M.S., PharmD, FASHP

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HEPARIN-INDUCED THROMBOCYTOPENIA

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therapy (first day of heparin is day 0).¹ This characteristic delay reflects the usual short interval required for heparin to initiate a humoral immune response.

Following the development of HIT, 38 to 76% of patients develop thrombotic complications, typically VTE, in the days to weeks after onset. VTE is associated with HIT infrequently (< 1%) in LMWH-treated patients, yet often (~ 5%) in unfractionated heparin-treated patients.²

Patients with HIT often have relative rather than absolute thrombocytopenia (a decrease of 50% in the platelet count yet a nadir > 150 × 10⁹/L). Platelet counts in HIT typically normalize within days of discontinuing heparin even though the thrombotic risk persists for weeks. Therefore, patients being discharged from the hospital with a recent history of HIT should be monitored closely for several weeks for the development of thrombosis.

It is also possible for heparin-treated patients to be discharged from the hospital

before their HIT manifests and then return with HIT-associated thrombosis. Most affected patients are exposed to heparin during hospitalization, then are discharged home only to return to the hospital in 1 to 2 weeks (rarely, up to 6 weeks) with new thromboses. However, there are reports of HIT occurring as late as 46 days following heparin initiation.³ Practitioners are encouraged to be vigilant in suspecting HIT in anyone presenting with thrombosis following recent (or current) heparin therapy or recent hospitalization; however, the likelihood that a new or recurrent VTE in a heparin-treated patient is associated with HIT remains unclear.¹

In a patient presenting with a thrombosis, careful history taking concerning any recent hospitalization, heparin exposure, heparin allergy, or platelet problems is important for risk assessment of HIT before initiating anticoagulant therapy. In patients with a thrombotic event and strongly suspected HIT, heparins should be avoided and

alternative anticoagulation (e.g., fondaparinux) should be initiated. Warfarin should not be used as sole therapy because it can temporarily worsen the thrombotic risk.

While the onset of disease is generally 5 to 12 days following the initial heparin exposure, the increasing recognition of delayed-onset HIT cases emphasizes that HIT must be considered whenever a hospitalized or recently hospitalized patient develops a new venous or arterial thromboses. With that in mind, a recent medication use evaluation of argatroban at The Medical Center revealed that the majority of suspected cases of HIT were ruled out with confirmatory antibody testing.

Carla Houston, PharmD
Pharmacy Practice Resident

REFERENCES FURNISHED UPON
REQUEST