

# Drugs & Therapy

B • U • L • L • E • T • I • N

## FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met January 17, 2012. 1 product was added in the *Formulary*, 1 product was designated a high-priority nonformulary drug, and no drugs were deleted from the *Formulary*. 7 products were designated nonformulary and not available. 1 interchange and 14 criteria for use changes were approved.

### ◆ ADDED

**Tadalafil** (Adcirca® and Cialis®)\*

\*Restricted: treated as a controlled substance

### ◆ REVIEWED, BUT NOT ADDED INTO THE FORMULARY

**Asparaginase** *Erwinia*

**Chrysanthemi** (Erwinaze®)†

†High Priority Nonformulary Drug

### ◆ DELETED

None

### ◆ INTERCHANGES

**Bupropion SR** (Generic) for  
Forfivo® XL

### ◆ CRITERIA-FOR-USE CHANGES

**Acetylcysteine Inhalation** (Generic)\*

\*Shortage resolved: restriction lifted

**Eltrombopag** (Promacta®)\*

\*No longer requires REMS; NOT listed in the *Formulary*

**Peripheral Parenteral Nutrition**  
(Compounded)\*

\*Limited to 900 mOsm for adults and pediatrics

**Romiplostim** (Nplate®)\*

\*No longer requires REMS

**Ruxolitinib** (Jakafi®)\*

\*Added in *Chemotherapy and Hazardous Drug Policies*

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## NEWS

### New Drugs in 2011

There were 32 new unique drugs approved in 2011 (see table on page 4). This was a large increase compared with last year and reverses the trend of fewer new drugs being approved over the last few years. FDA is touting faster approval times in the US compared with other countries, with 2 of every 3 new drugs being approved in the US before any other country. There were also many new dosage forms or combinations approved. A few examples are included in the table.

Several trends continued. For example, multiple drugs were approved for the treatment of cancer or cancer pain. Manufacturers seek approval of drugs used for the treatment of cancer, since these drugs are usually covered by third-party payers. Also, drugs for rare indications continue to be approved (eg, Factor XIII deficiency and hereditary angioedema).

FDA also approved 2 new drugs, 1 for melanoma (ie, vemurafenib) and 1 for lung cancer (ie, crizotinib), that are being touted as breakthroughs for personalized medicine. Each was approved with a diagnostic test that helps identify patients for whom the drug is most likely to be beneficial. At the January P&T Committee meeting, the first new subcommittee in many years was approved. The Personalized Medicine Subcommittee will be making recommendations to the P&T regarding when specific genetic information should be made clinically available to help guide drug effectiveness and safety.

The P&T Committee proactively reviews all new drugs and important new dosage forms. If the new drug might fulfill an important niche, the drug is often reviewed proactively and added in the *Formulary* (eg, belatacept, rilpivirine, rivaroxaban, and ticagrelor). Conversely, many new drugs are reviewed and deemed to be not needed for inpatient use at Shands (eg, adenovirus vaccine, aflibercept, bupivacaine liposomal, Centruroides immune fab, fentanyl nasal spray, fentanyl sublin-

qual, fidaxomicin, Forfivo® XL, Intermezzo®, phentermine, Rezira®, tapentadol, and Zutripro®). The nonformulary use of other new drugs is monitored to determine whether any additional actions are needed (see related article on page 6).

2011 was another big year for first-time generic approvals. Generic versions of blockbuster drugs continue to be marketed as patents expire. Many third-party payers encourage patients to use generics by requiring much lower copays. Some plans now have no copays for some generics, and many community pharmacies offer many generics for \$4 for a 1-month supply, and \$10 for a 3-month supply. Nearly 80% of all outpatient prescriptions are for generics and many predict that by 2015 90% of all outpatient prescriptions will be for generic drugs.

Important first-time generic versions of brand name drugs approved in 2011 included generic versions of common drugs used in the ambulatory setting like Lipitor® (atorvastatin), Concerta® (methylphenidate), Levaquin® (levofloxacin), Xalatan® (latanoprost), and Zyprexa® (olanzapine). Important generics expected in 2012 include Plavix® (clopidogrel), Lexapro® (escitalopram), Actos® (pioglitazone), Tricor® (fenofibrate), Provigil® (modafinil), Seroquel® (quetiapine), Singulair® (montelukast), and Diovan® (valsartan).

The growing arsenal of generics makes it easier to find a less expensive option in many therapeutic categories. After generics have been on the market for several months, the cost to health systems can drop by as much as 70% or more.

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## ◆ INSIDE THIS ISSUE

- ◆ New Drugs in 2011 table
- ◆ Personalized Medicine Subcommittee
- ◆ What is PML?

◆ Various Dose Rounding Changes

- Acetaminophen-Codeine Liquid 2.4 mg/mL [codeine]
- Ampicillin IV 20 mg/mL
- Diphenhydramine IV 50 mg/mL
- Gentamicin IV 10 mg/mL
- Ketorolac IV 30 mg/mL
- Morphine IV 2 mg/mL
- Oxycodone Liquid 1 mg/mL
- Oxycodone-Acetaminophen 1 mg/mL [oxycodone]
- Ondansetron IV 2 mg/mL

**Tadalafil** is a phosphodiesterase-5 (PDE-5) inhibitor traditionally used for the treatment of erectile dysfunction (ED). For this indication, it is marketed as **Cialis**<sup>®</sup>. **Cialis**<sup>®</sup> recently had its label changed to include a new indication for the treatment of benign prostatic hyperplasia (BPH) alone and when ED and BPH occur simultaneously. The efficacy data for tadalafil for the treatment of BPH are modest at best. They do not show an improvement of urinary flow rates, but do show improved subjective symptoms. The cost of tadalafil for treating BPH is roughly 50 times more than an alpha-blocker. Prescription benefit programs will likely have high copays and possibly step therapies before covering tadalafil for BPH. This therapy should not be started on inpatients and should only be used in patients admitted already receiving this therapy.

Tadalafil is also used to treat pulmonary arterial hypertension (PAH) under the brand name **Adcirca**<sup>®</sup>. This is similar to sildenafil, which is marketed as **Viagra**<sup>®</sup> for ED and **Revatio**<sup>®</sup> for PAH. Efficacy data for PAH are comparable to sildenafil and other PAH treatment therapies in regards to exercise improvement.

There is a trend of increasing outpatient use of tadalafil for PAH due to its once-daily dosing schedule. Conversion from tadalafil to sildenafil has been problematic in inpatients because of undefined dosage equivalencies. The cost of tadalafil is comparable to the cost of sildenafil for PAH.

Like sildenafil, tadalafil will be handled like a controlled substance in the inpatient setting because of the risk for diversion. Patients may not use their home supply of drugs in this class.

**Vardenafil**, another PDE-5 inhibitor, was designated nonformulary and not available. Its only labeled indication is erectile dysfunction.

There are limited data on the off-label use of vardenafil. Sildenafil and tadalafil should be sufficient to treat inpatients with PAH. Because this class of drugs is handled like a controlled substance, patients may not use their own supply from home. Their supplies will be sent home with their families or stored with their valuables.

**Erwinia asparaginase** has been used investigationaly for decades in patients with allergies to *E. coli*-derived asparaginase. However, FDA only recently approved an *Erwinia* product for marketing with a labeled indication for the treatment of patients with acute lymphoblastic leukemia who have developed hypersensitivity to *E. coli*-derived asparaginase. Asparaginase breaks down asparagine, which is essential for the growth of acute lymphoblastic leukemia cells. Normal cells can biosynthesize enough asparagine to avoid the toxic effects of asparaginase.

Allergic reactions can also develop to *Erwinia* asparaginase. Pancreatitis, liver toxicity, thrombosis, bleeding, nausea, vomiting, and hyperglycemia are all reported.

Cost is estimated to be \$15,000 per dose and \$96,000 per cycle. Patients usually receive three cycles. The need for *Erwinia* asparaginase in a particular patient should be known early enough to acquire product in a timely manner (ie, prior treatment with *E. coli* asparaginase should identify the patient's intolerance). Therefore, the *Erwinia* asparaginase was designated a high priority nonformulary drug and was restricted to patients who have demonstrated hypersensitivity to *E. coli*-derived asparaginase. It will only be acquired for inpatient use in patients who meet this criterion. Use is expected to be low and the storage costs are high.

**Aflibercept** is the newest angiogenesis inhibitor approved with a labeled indication for the treatment of wet (neovascular) age-related macular degeneration. Macular degeneration is a leading cause of vision loss in the elderly. Aflibercept is the fourth drug approved with this labeled indication. Other approved drugs include **pegaptanib** [Macugen<sup>®</sup>], **ranibizumab** [Lucentis<sup>®</sup>], and **verteporfin** [Visudyne<sup>®</sup>]. Bevacizumab [Avastin<sup>®</sup>] is an angiogenesis inhibitor commonly used off-label for this use because it is less expensive and equally effective to drugs like ranibizumab.

Aflibercept, like the other drugs for

this indication, should be given in an outpatient environment, not in the inpatient setting. For this reason, aflibercept, pegaptanib, ranibizumab, and verteporfin were designated nonformulary and not available for inpatient use. Since bevacizumab is used for many other uses, it remains listed in the *Formulary*.

Exparel<sup>®</sup> is a **liposomal injectable** dosage form for the amide local anesthetic **bupivacaine**. It has a labeled indication for single-dose infiltration into a surgical site [bunionectomy or hemorrhoidectomy] to produce postsurgical analgesia. Although the labeling only addresses dosing for bunionectomy or hemorrhoidectomy, it is possible that this agent will be requested off-label for other types of surgical wound site pain.

The P&T Committee designated bupivacaine liposomal injection nonformulary and not available. This product could be re-evaluated if published evidence provides sufficient evidence that it would be cost-effective in the inpatient setting.

**Zolpidem** is a short-acting nonbenzodiazepine hypnotic used for the short-term treatment of insomnia. Normal doses are typically 5-10 mg.

FDA approved lower dosages of zolpidem sublingual (1.75 mg in females and 3.5 mg in males) as **Intermezzo**<sup>®</sup> for insomnia characterized by middle-of-the-night waking followed by difficulty returning to sleep. This dosage form of zolpidem was designated nonformulary and not available. Since it is a controlled substance, patients may not use their own supply from home.

**Forfivo**<sup>®</sup> **XL** is a once-daily extended-release tablet formulation of the aminoketone antidepressant **bupropion**. It has a labeled indication for the treatment of major depressive disorder. As the brand name implies, the daily dosage is 450 mg (for = 4, fiv = 5, o = 0) once daily. Other dosage forms of bupropion are recommended to be used to titrate up to this dose. A 450-mg-per-day dose should only be used in patients who are receiving 300 mg daily of another form of bupropion for at least 2 weeks and who need an increased dosage. Patients currently being treated with other bupropion products at 450 mg per day can be switched to an equivalent 450-mg-per-day dosage. During their

(continued on next page)

**Formulary Update, from page 2**

hospitalization, patients will be switched to an equivalent dosage of bupropion SR.

The P&T Committee has previously reviewed the various oral solid dosage forms of bupropion (ie, immediate release [IR], sustained-release twice-daily formulary [SR], or once-daily extended-release [XL]). Currently, the IR- and XL-dosage forms are nonformulary and not available and are interchanged to an equivalent daily dose of the SR-dosage form with the last dose per day administered at 1600 to avoid the stimulant effect of bupropion. The SR-form can be crushed to get an IR dosage form, if needed. Forfivo® XL will be converted to the SR-dosage form with 300 mg given in the morning and 150 mg given at 1600. It is important that bupropion not be given too late in the day because bupropion may make it difficult for some patients to sleep.

**Acetylcysteine** is an acetylated form of the naturally occurring amino acid cysteine. The inhaled dosage form has a labeled indication as a mucolytic. At the June P&T Committee meeting, the use of inhaled N-acetylcysteine (NAC) was restricted to the oral off-label use for the prevention of radiocontrast-associated nephropathy. This restriction was intended to preserve our limited supply of NAC to prevent radiocontrast-induced nephropathy. Since the shortage has resolved, the restriction prohibiting the use of inhaled NAC was lifted per previously approved P&T policy.

**Eltrombopag** and **romiplostim** are thrombopoietin receptor agonists used to treat thrombocytopenia in patients with chronic immune thrombocytopenia who have not responded adequately to corticosteroids, immunoglobulins, or splenectomy.

Both drugs were restricted to distribution systems (Nplate NEXUS and Promacta CARES) that required anyone using, prescribing, or providing either drug to be enrolled in the monitoring networks due to limited experience. FDA removed these requirements in December 2011.

Romiplostim was added in the *Formulary* in January 2009 and restricted to use in patients enrolled in its restricted distribution program when prescribed by prescribers enrolled in the program. Eltrombopag was designated high priority nonformulary in February 2009 and required to follow the restric-

tions as outlined in the risk evaluation and mitigation strategy (REMS).

The P&T Committee removed the REMS restrictions on romiplostim. Eltrombopag remains nonformulary and is no longer “restricted” by the limited distribution program.

**Peripheral parenteral nutrition** (PPN) is the intravenous administration of nutrients via a peripheral vein, usually of the hand or forearm. Infusion of PPN requires careful consideration of the formulation’s osmolarity as well as monitoring of the venous access site for signs of phlebitis and/or infiltration. Osmolality is the measured osmotic concentration of a liquid expressed in osmoles or milliosmoles per kilogram of solvent. Osmolarity is the measured osmotic concentration of a liquid expressed in osmoles or milliosmoles (mOsm) per liter of solution. Osmolarity is used in clinical practice because it is expressed as a function of volume, but it cannot be measured; it is only calculated. Hypertonic intravenous solutions (ie, osmolarity higher than blood) have higher rates of phlebitis. Dextrose 5% (250 mOsm/L) and saline 0.9% [“normal saline”] (305 mOsm/L) are considered isotonic, and do not irritate veins. Human plasma’s osmolarity ranges between 275 and 300 mOsm/L.

The previously allowed maximum osmolarity for PPN in adult patients at Shands was 1250 mOsm/L. Hydrocortisone 5 mg/L is often added to peripheral PPN solutions to prevent phlebitis. Higher osmolarity PPN is often desired to deliver as much intravenous nutrition as possible. Usually PPN is not able to meet a patient’s nutritional needs, but mitigates the nutrition deficit.

Various professional societies endorse the recommendation of central administration of total parenteral nutrition (TPN) solutions of high osmolarity. The American Society for Parenteral and Enteral Nutrition (ASPEN) recommends limiting peripheral administration of parenteral nutrition solutions to 900 mOsm/L and reserving central venous access administration for solutions of greater than 900 mOsm/L. The Task Force for the Revision of Safe Practices for Parenteral Nutrition also recommends not exceeding 900 mOsm/L for peripheral administration of intravenous nutrition. The Infusion Nurses Society recommends administration of parenteral nutrition through central venous access when osmolarity exceeds 600 mOsm/L.

The P&T Committee revised the PPN

policy that now limits osmolarity to 900 mOsm/L or less for both adults and children. The most recent pediatric ASPEN guidelines were published in 2005 and do not specify an osmolarity limit for PPN in children. No literature has been published to support such a limit, but pediatric nutrition experts have advocated limiting PPN osmolarity to 900 mOsm/L in children and local experts agree with this change. The previous maximum for PPN osmolarity in children was 1000 mOsm.

**Ruxolitinib** is an oral kinase inhibitor indicated for treatment of patients with intermediate or high-risk myelofibrosis, including primary myelofibrosis and post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis. Thrombocytopenia, anemia, and neutropenia can occur, which is managed by dose reduction or interruption of therapy.

Ruxolitinib is the first FDA approved drug to treat bone marrow myelofibrosis. It was approved under the FDA priority review program. It is an orphan drug (ie, approved for use to treat a disease that affects fewer than 200,000 patients). Although not added in the *Formulary*, ruxolitinib was added in the Chemotherapy Policy and Hazardous Drug Policy. Most patients will use their own home supply of ruxolitinib if they are hospitalized.

The P&T Committee approved revised dose rounding for **acetaminophen liquid** 2.4 mg/mL [codeine], **ampicillin IV** 20 mg/mL, **diphenhydramine IV** 50 mg/mL, **gentamicin IV** 10 mg/mL, **ketorolac IV** 30 mg/mL, **morphine IV** 2 mg/mL, **oxycodone liquid** 1 mg/mL, **oxycodone-acetaminophen liquid** 1 mg/mL [oxycodone], and **ondansetron IV** 2 mg/mL.

Dose rounding functionality in EPIC allows medications prescribed by weight-based dosing to be rounded; however, rounding does not always equal a dose that is practical for preparation and administration. This has become problematic because of the need to waste drug due to preparation based on the ordered dose. Based on feedback from nursing staff, the above rounding changes were made. The percent variation from the weight-based dose is not greater than 15% for any rounded dose and most are less than 5%. These changes are supported by the medical staff and Shands Jacksonville, which shares the same rounding protocols in EPIC.

**NEW DRUGS, BIOLOGICALS, & SELECTED DOSAGE FORMS APPROVED BY THE FDA IN 2011**

<b>GENERIC NAME</b>	<b>TRADE NAME</b>	<b>INDICATION</b>
Abiraterone acetate <sup>^</sup>	Zytiga <sup>®</sup>	Cancer: Prostate
Adenovirus Vaccine <sup>^†</sup>	None	Adenovirus Prevention
Aflibercept <sup>^†</sup>	Eylea <sup>®</sup>	Macular Degeneration
Asparaginase, <i>Erwinia</i> <sup>^</sup>	Erwinaze <sup>®</sup>	Cancer: ALL
Azficel-T <sup>^</sup>	Laviv <sup>®</sup>	Cosmetic: Nasolabial folds
Azilsartan <sup>^</sup>	Edarbi <sup>®</sup>	Hypertension
Azilsartan + Chlorthalidone <sup>†</sup>	Edarbyclor <sup>®</sup>	Hypertension
Belatacept <sup>^*</sup>	Nulojix <sup>®</sup>	Prevent Transplant Rejection
Belimumab <sup>^</sup>	Benlysta <sup>®</sup>	Lupus
Boceprevir <sup>^</sup>	Victrelis <sup>®</sup>	Hepatitis C
Brentuximab Vedotin <sup>^</sup>	Adcentris <sup>®</sup>	Cancer: Lymphoma
Bupivacaine Liposomal <sup>††</sup>	Exparel <sup>®</sup>	Surgical Wound Anesthesia
Bupropion ER <sup>††</sup>	Forfivo <sup>®</sup> XL	Depression
Centruroides Immune Fab <sup>^</sup>	Anascorp <sup>®</sup>	Scorpion Bites
Clobazam <sup>^</sup>	Onfi <sup>®</sup>	Seizures
Crizotinib <sup>^</sup>	Xalkori <sup>®</sup>	Cancer: Lung
Deferiprox <sup>^</sup>	Ferriprox <sup>®</sup>	Iron Overload
Ezogabine <sup>^</sup>	Potiga <sup>®</sup>	Seizures
Factor XIII <sup>^</sup>	Corifact <sup>®</sup>	Factor 13 Deficiency
Fentanyl Nasal Spray <sup>††</sup>	Lazanda <sup>®</sup>	Cancer: Pain
Fentanyl Sublingual <sup>††</sup>	Abstral <sup>®</sup>	Cancer: Pain
Fidaxomicin <sup>^†</sup>	Dificid <sup>®</sup>	<i>C. difficile</i> Diarrhea
Gabapentin <sup>††</sup>	Gralise <sup>®</sup>	Post-Herpetic Neuralgia
Gabapentin Enacarbil <sup>††</sup>	Horizant <sup>®</sup>	Restless Leg Syndrome
Gadobutrol	Gadavist <sup>®</sup>	MRI Contrast Agent
Hydroxyprogesterone Caproate	Makena <sup>®</sup>	Preterm Birth Prevention
Hydrocodone-Pseudoephedrine <sup>††</sup>	Rezira <sup>®</sup>	Cold Symptoms
Hydrocodone-Pseudoephedrine -Chlorpheniramine <sup>††</sup>	Zutripro <sup>®</sup>	Cold or Allergy Symptoms
Icatibant Acetate <sup>^</sup>	Firazyr <sup>®</sup>	Hereditary Angioedema
Indacaterol <sup>^</sup>	Arcapta <sup>®</sup>	COPD
Ioflupane I-123 <sup>^</sup>	Datscan <sup>®</sup>	Diagnostic: SPECT Imaging
Ipilimumab <sup>^</sup>	Yervoy <sup>®</sup>	Cancer: Melanoma
Ipratropium-Albuterol <sup>†</sup>	Combivent <sup>®</sup> Respimat <sup>®</sup>	COPD
Linagliptin <sup>^</sup>	Tradjenta <sup>®</sup>	Diabetes: Type 2
Nevirapine ER <sup>*</sup>	Viramune <sup>®</sup> XR	HIV
Nitroglycerin Ointment 0.4% <sup>†</sup>	Rectiv <sup>®</sup>	Anal Fissures
Oxybutynin Gel 3% <sup>†</sup>	Anturol <sup>®</sup>	Overactive Bladder
Phentermine <sup>††</sup>	Suprenza <sup>®</sup>	Obesity
Rilpivirine <sup>^*</sup>	Edurant <sup>®</sup>	HIV
Rilpivirine-Emtricitabine-Tenofovir <sup>††</sup>	Complera <sup>®</sup>	HIV
Rivaroxaban <sup>^*</sup>	Xarelto <sup>®</sup>	DVT-PE-Stroke Prophylaxis
Roflumilast <sup>^</sup>	Daliresp <sup>®</sup>	COPD
Ruxolitinib <sup>^</sup>	Jakafi <sup>®</sup>	Cancer: Myelofibrosis
Sitagliptin-Simvastatin <sup>††</sup>	Juvisync <sup>®</sup>	Diabetes & Hyperlipidemia
Sodium Fluoride F-18 <sup>^</sup>	None	PET Scan Contrast Agent
Sodium Nitrite-Sodium Thiosulfate	Nithiodote <sup>®</sup>	Cyanide Poisoning
Spinosad <sup>^</sup>	Natroba <sup>®</sup>	Head Lice
Tadalafil <sup>††</sup>	Cialis <sup>®</sup>	Benign Prostatic Hypertrophy
Tapentadol ER <sup>††</sup>	Nucynta <sup>®</sup> ER	Pain
Telaprevir <sup>^</sup>	Incivek <sup>®</sup>	Hepatitis C
Ticagrelor <sup>^*</sup>	Brilinta <sup>®</sup>	ACS-PCI Thrombosis Prevention
Vilazodone <sup>^</sup>	Viibryd <sup>®</sup>	Depression
Vandetanib <sup>^</sup>	Caprel <sup>®</sup> SA	Cancer: Thyroid
Vemurafenib <sup>^</sup>	Zelboraf <sup>®</sup>	Cancer: Melanoma
Zolpidem <sup>††</sup>	Intermezzo <sup>®</sup>	Insomnia

<sup>^</sup>New Drugs and Biologicals<sup>†</sup>New Dosage Form, Combination, or Indication<sup>\*</sup>Listed in the Formulary<sup>††</sup>Nonformulary and not available

## Pardon My Language: What is PML?

**R**ecent drug safety alerts have brought a serious virus to the attention of clinicians and patients – progressive multifocal leukoencephalopathy (PML). Many people may not be aware of what PML is despite the frequent mention of this rare condition in recent drug safety news.

This severe demyelinating disease of the central nervous system is caused by reactivation of the polyomavirus, JC virus (JCV), so named for the initials of the patient whose tissue samples allowed the first successful culture.<sup>1</sup> Asymptomatic infection is prevalent and antibodies can be found in over 80% of adults.<sup>2</sup> JCV may remain latent in kidneys and lymphoid organs until profound immunosuppression allows reactivation and spread to the brain.

Clinical manifestations include subacute neurologic findings including altered mental status, ataxia, and visual disturbances. Disease course is usually progressive and fatal, with a median survival of 3 months in patients without HIV.<sup>1</sup>

In January 2012 alone, FDA revised the labels of 2 drugs – natalizumab (Tysabri®) and brentuximab (Adcetris®) – to reflect concern over association with PML due to JCV. In recent years, similar immunosuppressive drugs also received warnings on the risk of PML – rituximab (Rituxan®), efalizumab (Raptiva®), and mycophenolate mofetil (CellCept®). Not all of these medications are listed in the *Formulary*, but patients may receive them at clinics or present after courses of treatment.

The Tysabri® label was updated to include a boxed warning and information on estimation of PML incidence.<sup>3</sup> Data are based on approximately 200 cases in 100,000 treated patients and estimates risk at less than 1 to 11 per 1000 patients based on drug exposure and JCV antibody status. Data beyond 4 years of treatment are limited.

The August 2011 Adcetris® label originally included a warning based on a single case of PML identified before approval.<sup>1</sup> It has been updated to describe 2 additional cases, both reported in patients

with Hodgkin lymphoma.

Immunosuppressive conditions are most commonly associated with PML, though no individual condition is a leading risk factor. A retrospective population-based study estimated incidence in various conditions, including systemic lupus erythematosus, non-Hodgkin lymphoma, chronic lymphocytic leukemia, and bone marrow transplantation. No statistically significant difference in PML incidence was identified.<sup>4</sup>

The lack of a specific treatment for PML makes the condition concerning and management can be clinically counterintuitive. Discontinuation or dose decreases of immunosuppressive drugs clearly increases risk of negative outcomes such as transplant rejection, but case reports of transplant recipients and patients

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### Discontinuation or dose decreases of immunosuppressive drugs is supported by case reports of patients with drug-induced PML.

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with dermatomyositis support such a strategy.<sup>5</sup>

Definitive treatment recommendations are few. Natalizumab should be immediately discontinued in patients with PML associated with this drug, with consideration of plasma exchange due to its prolonged duration of action.<sup>3</sup> Case reports and series have described success with mirtazepine, owing to the possible infection mechanism of JCV through 5-HT<sub>2a</sub> receptors. Several controlled trials suggest possible benefit from topotecan and cytarabine (in patients with and without HIV, respectively) for improvement of functional status but not prognosis.<sup>6,7</sup> Data do not support use of cidofovir in patients with PML and HIV, a recommendation endorsed in HIV opportunistic infection guidelines.<sup>8</sup>

Estimating an accurate incidence of very rare drug-associated conditions is difficult due to suboptimal

reporting of cases and exposures. However, heightened emphasis on reporting and distribution systems with high-risk drugs may increase detection and clarify incidence. Additionally, the expanding use of biological immunosuppressants to off-label indications may further reveal rare adverse effects like PML. Though the condition is rare, clinicians should be aware of drugs associated with PML, particularly those with FDA boxed warnings.

By Ryan Rodriguez, PharmD

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**NEWS**

## New Personalized Medicine Subcommittee

**A**t the January meeting, the first new P&T subcommittee in many years was approved. A Personalized Medicine Subcommittee was established to review the available evidence and make recommendations to the P&T Committee about what genetic information will be used clinically.

This subcommittee will function like the other P&T subcommittees (ie, Formulary Subcommittee and Anti-infective Subcommittee). The Personalized Medicine Subcommittee will have experts who will review the available evidence and make recommendations to the P&T Committee. The P&T Committee is the medical staff committee that acts as the formal line of communication between the medical staff and the hospital on all drug-related matters.

What pharmacogenetic information should be included in patients' charts will be important decisions as more data become available in this emerging area. For example,

clopidogrel has a labeled indication for acute coronary syndrome (ACS) when a patient undergoes coronary revascularization. Clopidogrel also has a black box warning that states that poor metabolizers (ie, inadequate CYP2C19 activity to activate clopidogrel) are at higher risk for cardiovascular event rates following percutaneous coronary intervention (PCI). Laboratory tests are available to identify a patient's CYP2C19 genotype and can be used to aid in determining therapeutic strategies.

Clopidogrel should be available as a generic in 2012 (see *New Drugs in 2011* article). It is a good choice for most patients, but there may be patients who will require a higher dose or an alternative therapy (eg, prasugrel or ticagrelor). The Personalized Medicine Subcommittee will recommend which genetic testing should be available in the medical record, what alerts prescribers and others should receive, and what alternative strategies should be considered to guide drug therapy.

## Drug information questions?

**Contact the  
Drug Information Service**



**Call 265-0408**



**Or submit your  
question online at  
[www.shands.org/  
professionals/druginfo/  
default.asp](http://www.shands.org/professionals/druginfo/default.asp)**

- This service is for referring physicians and other healthcare professionals taking care of Shands patients
- Phones are staffed from 9 am to 4:30 pm, Monday – Friday
- All answers are thoroughly researched and referenced

*For emergent questions that do not need thorough research, go to the pharmacy servicing your area.*