



Script Notes



The Pharmacy and Therapeutics Newsletter for Keystone Mercy Health Plan Participating Providers

FDA Alerts

Increased Risk of Pulmonary Arterial Hypertension (PAH) with Sprycel® (dasatinib)

The FDA announced to health care professionals that there may be an increased risk of PAH in patients who are currently taking and who have previously taken the kinase inhibitor Sprycel® to treat their Chronic Myeloid Leukemia or Acute Lymphoblastic Leukemia. Health care professionals are encouraged by the FDA to thoroughly examine their patients for PAH before beginning therapy with Sprycel and to discontinue treatment if the patient develops PAH while undergoing therapy.

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Abnormal Heart Rhythms Associated With Use of Zofran® (ondansetron)

The FDA has notified health care professionals and patients about labeling changes for ondansetron. Changes include the QT prolongation risk warning on all ondansetron-containing products that is expanded to specifically address those individuals at greatest risk for developing Torsades de Pointes. The label has been updated to include avoidance of ondansetron use in individuals diagnosed with congenital long QT syndrome along with the recommendation of ECG monitoring in patients with electrolyte irregularities, heart failure, certain arrhythmias, and for patients taking additional QT prolonging medications (e.g.ciprofloxacin, levofloxacin, amiodarone, sotalol, dasatinib, nilotinib, amitriptyline, clomipramine, vardenafil) concurrently with ondansetron. GlaxoSmithKline, the manufacturer of Zofran®, is also conducting an FDA mandated study on the QT prolonging potential of the drug with results and possible subsequent labeling alterations anticipated in 2012. Providers are encouraged to follow these labeling updates and educate their patients on what to do should they experience warning symptoms of QT prolongation such as syncope or difficulty breathing while on ondansetron therapy.

Tumor Necrosis Factor-alpha (TNFα) blockers: BOXED WARNING

The FDA notified health care professionals that the drug class known as the TNFα blockers which include: Enbrel® (etanercept), Remicade® (infliximab), Cimzia® (certolizumab pegol), Humira® (adalimumab), and Simponi® (golimumab) have recently underwent labeling updates. These updates reflect concerning findings from a recent review of the FDA's Adverse Event Reporting System (AERS), where several cases of severe infection and even fatalities were identified in individuals undergoing TNFα blocker therapy. Boxed warnings for the entire class now contain a statement regarding an increased risk of susceptibility to infections caused by the bacteria Legionella and Listeria. Patients are being encouraged to read the Medication Guides that they receive and to report any serious adverse effects directly to the FDA's MedWatch program. Providers are encouraged to cautiously weigh the risks and benefits of TNFα blocker therapy in their patients and to report any adverse events to MedWatch.

1. FDA MedWatch. Available from: <http://www.fda.gov/Safety/MedWatch/SafetyInformation/default.htm>. Accessed October, 2011.
2. FDA Drug Safety Communications. Available from: <http://www.fda.gov/Drugs/DrugSafety/ucm199082.htm>. Accessed October, 2011.
3. FDA Alerts. Available from: http://www.drugs.com/fda_alerts.html. Accessed October, 2011.

4. MedWatch Safety Alert RSS Feed. Available from: <http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/MedWatch/rss.xml>. Accessed October, 2011.
5. Medscape: Alerts, Approvals and Safety Changes. Available from: http://www.medscape.com/index/section_3093_0. Accessed October, 2011.

Formulary Website Access

Access the Keystone Mercy Website 24 hours/7 days a week at <http://www.keystonemercy.com/apps/formulary/index.aspx>
The formulary is updated on a quarterly basis.
We recommend adding this link as a favorite in your computer's web browser for easy access.

Steven Feinstein, M.D.
P&T Committee Chair

Andrew Maiorini, Pharm.D.
Director, Formulary & Clinical Outcomes

Margaret Shepherd, R.Ph.
Associate Vice President, Clinical Services

Editor:

Norbert Becker, R.Ph.
Clinical Pharmacist, Formulary/DUR

Contributing Editors:

Satya Bontha, R.Ph., M.S.
Clinical Pharmacist, Formulary/DUR

Lauren Brophy, Pharm.D.
Manager, Drug Therapy Management

Candice Carbaugh
Pharmacy Student

Angela Guldin, Pharm.D.
Clinical Pharmacist, Formulary/DUR

Jamila J. Jorden, Pharm.D.
Clinical Pharmacist, Formulary/DUR

We welcome your thoughts, comments and/or suggestions. Do you have an idea for a story? Is there information we can provide to help you?

All correspondence concerning Script Notes should be sent to:

Norbert Becker, R.Ph.
contact with any questions 215-863-5670



Formulary Update Additions

Drug	Indication	Usual Dose	Dosage Form and Strength
Latuda® (Lurasidone)	Atypical antipsychotic for the treatment of schizophrenia.	Initial dose is 40 mg once daily. Maximum recommended dose is 80 mg once daily.	Tablets: 40 mg, 80 mg

Formulary Update

2011-2012 Flu Vaccines - several new products have been introduced which process in the same manner as previous years. They are Fluvirin products and Afluria Products.

References:

1. **Latuda®**. Prescribing Information. May 2011
2. **Lexi-Comp Online**. Available at: <http://online.lexi.com/crlsql/servlet/crlonline>. (Accessed October 25, 2011).
3. **Facts and Comparisons**. Available at: <http://online.factsandcomparisons.com/MonoDisp.aspx?monolD=fandc-hcp12303&quick=278274%7c5&search=278274%7c5&isstemmed=true> (Accessed October 25, 2011).

Product Updates

Drug	Indication	Mechanism of Action	Usual Dose	Dosage and Strength
Ferriprox® (deferiprone)	Indicated for the treatment of patients with transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate.	Deferiprone is a chelating agent with an affinity for ferric ion (iron III) and binds with ferric ions to form neutral 3:1 (deferiprone:iron) complexes that are stable over a wide range of pH values.	For oral use: 25 mg/kg to 33 mg/kg body weight, orally, three times per day, for a total daily dose of 75 mg/kg to 99mg/kg body weight.	Film-coated scored tablets (deferiprone): 500 mg
Combivent® RespiMAT® (ipratropium bromide and albuterol sulfate)	Inhalation Spray indicated for: Patients with chronic obstructive pulmonary disease (COPD) on a regular aerosol bronchodilator who continue to have evidence of bronchospasm and who require a second bronchodilator. COMBIVENT® RESPIMAT® combination does not have a contraindication to patients with hypersensitivity to soya lecithin or related food products such as soybean and peanut unlike the COMBIVENT® alone.	COMBIVENT® RESPIMAT® is a combination of the anticholinergic ipratropium bromide and the beta2-adrenergic agonist albuterol sulfate. Simultaneous administration of both an anticholinergic and a beta2-sympathomimetic is designed to produce a greater bronchodilator effect than when either drug is utilized alone at its recommended dosage.	For oral inhalation only: One inhalation four times a day, not to exceed six inhalations in 24 hours.	Inhalation spray: 20 mcg ipratropium bromide (monohydrate) and 100 mcg albuterol (equivalent to 120 mcg albuterol sulfate) per actuation with the COMBIVENT RESPIMAT inhaler

Product Updates continued

Onfi™ (clobazam)	Onfi (clobazam) is an oral antiepileptic drug used along with other medicines to treat seizures associated with Lennox-Gastaut syndrome in people 2 years of age or older.	Onfi is a 1,5 benzodiazepine. The exact mechanism of action for Onfi is not fully understood, but is thought to involve potentiation of GABAergic neurotransmission resulting from binding at the benzodiazepine site of the GABA receptor.	Adult dosing : 5-15 mg/day initially and may be gradually adjusted to a maximum dose of 80 mg/day based on tolerance and seizure control. Pediatric dosing : < 2 years : Initial 0.5-1 mg/kg/day 2-16 years :Initial 5 mg/day ; may be increased to a maximum dose of 40 mg/day (no more frequently than every 5 days).	Available as 5 mg, 10 mg, 20 mg tablets
Remicade® (infliximab)	Indicated for treatment of Crohn's Disease, Pediatric Crohn's Disease, Ulcerative Colitis, Pediatric Ulcerative Colitis, Rheumatoid Arthritis, Ankylosing Spondylitis, Psoriatic Arthritis, Plaque Psoriasis	Infliximab neutralizes the biological activity of TNFα by binding with high affinity to the soluble and transmembrane forms of TNFα and inhibits binding of TNFα with its receptors.	For Pediatric Ulcerative Colitis: 5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks.	I.V. Infusion (infliximab): 100 mg of lyophilized infliximab in a 20 mL vial
Prolia® (denosumab)	Indicated for the treatment of osteoporosis in postmenopausal women, for men receiving androgen deprivation therapy for non-metastatic prostate who are at high risk of fracture and in women receiving adjuvant aromatase inhibitor therapy for breast cancer and who are at high risk of fracture	Prolia is a RANK ligand inhibitor. It binds to RANKL, and prevents RANKL from activating its receptor, RANK, on the surface of osteoclasts and their precursors. This inhibition decreases bone resorption and increases bone mass and strength in cortical and trabecular bone.	Patient should receive 60 mg every 6 months as a subcutaneous injection in the upper arm, upper thigh, or abdomen.	Solution (denosumab): Available as a prefilled syringe and single-use vial containing 60 mg in 1 mL
Juvisync® (simvastatin and sitagliptin)	Indicated in patients for whom treatment with both sitagliptin and simvastatin is appropriate. (i.e. in individuals requiring treatment of type 2 diabetes and hyperlipidemia).	Juvisync contains two active ingredients, simvastatin and sitagliptin. Simvastatin is a 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitor which prevents the synthesis of cholesterol. Sitagliptin is a dipeptidyl peptidase-IV (DPP-IV) inhibitor that slows the inactivation of incretin hormones, thereby increasing the release of insulin and decreasing glucagon levels in the circulation in a glucose-dependent manner in type 2 diabetics.	Usual starting dose: 100 mg/40 mg once daily in the evening. Individuals already taking simvastatin (10 mg, 20 mg, or 40 mg): May start at a 100 mg sitagliptin and the dose of simvastatin that they are currently on.	Fixed-dose Tablets (sitagliptin/simvastatin): 100 mg/10 mg, 100 mg/20 mg 100 mg/40 mg
Xalkori® (crizotinib)	Indicated for the treatment of individuals diagnosed with locally advanced or metastatic non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.	Crizotinib is an oral tyrosine kinase inhibitor. It inhibits anaplastic lymphoma kinase (ALK) in NSCLC tumors which are ALK-positive.	Usual Dosing: 250 mg taken by mouth twice daily without regard to food. Dosing interruption and/or dose reduction: 200 mg taken twice daily may be required based on the patient's tolerability and safety. Further reduction: 250 mg taken orally once daily may also be necessary.	Capsules (crizotinib): 200mg, 250 mg

References:

- Juvisync® Prescribing Information. Merck. October 2011.
- Xalkori® Prescribing Information. Pfizer. October 2011.
- Soliris® Prescribing Information. Alexion Pharmaceuticals, Inc. October 2011.
- Prolia® Prescribing Information. Amgen, Inc. October 2011.
- Anascorp® Prescribing Information. Instituto Bioclon S.A. de C.V., October 2011.
- FERRIPROX® Prescribing Information. ApoPharma USA, Inc., October 2011.
- Remicade® Prescribing Information. Janssen Biotech, Inc., October 2011.
- Onfi™ Full Prescribing Information. Lundbeck, Inc. October 2011.
- COMBIVENT® RESPIMAT® Full Prescribing Information. Boehringer Ingelheim Pharmaceuticals, Inc. October 2011.
- CenterWatch. Drug Info: FDA-Approved Drugs. Available from: www.centerwatch.com/drug-information. Accessed October, 2011.
- Drugs.com. New Drug Approvals Archive. Available from: <http://www.drugs.com/newdrugs-archive/September-2011.html>. Accessed October, 2011.

Claims Processing and Update on Copays for Pregnant Members of Keystone Mercy Health Plan

Effective immediately, your pharmacy should enter a '2' in their prior authorization type field which is also NCPDP field 461-EU to override copays for pregnant members. The Prescriber will state that the member is pregnant on the script or the member will need to tell the pharmacist that she is pregnant.

According to Pennsylvania 55 Pa Code, Chapter 1101, Section 63, payment in full, services and items furnished to pregnant women are excluded from copayment requirements for all categories of recipients. This update to your system will enable you to process prescriptions with no copayment due for pregnant members in the event that their pregnancy status has not yet been updated by the county assistance office.

Members are encouraged to update their pregnancy status through Department of Public Welfare's statewide change center at 1-877-395-8930.

Please contact the Pharmacy Call Center at 1-800-588-6767, if you have questions or experience system problems.

The Role of the Health Care System In Improving Patients' Medication Adherence

"Drugs don't work in patients who don't take them." - C. Everett Koop

Medication adherence is defined as "the extent to which patients take medications as prescribed by their providers which includes taking the right dose at recommended time and frequency." Any medical intervention is successful only if the patients follow the recommended regimen of medication. Medication non-adherence remains a key challenge across all sectors of the health care industry resulting in estimated costs of \$100 billion per year, accounting for about 4 to 11.4 percent of all hospitalizations and 7.6 percent of all emergency room visits. Non-adherence to medications affects Americans of all ages but is most prevalent among the elderly, and patients on long-term therapy for chronic conditions such as diabetes, hypertension, cardiovascular disease and asthma.

Reasons for non-adherence: There are many reasons for non-adherence to medications. The world health organization classifies the barriers to medication adherence into five categories: (1) patient-related factors, (2) socio-economic factors, (3) factors associated with health care team, (4) disease-related factors and (5) treatment-related factors.

Patient-related factors include lack of understanding of the disease, involvement in the treatment decision-making process and health literacy. Patient's health beliefs and their attitude concerning the effectiveness of the treatment can also affect their degree of adherence. Some of the socioeconomic factors contributing to non-adherence are the high cost of medications, lack of transportation or ability to get to the pharmacy, lack of family support and the mental status of the patient. Cognitive diseases and conditions that affect the mobility of the patients also contribute to the medication non-adherence.

Health care related factors such as complex treatment regimens, failure to explain the benefits of the treatment or adverse effects of medications have a significant contribution to the patient's medication adherence. Lack of collaboration between the patients' primary care physician (PCP) and the specialists are often the contributing factors for the non-adherence. For example, it has been reported in the literature that between 2000 and 2002 a typical Medicare beneficiary saw a median of seven physicians per year: two primary care and five specialists. This finding highlights the need for collaboration between the health care professional in addressing the medical needs of the patients.

Role of the health care team: The problem of medication non-adherence is a great matter of importance to policy makers, health plan sponsors, physicians and patients. Adherence to medications results in better health outcomes and less use of emergency and inpatient services resulting in declined health care costs. Focusing on increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatment.

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The Role of the Health Care System In Improving Patients' Medication Adherence *(continued)*

Role of the provider: Literature on strategies to enhance medication adherence supports that improving patient's adherence to therapy begins with the recognition by physicians of the necessity of patient involvement in decision making of their treatment regimen. One strategy for involving patients in the management of their treatment is writing a treatment plan. The involvement of the patient in the decision making process of the treatment regimen gives them a sense of empowerment and patients are more likely to be motivated to adhere to medications and manage their disease. Additionally, involvement of the patient's family in certain cases may increase the medication adherence.

It should be recognized that dealing effectively with the psychosocial complexities of patient care is as much a scientific undertaking as any other intervention in medical care. Substantially improved adherence rates were reported by patients who have a good relationship with their physician. The key to successful patient-physician relationship is effective communication. The physician should consider the patient's cultural beliefs and attitudes in the treatment process. One example would be if a diabetic patient has a strong belief in herbal remedies, the physician should reassure the patient by saying that metformin is extracted from a plant called French Lilac which was used in folk medicine for centuries.

Finally, physicians should consider simplification of the treatment regimen if possible. For example, combination of two active ingredients instead of administering them as single pills is one way of simplifying the therapy for hypertensive or diabetic patients. Also, products that are dosed once a day can improve a patient's medication adherence.

Physician's Action Plan:

- Engage patients in decision making process of the treatment regimen and drafting the treatment plan.
- Confirm that the patient understood the treatment plan and ask the patient to repeat the instructions.
- Consider simplification of the treatment (combination pills, once daily dosing) when possible.

Role of a pharmacist: Being an integrated member of the health care system, pharmacists have a great responsibility in addressing the problem of medication non-adherence. Pharmacists are the first point of contact for the patients with health inquiries. The patient encounters the pharmacist each time he or she refills a prescription. Pharmacists can achieve long-term medication adherence by having open communication with their patients and by collaborating with other health care providers.

One of the major reasons for non-adherence of the medication is the adverse effects and drug interactions of the medications. When working with the physician, a pharmacist can educate the patient about the medication and its potential adverse effects which could greatly help in adherence to therapy. Through patient counseling, including Medication Therapy Management (MTM) services, the pharmacists can identify potential barriers causing the patient's non-adherence to medications and create an action-plan to address the identified issues. The pharmacist can also identify the patients with adherence issues and could set up automated refill reminders for those members.

Pharmacist's Action Plan:

- Reinforce the importance of long-term medication adherence with the patients.
- Encourage the patients to enroll in auto-refill programs or use of pillboxes which might help patients remember to take their medications.
- Collaborate with the provider to discuss any medication-related concerns (nonadherence due to side effects of the drug) of the patient.

Role of a health plan: The health plans should play an active role in improving the medication adherence among their beneficiaries as improved adherence is the hallmark of better quality care, healthier patients, and reduces the overall medical costs. Health plans should utilize the modern day technology to implement initiatives such as e-prescribing, as there is evidence in literature which suggests that 20 percent of the written prescriptions remain unfilled by the patients. Electronic transmission of a prescription to pharmacies not only increases the medication adherence but can also lower the prescription drug costs. Physicians can select the optimal therapy, in terms of efficacy and cost, from the plan's formulary and the patient's health records that can be accessed through the e-prescribing systems.

Medication adherence is a complex problem, impacts the effectiveness of a therapy and is a great financial burden to the health care system. It is the responsibility of all stakeholders in the health care system to address the issue and help patients better achieve the benefits of their therapy. Through a sustained and coordinated effort from clinicians, pharmacists and the health plans, the goal of long-term medication adherence can be achieved.

Take Home Message:

- Nonadherence to medications remains as a key challenge to our healthcare industry.
- The consequences of nonadherence are poor health outcomes and increased healthcare costs.
- The healthcare team: providers, pharmacists and the health plans need to collaborate and take active steps towards improving the long-term medication adherence in patients..

References:

1. **Mariet T. Brown, MD and Jennifer K. Buseell, MD. Medication Adherence: WHO Cares?** Mayo Clin Proc.2011; 86(4):304-314
2. **Sandra C Thompson, Adrian T Walker.** Use of Modern Technology as an aid to Medication Adherence: an Overview. Patient intelligence 2011;(3) 49-55
3. **M.Christopher Roebuck, Joshua N. Liberman, Marin Gemmill-Toyoma and Troyen A. Brennan**
Medication Adherence Leads To Lower Health Care Use And Costs Despite Increased Drug Spending. Health Affairs 2011,30(1):91-99