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Pharmacy & Therapeutics Update: Drug Information for Health Care Professionals, November/December 2009

Medical University of South Carolina

Heather Kokko
Medical University of South Carolina

Kelli Garrison
Medical University of South Carolina

Jason Cooper
Medical University of South Carolina

Chris Wisniewski
Medical University of South Carolina

See next page for additional authors

Authors

Medical University of South Carolina, Heather Kokko, Kelli Garrison, Jason Cooper, Chris Wisniewski, and James New

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Drug Information Center
Department of Pharmacy Services
RT Annex, Room 604
Phone: 792-3896
E-mail: druginfo@musc.edu

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In This Issue

Evaluation of Adherence to FDA Boxed Warnings and Reimbursement Guidelines for Erythropoiesis Stimulating Agents: Medication Use Evaluation

By: John Bossaer, PharmD; Brie Dunn, PharmD; Libby Hinds, PharmD; James New, PharmD; Amanda Schutt, PharmD; Lynn Uber, PharmD; Kelli Garrison, PharmD, BCPS

In December 2004, the first of several FDA mandated boxed warnings and labeling changes to the erythropoiesis stimulating agents (ESAs), darbepoetin alfa (Aranesp®) and epoetin alfa (Procrit®, Epogen®), emerged. The purpose was to warn prescribers of the potential life-threatening adverse effects and death in patients with cancer and chronic renal failure (CRF) when treated to near normal hemoglobin (Hb) concentrations. Reimbursement guidelines have also changed in accordance with these boxed warnings. These updates have forced institutions to re-examine ESA prescribing practices to continue to optimize patient safety and reimbursement.

Warnings issued for CRF focus on lower goal Hb concentrations when using ESAs (Table 1). When target Hb concentrations are higher, there has been a noted increased risk of death and cardiovascular events. Other warnings include an increased need for antihypertensive medications, risk of seizures, and pure red cell aplasia. Dosing recommendations include individualizing regimens to keep the Hb between 10 and 12 g/dL.[1,2] Findings in the CHOIR and CREATE studies support the aforementioned warnings. In these studies, higher target Hb concentrations (13.5 and 13 to 15 g/dL, respectively) resulted in statistically significant increases in composites of cardiovascular events or death.[3,4]

Warnings issued for cancer patients were a result of decreased survival and/or increased risk of tumor progression (Table 1). These warnings were based on several post-marketing studies.

Metastatic breast cancer patients in the BEST trial receiving ESAs targeting Hb concentrations of 12 to 14 g/dL experienced decreased overall survival at 1 year compared with placebo.[5] The ENHANCE study investigated the effects of ESA therapy compared

Table 1. Appropriate ESA Administration

Boxed Warnings	CMS NCD Guidelines
Cancer ▪ ESA shortened overall survival and/or increased the risk of tumor progression or recurrence in clinical studies in patients with breast, non-small cell lung, head, neck, lymphoid, and cervical cancer ▪ To decrease these risks, as well as the risk of serious cardio- and thrombovascular events, use the lowest dose needed to avoid RBC transfusion** ▪ Use ESAs only for treatment of anemia due to concomitant myelosuppressive chemotherapy ▪ ESAs are not intended for patients receiving myelosuppressive therapy when the anticipated outcome is cure ▪ Discontinue following the completion of chemotherapy course **Renal Failure** ▪ Patients experienced greater risk for death and serious cardiovascular events when administered ESAs to target higher versus lower Hb concentrations (13.5 vs. 11.3 g/dL; 14 vs. 10 g/dL) in 2 clinical studies** ▪ Individualize dose to achieve and maintain Hb concentrations within the range of 10 to 12 g/dL** **Perisurgery** ▪ DVT prophylaxis is strongly recommended for those receiving ESAs (EPOGEN and PROCRIT only) pre-operatively to avoid blood transfusions	**Covered Indications – Cancer** ▪ Hb concentration prior to ESA initiation <10 g/dL ▪ Initial dose is the recommended FDA label starting dose or equivalent doses over other approved time periods. – Epoetin: 150 units/kg, 3 times weekly or 40,000 units weekly – Darbepoetin: 2.25 mcg/kg/wk or ≤ 500 mcg every 3 weeks ▪ Hb concentration remains < 10 g/dL in 4 weeks after initiation of therapy and rise in Hb is ≥ 1 g/dL with no adjustment ▪ Hb rate of rise > 2 g/dL in 4 weeks with dose adjustment ▪ Hb rate of rise > 1 g/dL in 2 weeks with dose adjustment ▪ Chemotherapy given < 8 weeks prior **Non-covered Indications – Cancer** ▪ Anemia due to folate, B12, or iron deficiency; hemolysis; bleeding; or bone marrow fibrosis ▪ Anemia associated with the treatment of CML and AML or erythroid cancers ▪ Anemia of cancer not related to cancer treatment ▪ Any anemia associated only with radiotherapy ▪ Prophylactic use to prevent chemotherapy-induced anemia ▪ Prophylactic use to reduce tumor hypoxia ▪ Patients with erythropoietin-type resistance due to neutralizing antibodies ▪ Anemia due to cancer treatment if patients have uncontrolled hypertension

**To assess individualized dosing for cancer and CRF, the FDA-approved dosing guidelines were used.
Abbreviations: ESA - erythropoiesis stimulating agent; RBC - red blood cell; CMS - Center for Medicare and Medicaid Services; NCD - National Coverage Determination; Hb - hemoglobin; DVT - deep vein thrombosis; CML - chronic myelogenous leukemia; AML - acute myelogenous leukemia

with placebo in patients receiving radiotherapy for head and neck cancer. Patients receiving ESAs were dosed targeting a goal Hb concentration of 14.5 and 15 g/dL in women and men, respectively. The primary outcome of locoregional progression-free survival was statistically significant for the patients receving placebo.[6] The EPO-CAN-20 study examined quality of life (QOL) as its primary endpoint in non-small cell lung cancer (NSCLC) patients who were not candidates for curative treatment. A goal Hb concentration of 12 to 14 g/dL was used. An unplanned safety analysis (based on reports of thrombotic events in other trials) revealed a significant difference in overall survival favoring placebo.[7]

In accordance with the boxed warnings, the American Society of Clinical Oncology (ASCO) recommends ESA therapy for anemia of chemotherapy in patients with Hb concentrations approaching or below 10 g/dL to avoid RBC transfusion.[11] These recommendations are based on emerging evidence questioning the safety of ESAs and the lack of a survival benefit with ESA use. The guidelines do support ESA use in low risk myelodysplasia (MDS) due to improvements in QOL surveys, despite a lack of survival benefit.[12]

Also in correlation with the aforementioned clinical evidence, the Center for Medicare and Medicaid Services (CMS) implemented a National Coverage Determination (NCD) for the use of ESAs in cancer and other neoplastic conditions in July 2007.[13-14] The NCD specifies the conditions for which ESA treatment will be reimbursed. These recommendations are also listed in Table 1.

Methods

A retrospective chart review of patients receiving ESAs from July 2007 through September 2008 in ambulatory clinics were evaluated for adherence to boxed warnings and CMS NCD guidelines. Any ambulatory care patient who was billed for darbepoetin alfa or epoetin alfa was identified from the pharmacy order entry system.

The primary outcome was defined as adherence to boxed warnings and CMS NCD guidelines. Secondary outcomes included incidence of adverse clinical outcomes and assessment of potential revenue losses.

Patient-specific data collected included demographics, insurance provider, and reimbursement data. For each dose of ESA given, data were gathered about the prescribing service, indication for ESA, and number of doses administered. Clinical outcomes data collected included all Hb concentrations during the specified time frame, appropriateness of initial dose and subsequent dosing adjustments, and adverse events.

Initial dosing and adjustments were deemed appropriate based on standards set forth by FDA boxed warnings,[1,2] FDA-approved product labeling, and CMS NCD guidelines.[13] Indications for ESAs other than those listed in Table 1 were also recorded to assess usage. Average doses of ESAs and Hb concentrations were calculated as well.

Patients admitted to the hospital with a recent diagnosis of an acute myocardial infarction (AMI), deep vein thrombosis (DVT), pulmonary embolism (PE), or cerebrovascular accident (CVA) were documented as having an adverse event.

Reimbursement data for outpatient clinic use of ESAs was collected in order to evaluate average collection rates according to differing insurance payors and indication. Average collection rates were determined by the percent of charges and total reimbursement (drug charge / total charges x total reimbursement = drug reimbursement). Total profit per payor was also analyzed by subtracting drug cost from drug reimbursement. This review was approved by the MUSC institutional review board.

Table 2. Patient Demographics (N = 306)

Age	
Average (years)	59 ± 14
Race	
African American	156 (51%)
Caucasian	135 (44%)
Other	15 (5%)
Sex	
Female	183 (60%)
Male	123 (40%)
Prescribed ESA	
Darbepoetin alfa	227 (74%)
Epoetin alfa	76 (25%)
Both	3 (1%)
Average Number of Injections per Patient	
Darbepoetin alfa	3.7 ± 4.6
Epoetin alfa	2.5 ± 5.4
Indication	
Anemia of CRF	151 (49.3%)
Anemia in cancer	126 (41.2%)
Perisurgery	1 (0.3%)
Other	28 (9.2%)
Prescribing Service	
Nephrology	105 (34%)
Hematology/Oncology	102 (33%)
Infectious Disease	3 (1%)
Internal Medicine	35 (12%)
Transplant	49 (16%)
Gynecology/Oncology	12 (4%)
Weight	
Average (kg)	79.7 ± 21.6
Average Dose	
Darbepoetin alfa (mcg)	205 ± 131
Epoetin alfa (units)	27,944 ± 14,892
Hemoglobin	
Average (g/dL)	9.7 ± 1.1
Funding	
Medicare	137 (45%)
Medicaid	30 (10%)
Private	101 (33%)
Other	7 (2%)
Unfunded	31 (10%)

Data Analysis

A total of 306 patients were included in the analysis. Patient demographics are listed in Tables 2 and 3. Nephrology (34%, n = 105) and hematology/oncology (33%, n = 102) were the most common services that prescribed ESAs. Likewise the most common indications for ESAs were anemia of CRF (49%, n = 151) and anemia in cancer (41%, n = 126). Darbepoetin was prescribed more frequently compared with epoetin (74 vs. 25%, 1% were prescribed both). The average number of injections, doses, and Hb concentrations are seen in Tables 2 and 3. Racial demographics differed by indication (Table 3).

Twenty-nine patients were prescribed ESAs for indications other than CRF or cancer. The "other" category included patients with HIV, anemia of chronic disease, myelodysplastic disorder and perisurgery. One patient was prescribed an ESA for perisurgery and the indication was deemed

inappropriate according to the boxed warnings.

As expected, the average doses prescribed for anemia in cancer were higher than those used for anemia of CRF. However, the average Hb for patients with anemia of CRF was significantly higher than patients with anemia in cancer (9.96 ± 1.2 vs. 9.6 ± 0.8 g/dL, p = 0.0033).

Significant differences were also found in regards to insurance data. More patients with anemia of CRF were covered by Medicare (56%) compared with patients with anemia in cancer (30%), (p = 0.001). Also, fewer patients with anemia of CRF compared with cancer were unfunded (5 vs. 15 %, respectively).

Overall, adherence to boxed warnings was met in 62% of cases in the CRF and cancer populations (other indications were not included in analysis of adherence) (Table 4). Appropriateness did not differ significantly after analysis by indication. A trend was noted for boxed warning adherence after analysis by date. Adherence was 48% in 2007 compared with 76% in 2008 (Table 5). The most common reasons for non-adherence in the CRF population were Hb concentrations not being checked every 4 to 6 weeks and doses not being adjusted to maintain Hb concentrations between 10 and 12 g/dL (Table 6). The primary reason for non-adherence in the cancer population was initiation of ESA or administration of maintenance dose when Hb was > 10 g/dL.

Table 3. Patient Demographics by Indication

	CRF N = 151	Cancer N = 126	Other N = 29
Age			
Average (years)	58.6 ± 16	59.2 ± 12.6	59.3 ± 13.5
Race			
African American	93 (62%)	48 (38%)	15 (52%)
Caucasian	56 (37%)	67 (53%)	12 (41%)
Other	2 (1%)	11 (9%)	2 (7%)
Sex			
Female	85 (56%)	80 (63%)	18 (62%)
Male	66 (44%)	46 (37%)	11 (38%)
Prescribed ESA			
Darbepoetin alfa	100 (66%)	111 (88%)	16 (55%)
Epoetin alfa	49 (33%)	14 (11%)	13 (45%)
Both	2 (1%)	1 (1%)	0 (0%)
Average Number of Injections per Patient			
Darbepoetin alfa	5.8 ± 6.1	2 ± 1.4	2.3 ± 2.3
Epoetin alfa	1.6 ± 1.9	3 ± 1.7	5.3 ± 12.6
Weight			
Average (kg)	84.5 ± 22.6	73.4 ± 18	82.2 ± 24.1
Average Dose			
Darbepoetin alfa (mcg)	82 ± 42	310 ± 83	254 ± 104
Epoetin alfa (units)	22,072 ± 8,848	45,667 ± 13,478	30,529 ± 18,893
Hemoglobin			
Average (g/dL)	9.96 ± 1.2	9.6 ± 0.8	8.8 ± 1.4
Insurance Provider			
Medicare	85 (56%)	38 (30%)	14 (48%)
Medicaid	15 (10%)	13 (10%)	2 (7%)
Private	42 (28%)	51 (41%)	8 (28%)
Other	2 (1%)	5 (4%)	0 (0%)
Unfunded	7 (5%)	19 (15%)	5 (17%)

Table 4. Appropriateness by Indication

	CRF and Cancer Indications		CRF Indication		Cancer Indication	
	Boxed Warning n=277	CMS Guidelines n=127*	Boxed Warning n=151	CMS Guidelines n=151	Boxed Warning n=126	CMS Guidelines n=126
Appropriate	62%	48%	61%	N/A	63%	48%
Not appropriate	38%	52%	39%	N/A	37%	52%
Adverse events (n)	2.9% (8)		0%		6.3% (8)	

*One patient had a primary indication of CRF, but also was receiving chemotherapy; therefore CMS NCD guidelines were evaluated.

Table 5. 2007 and 2008 Appropriateness for CRF and Cancer Indications

	2007		2008	
	Boxed Warning n=137	CMS Guidelines n=62	Boxed Warning n=140	CMS Guidelines n=65
Appropriate	48%	27%	76%	68%
Not appropriate	52%	73%	24%	32%
Adverse events (n)	1.5% (2)		4.3% (6)	

Adherence to CMS NCD guidelines was 48% overall. However, adherence to guidelines improved from 2007 to 2008 (27% vs. 68%, respectively, Table 5). Interestingly, this corresponded with the CMS NCD implementation date. The most prevalent reasons for non-adherence were inappropriate initial doses and Hb concentration not being maintained ≤ 10 g/dL (Table 6).

Lastly, of the 2.9% of patients experiencing a DVT or PE during the evaluation period, all of the adverse events experienced were found in patients also receiving chemotherapy. When compared with 2007, the number of reported adverse events increased from 2 to 6 in 2008.

The average collection rate of ESAs used in Medicare patients treated in the outpatient clinics was 21% of charges. There was a similar collection rate in Medicare patients when separated by indication. Medicare collection rates for 2007 and 2008 were similar (0.21% and 0.20%, respectively). The highest collection rates came from private insurance payors with an average collection rate of 52% of charges for all indications. The collection rate for Medicaid and unfunded patients was poor.

Overall, the profit margin for ESA use was $407,608.32 including all indications and all insurance payors. The largest profits were seen with private insurance payors while there was a net loss of income from Medicaid and unfunded patients. Of note, the Medicare profit margin for CRF was positive while the profit margin for cancer patients was in the negative possibly due to the CMS NCD.

Conclusions

Adherence to black box warnings and the CMS NCD guidelines was suboptimal. Over the study period of July 2007 through September 2008, 62% of ESA doses for CRF and cancer were deemed appropriate per boxed warnings and 47% were deemed in accordance with CMS guidelines. However, adherence improved significantly from 2007 to 2008 once the CMS NCD went into effect.

While adherence rates appear to be on the rise, reimbursement opportunities still exist especially in the Medicare and Medicaid populations. Mandating use of anemia order forms outlining boxed warnings and CMS NCD guidelines would increase adherence and increase potential for optimal reimbursement. Another issue noted during this project was the lack of documentation of doses given in clinic. Doses not documented will not receive reimbursement. Use of medication templates in Practice Partner is highly recommended.

Table 6. Percentage of Inappropriate Use

	2007 - 2008	2007	2008
Boxed Warning – CRF	**n=151**	**n=75**	**n=76**
Initial dose was not appropriate	10.6%	9.1%	11.6%
Hb was not checked every 4 to 6 weeks	**21.2%**	**28.0%**	14.5%
Doses were not adjusted to maintain Hb between 10 and 12 g/dL	**23.2%**	**32.0%**	14.5%
There was not an appropriate intervention for Hb rise > 2 in 4 weeks, or > 1 in 2 weeks	5.3%	8.0%	2.6%
Doses were increased more than once monthly	0.0%	0.0%	0.0%
Boxed Warning – Cancer	**n=127**	**n=62**	**n=65**
ESA was not prescribed for an appropriate indication	5.5%	4.8%	6.3%
ESA was not discontinued within 8 weeks of discontinuation of chemotherapy	5.5%	8.1%	3.1%
ESA was not initiated when Hb was <10 g/dL	**28.3%**	**45.2%**	12.5%
There was not an appropriate intervention for Hb rise > 2 in 4 weeks, or > 1 in 2 weeks	4.7%	6.5%	3.1%
Hb was not maintained at a concentration to avoid RBC transfusion	3.1%	3.2%	3.1%
CMS NCD Guidelines	**n=127**	**n=62**	**n=65**
Initial dose was not appropriate	24.0%	34.5%	14.3%
Hb was not obtained within 1 week of all doses	**8.7%**	**9.7%**	7.7%
Hb was not maintained at <10 g/dL	**37.0%**	**53.2%**	21.5%

Abbreviations: CRF - chronic renal failure; Hb - hemoglobin; ESA - erythropoiesis stimulating agent; RBC - red blood cell; CMS - Center for Medicare and Medicaid Services; NCD - National Coverage Determination

As private insurers often follow trends set forth by CMS, it is possible private insurers will begin following similar reimbursement guidelines. Periodic monitoring of reimbursement should be performed to ensure reimbursement rates do not decline further. Overall, a greater adherence to guidelines could potentially not only increase safety for patients being treated with ESAs but could also increase the overall reimbursement for ESAs provided to all of our patients.

References available upon request

Incomplete Orders….Not Being Accepted As of January 4, 2010

After a recent review, it was noted that MUSC prescribers are not following our guidelines on proper medication order writing. This is a significant safety issue for our patients. **Beginning January 4, 2010, orders not written correctly will not be accepted by nursing or pharmacy staff.** The prescriber will be contact regarding any incomplete so that the order can be re-written. Please refer to Policy C78: Medication Orders for the order writing guidelines https://www.musc.edu/medcenter/policy/Med/C078.pdf.

Did You Know…
Peramivir H1N1 Emergency Use Authorization

Recently, the Commissioner of the FDA issued an Emergency Use Authorization (EUA) of the investigational intravenous (IV) antiviral medication, peramivir, for the treatment of specific adult or pediatric inpatients with suspected or confirmed 2009 H1N1 influenza infection. Peramivir is a neuramidase inhibitor similar to oseltamivir and zanamivir. Emergency use of this medication is restricted to adult and pediatric inpatients who require IV therapy because they are not responding to oral or inhaled antiviral therapy or drug delivery other than IV is not feasible. Adult inpatients may also be treated if the clinician determines IV use is clinically appropriate for other circumstances.

The following requirements for emergency use must be fulfilled when using peramivir:

- Be aware of the EUA and read the *Fact Sheet for Health Care Providers* (link below)
- Ensure that the *Fact Sheet for Patients and Parents/Caregivers* (link below) are made available to the patients or caregivers and document in the medical record that the patient or caregiver has received the *Fact Sheet*, has been informed of the alternatives to peramivir therapy, and has been informed that peramivir is an unapproved drug authorized for use under an EUA
- Ensure that adverse events and medication errors associated with peramivir will be reported to the FDA's MedWatch program, reports of adverse events will include the words "Peramivir EUA" and peramivir request number in the description field, and reports of adverse events will be made within 7 calendar days of the event
- Prescribe and administer peramivir only for the indications listed above
- Ensure that a patient's creatinine clearance will be determined prior to administration of the first dose
- Ensure that any patient who has had a past severe allergic reaction to any neuramidase inhibitor will not receive peramivir
- Only provide additional written information relating to the emergency use of peramivir to the degree that it is consistent with the terms of the EUA
- Make records and information in connection with the EUA and the use of peramivir available at the request of the FDA and CDC

These requirements, along with dosing, preparation, and contraindication information, are listed in the *Emergency Use Authorization of Peramivir IV Fact Sheet for Health Care Providers* available on the FDA web site (link below). Formal requests for use in specific patients must be submitted electronically through the CDC. Once the request is accepted and processed, it is estimated to take approximately 24 hours for the product to arrive.

Use will be restricted to the approval of the Infectious Diseases or Pulmonary/Critical Care attending physicians and will be coordinated through the Pharmacy Distribution Center's appointed designee to ease the EUA approval process and expedite acquisition of the medication. The physician will be required to enter specific information, including licensure and attestantions in the approval system provided by CDC.

FDA Health Care Provider and Patient/Caregiver Information:

Emergency Use Authorization of Peramivir Fact Sheet for Patients and Parents/Caregivers
Emergency Use Authorization of Peramivir IV Fact Sheet for Health Care Providers

FORMULARY UPDATE FOR NOVEMBER 2009

In October 2009, the Pharmacy and Therapeutics Committee approved the actions listed below. The changes are considered formulary effective unless stated otherwise.

Additions:

Basiliximab (Simulect®)
The current formulary IL-2 antagonist daclizumab (Zenapax®) is no longer being produced by the manufacturer. Basiliximab has a similar mechanism of action and is considered to be a suitable alternative to daclizumab for renal transplant patients. Pre-printed order forms have been updated.
20-mg vials

Additions with Restriction:

Recombinant thrombin (Recothrom®)
This agent is a topical thrombin product that is effective at reducing hemostasis in patients developing post-surgical bleeding and oozing. Due to the potential need for this product in situations of suspected anti-thrombin antibody coagulopathy, recombinant thrombin was added to the formulary with prescribing restricted to Cardio-thoracic Surgery service. Bovine thrombin (Thrombin-JMI®) will remain on the formulary.
5000-IU powder for suspension

Fibrinogen concentrate [human] (RiaSTAP®)
This agent is for treatment of acute bleeding episodes in patients with congenital fibrinogen deficiency including afibrinogenemia and hypofibrinogenemia. It will be centralized with other high-cost medications in the pharmacy distribution center. This agent will be restricted to the Hematology service and patients with afibrinogenemia and hypofibrino-genemia suffering from acute bleeding episodes.
900 to 1300 mg-vials *[exact potency labeled on vial]*

Trisodium citrate 4%
This concentration has been studied as an alternative to heparin for the storage of dialysis catheters. However, it is not FDA approved for this indication. Due to the low theoretical risk from accidental systemic administration and the potential for maintaining catheter patency, this agent was added to the formulary for the storage of dialysis catheters with prescribing restricted to patients with contraindications to heparin products.
250-mL bags

Addition of Restriction:

Hydroxyzine pamoate suspension
The 25-mg/mL extemporaneous oral suspension will now be restricted to the Pediatric Dentistry clinic. All other uses of hydroxyz-ine paomate will be substituted with hydroxyzine hydrochloride.

Change in Restrictions:

Clevidipine (Cleviprex®) and Nicardipine (Cardene®)
Due to the needs of these agents in various units, the restrictions have been expanded with specific monitoring parameters for use in the following areas:

Clevidipine (Cleviprex®)
- *Critical care areas*: ICU, OR, ED
- *Non-critical care areas*: Interventional Radiology (to be monitored by Anesthesia), 6 East (MUH), 9 East (MUH), DDPCU (ART)

Nicardipine (Cardene®)
- *Critical care areas*: ICU, OR, ED
- *Non-critical care areas*: Labor and Delivery, 6 East (MUH), 9 East (MUH), DDPCU (ART)

The formulary effective date is to be determined to allow for the up-dating of pre-printed forms.

Automatic Therapeutic Substitu-tion (ATS) Protocol Addition:

Hydroxyzine products
A protocol for the conversion of hydroxyzine pamoate (Vistaril®) to hydroxyzine hydrochloride (Atarax®) has been approved. These salts forms are considered equivalent. The hydroxyzine pamoate extemporaneous suspension will remain on formulary restricted to the Pediatric Dentistry clinic. The protocol is available on the *MUSC Formulary and Drug Information Resources Web page.*

Line Extensions:

- Mycophenolic sodium (Myfortic®) 180- and 360-mg delayed-release tablets
- Aztreonam (Azactam®) 1- and 2-g/50-mL premixed bags
- Benztropine (Cogentin®) 2-mg/mL vials *[generic]*
- Tetracaine (Pontocaine®) 2% solution *[restricted to the outpatient clinics]*
- Povidone-iodine (Betadine®) 5% ophthalmic solution *[restricted to Ophthalmology]*
- H1N1 vaccine intranasal and injectable products *[formulary effec-tive at first availability]*
- Nevirapine (Viramune®) 50-mg/mL oral suspension

Deletions:

- Daclizumab (Zenapax®) 5-mg/mL injection
- Dipivefrin (Propine®) ophthalmic solution
- Benztropine (Cogentin®) 2-mg/mL ampules *[brand]*
- Aztreonam (Azactam®) 500-mg, 1-g, and 2-g vials
- Pentazocine-naloxone (Talwin NX®) 50/0.5-mg tablets
- Hydroxyzine pamoate (Vistaril®) 25- and 50-mg capsules

FORMULARY UPDATE FOR DECEMBER 2009

In November 2009, the Pharmacy and Therapeutics Committee approved the actions listed below. The changes are considered formulary effective unless stated otherwise.

Additions with Restriction:

Plerixafor (Mozobil®)

Plerixafor is a CXCR4 antagonist used as a stem cell mobilizing agent in patients with non-Hodgkin's lymphoma (HNL) and multiple myeloma (MM). Use of this medication may entail higher up-front cost; however, there is a potential to improve patient quality of care and reduce long-term institutional cost. Therefore, plerixafor was added to the formulary with prescribing restricted to the Hematology/ Oncology service under outpatient settings. Additionally, each patient should be evaluated for appropriate reimbursement prior to initiation of therapy.

20 mg/mL, 1.2-mL vial

Peramivir

Peramivir is a neuramidase inhibitor similar to oseltamivir and zanamivir that was recently granted an Emergency Use Authorization (EUA) by the FDA for the treatment of specific adult or pediatric inpatients with suspected or confirmed 2009 H1N1 influenza infection. See the page 6 more detailed information. Due to the highly specialized acquisition, prescribing, and monitoring process, peramivir was added to the formulary with restrictions to attending level approval from Infectious Diseases and Pulmonary & Critical Care. Services requesting use of peramivir must work with the Distribution Center to complete the online form.

10-mg/mL vial

Change in Restrictions:

Bortezomib (Velcade®)

Bortezomib is indicated for the treatment of patients with multiple myeloma and for the treatment of patients with mantle cell lymphoma who have received at least 1 prior therapy. However, newer evidence from a series of case reports has shown that bortezomib may also be effective in preventing antibody- and cell-mediated acute rejection in transplant patients. Due to this evidence, the restriction for bortezomib will be expanded to include use by Solid Organ Transplant physicians per the Chemotherapy Prescribing Restrictions. Administration will require a chemotherapy-certified nurse from 7W university hospital.

Addition of Nonformulary Restriction:

Domperidone maleate

Currently, domperidone does not have FDA approval for any indication and is not commercially available for any use in the United States because of recognized health risks. Domperidone can **ONLY** be given as part of an Investigational New Drug (IND) application through the FDA.

Inpatient use of a home supply of domperidone with or without evidence of an IND will be brought before MUSC Legal Affairs Department for recommendations on usage allowance. Currently, use of domperidone by inpatients of MUSC **WILL NOT** be allowed unless evidence of a current IND is provided and the prescriber verifies that the patient is appropriately receiving the medication through the FDA.

Line Extension:

- Calcium carbonate (Tums Ultra®) 1000-mg tablets

Deletion:

- Morphine sulfate 0.2-mg/mL oral extemporaneous suspension

Changes in Anti-retroviral Formulary Medications

The anti-retroviral agents available on the formulary have been modified based on guidelines and prescribing in the Infectious Diseases clinic.

Additions or Line extensions:

- Atazanavir (Reyataz®) 300-mg tablets
- Darunavir (Prezista®) 400- and 600-mg tablets
- Efavirenz (Sustiva®) 600-mg tablets
- Emtricitabine/tenofovir (Truvada®) 200/300-mg tablets
- Efavirenz/emtricitabine/ tenofovir (Atripla®) 600/200/300-mg tablets
- Lamivudine (Epivir®) 300-mg tablets
- Lopinavir/ritonavir (Kaletra®) 100/25-mg tablets
- Raltegravir (Isentress®) 400-mg tablets

Deletions:

- Atazanavir (Reyataz®) 100- and 150-mg tablets
- Efavirenz (Sustiva®) 200-mg tablets
- Lamivudine (Epivir®) 150-mg tablets
- Nelfinavir (Viracept®) 250-mg tablets
- Didanosine (Videx® EC) 125- and 200-mg tablets
- Fosamprenavir (Lexiva®) 700-mg tablets

Updated Opioid Comparison/ Conversion Chart

The Chart has been revised to include more detailed information regarding conversion calculations, fentanyl dosing, methadone dosing, and use of naloxone. This chart will be made available on the Department of Pharmacy Services and *Formulary and Drug Information Resources* web sites. Pocket cards are being printed and can be orders through the Department.