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# First Script Prescription Benefit News
## for Workers' Compensation

**April/May 2018**

**Drug of the Month**

### Ixifi™ (infliximab-qbtx)

The third biosimilar drug for Remicade® was approved by the Food and Drug Administration (FDA) in December of 2017. Ixifi (infliximab-qbtx) is made by Pfizer Inc. and joins Inflectra® (infliximab-dyyb) and Renflexis™ (infliximab-abda), with all three biosimilar drugs based on the reference product from Janssen Biotech Inc., Remicade (infliximab). Remicade is a biologic medication indicated in the treatment of various inflammatory conditions including Crohn's Disease, ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis. The biosimilar, Ixifi, was FDA-approved for all of Remicade's indications.

Ixifi is an injectable product available as 100 mg infliximab-qbtx in a 15 mL vial for intravenous use. The approved dosing for Ixifi varies based on the condition being treated, but in general, the drug is injected on a specific regimen usually involving an intravenous induction period with administration at 0, 2, and 6 weeks followed by a regular maintenance dose given every eight weeks (every six weeks in the case of ankylosing spondylitis). Ixifi is immunosuppressive in nature as it works by blocking tumor necrosis factor (TNF) within the body, a regulator of immune cells. Patients should be monitored for the occurrence of opportunistic infections during therapy as they may be at an increased risk of hospitalization or death from serious infections such as tuberculosis (TB), bacterial sepsis, and invasive fungal infections (e.g., histoplasmosis). Due to these risks, it is recommended that the patient undergo a test for latent TB before starting Ixifi, and the patient should continue to be evaluated for active TB periodically throughout Ixifi treatment. Patients with any active infection should not be started on Ixifi, and live vaccines or therapeutic infectious agents should not be given with Ixifi.

Adverse effects reported during administration of Ixifi infusion include flu-like symptoms, headaches, shortness of breath, low blood pressure, fever, chills, gastrointestinal symptoms, and skin rashes. A severe allergic reaction known as anaphylaxis may also occur at any time during Ixifi infusion. The medical provider may choose to premedicate the patient with antihistamines, acetaminophen, and/or corticosteroids before Ixifi administration in an effort to mitigate these effects. Along with infusion-related reactions, the other most common adverse reactions associated with Ixifi use include infections (e.g., upper respiratory, sinusitis, pharyngitis), headache, and abdominal pain.

Biosimilar products are often less costly than their biologic reference product counterparts. According to Medi-Span, the cost comparison (based on Average Wholesale Price [AWP]) between the reference biologic (Remicade) and the first available biosimilars is as follows: Remicade $1,401.38/vial vs. Inflectra $1,135.54/vial or Renflexis $904.07/vial. Pricing is not yet available for the newest biosimilar product, Ixifi; however, it can be reasonably expected to follow the lower comparative price point typical of biosimilar drugs. If an injured worker is currently receiving a work comp approved prescription for Remicade, this may be an opportunity to engage in a discussion with the provider regarding a switch to one of the available biosimilar medications. The prescriber would need to contact the pharmacy to expressly authorize a change from Remicade to the biosimilar product, or they may simply write the prescription for the specific biosimilar medication going forward.

In any case, biosimilar medications like Ixifi fall in the "specialty" drug category, and additional oversight is recommended due to the complex or costly nature of these types of drugs. Furthermore, the conditions treated by Ixifi are not typically considered to be work-related as a person is genetically predisposed to have these diagnoses. The appropriateness for use of Ixifi in relation to the work injury should be determined prior to coverage consideration.

Reference: www.accessdata.fda.gov/scripts/cder/daf/

## Ask The Pharmacist

*To suggest a topic, send an email to: AskThePharmacist@cvty.us.com*

# I know that taking opioids and benzodiazepines together is bad, but what if the injured worker is being prescribed an opioid specifically for opioid dependence treatment?

You are correct that, in general, combined use of opioid medications, benzodiazepines, and other central nervous system (CNS) depressants is not recommended. This is primarily due to the increased risk of respiratory depression which can lead to serious medical issues including death from overdose. You may recall that the FDA added a boxed warning to the labels of all opioid analgesics, opioid-containing cough products, and benzodiazepines in August 2016 relating to these adverse effects if the medications were used together. Our March 2017 newsletter reviewed some of these risks and recommendations along with a link to a full list of opioid pain and cough medications, benzodiazepines, and other CNS depressants.

Interestingly, the FDA has since issued a second alert that speaks more to your question. In September 2017, the FDA issued an updated safety announcement addressing careful medication management for patients taking an opioid for opioid use disorder along with benzodiazepines or CNS depressants. The communication focused on two specific opioids: buprenorphine (including products containing buprenorphine-naloxone) and methadone. Both medications fall within the opioid class, but their unique indication for use as part of medication-assisted treatment (MAT) for opioid dependence calls for additional consideration. Essentially, the FDA stated that these types of opioid medications should not be withheld from a patient simply because that patient is receiving other drugs that depress the CNS. Upon review, the FDA reasoned that "[t]he combined use of these drugs increases the risk of serious effects; however, the harm caused by untreated opioid addiction can outweigh these risks."[1] This information has since been added to the drug labeling for buprenorphine and methadone products, along with guidance for reducing the use of such drugs with benzodiazepines.

The FDA has provided the following recommendations for health care professionals managing patients who will be using both an opioid for MAT along with benzodiazepines or other CNS depressants:[1]

- Educate patients about the serious risks of combined benzodiazepine/opioid use, including overdose and death, that can occur with CNS depressants even when used as prescribed, as well as when used illicitly.
- Develop strategies to manage the use of prescribed or illicit benzodiazepines or other CNS depressants when starting MAT.
- Taper the benzodiazepine or CNS depressant to discontinuation if possible.
- Verify the diagnosis if a patient is receiving prescribed benzodiazepines or other CNS depressants for anxiety or insomnia, and consider other treatment options for these conditions.
- Recognize that patients may require MAT medications indefinitely and their use should continue for as long as patients are benefiting and their use contributes to the intended treatment goals.
- Coordinate care to ensure other prescribers are aware of the patient's buprenorphine or methadone treatment.
- Monitor for illicit drug use by conducting urine or blood screening, for example.

Essentially, the FDA's stance is that a patient should not be removed or barred from starting an MAT program if they test positive for benzodiazepine use, but rather a thoughtful treatment plan should be developed, and careful oversight is needed to determine the best approach given some of the recommendations outlined above. Patients who are using buprenorphine or methadone products for MAT should not stop taking those medications abruptly but should instead follow-up with a health care professional if they wish to discontinue use. Patients should also be guided to speak with their health care provider whenever they start a new medication while using an opioid for MAT to assist in evaluation and management of any ongoing risk. For further insight into drug-drug interactions or for questions related to a specific injured worker's care, please consider contacting our team of clinical pharmacists at askthepharmacist@cvty.com.

Reference:. www.fda.gov/Drugs/DrugSafety/ucm575307.htm

# Allergan Patent Update

In our November newsletter, we discussed the FDA's recent approach to speeding more generics to market in our article entitled "FDA spurs new interest in expediting generic drug opportunities to market." The article mentioned Allergan had attempted to extend exclusive selling rights for Restasis®, a popular eye medication, by selling their product patent to the Saint Regis Mohawk Tribe in upstate New York. By doing so, the tribe could claim sovereign immunity on the patent, and dismiss the patent challenge through the United States Patent and Trademark Office (USPTO).

In response, Mylan, a generic drug manufacturer, asked the United States administrative court to invalidate the transfer between Allergan and the Mohawk Tribe, calling the move a "sham."[1] Allergan appealed to the Patent Trial and Appeal Board (PTAB), who ruled in Mylan's favor. The PTAB indicated that tribal immunity doesn't apply to patent review proceedings and, Allergan retained a substantial ownership interest in the patents.

"U.S. lawmakers from both political parties have criticized Allergan's maneuver, with one U.S. senator introducing a bill to ban attempts to take advantage of tribal sovereignty."[1] Last October Mylan asked a federal judge in Texas to invalidate the patent, which he did, and rendered Allergan's "tribal maneuver" meaningless.

Reference: www.reuters.com/article/us-allergan-patent-tribe/u-s-patent-court-deals-setback-to-allergans-restasis-strategy-idUSKCN1GA239

## Regulatory Update

### Arizona

AZ S 2633 has adopted amendments to the opioid prescribing limitation and exception rules within AZ S 1001. The bill will become effective 90 days after the session ended (May 3, 2018) and will be effective retroactively to April 25, 2018.

AZ S 1111 has adopted amendments to Sections 23-908 and D 23-1062.02 regarding physician prescribing and utilization reporting requirements. The effective date is 90 days after the legislative session adjourned (May 3, 2018).

AZ HB 2549 has adopted changes regarding prescription dosage limitations. Changes include the dispensing of Schedule ll controlled substances for naturopathic physicians, osteopathic physicians, physician assistants, and other health professionals. The bill became effective 90 days after the session ended (April 21, 2018), and will be effective retroactively to May 5, 2018.

### Florida

HB 21 regarding opioid prescribing limitations was signed into law by Florida Governor Rick Scott on March 3, 2018, with an effective date of July 7, 2018. The rule requires that prescriptions for a Schedule II opioid to treat acute pain not exceed a three-day supply. The bill also stipulates that a seven-day supply of a Schedule II opioid to treat acute pain can be prescribed when specific requirements are met.

### Georgia

The State has updated their Workers' Compensation Medical Fee Schedule rules in regards to section IV general reimbursement requirements for fee schedule, compounds, and over-the-counter drugs effective April 1, 2018.

### Kentucky

HB 2 regarding reimbursement, drug formulary, and treatment guidelines has been adopted with an effective date of July 12, 2018. The commissioner plans to develop or adopt a pharmaceutical formulary for medications prescribed for the cure of and relief from the effects of a work injury or occupational disease, and publish administrative regulations to implement the developed or adopted pharmaceutical formulary on or before December 31, 2018. More information can be found here.

### Maryland

Maryland has adopted COMAR 10.13.01, 10.32.12, and 10.32.23 regarding the dispensing of prescription drugs. The adopted rules became effective March 26, 2018 and available on April 18, 2018. The rules address the following changes:

- Allows a licensed physician to dispense a prescription written by a physician assistant under specified conditions
- Defines the parameters under which a physician is required to obtain a permit to dispense prescription drugs
- Addresses the delegation of dispensing functions and other requirements of the permit holder

More information can be found here.

## Michigan

Effective July 1, 2018 SB 274 enacts opioid prescription limitations for claimants injured in the state; including opioids used for acute pain treatment, which are limited to no more than a seven-day supply of an opioid within a 90-day period. To adhere to the state's requirements, all attempts to fill opioids in the state of Michigan will reject if the day supply is over seven, and if the injured worker has not previously obtained that opioid in the previous 90 days.

Michigan also updated their Workers' Compensation Administrative Rules, citation R 418.10106 - .101503. There were no updates to the pharmacy fee schedule other than a new effective date of March 15, 2018.

## Montana

The Montana Labor Management Advisory Council (LMAC) voted to adopt ODG guidelines as part of their formulary utilization and treatment guidelines. This resulted from the enactment of MT SB 312 earlier this year. Several issues are being worked out as the state proceeds, including how to deal with prior authorizations, legacy claims, and dispute resolution. The tentative time-line is as follows:

- Final draft to be completed by October 1, 2018
- Formal rule-making procedures expected during October - December, 2018
- Expected effective date by or after December 31, 2018
- Administrative rules complete by December 31, 2018

## North Carolina

Effective May 1, 2018, North Carolina has adopted Rule 04 NCAC 10M.0100 - .0501 regarding the utilization and limitation of opioids, related prescriptions, and pain management. Changes include, but are not limited to:

- Definitions added for acute and chronic phase, confirmatory and presumptive urine drug tests, long-acting or extended-release opioid, short-acting opioid, and targeted controlled substances.
- Limitations and regulations on prescribing targeted controlled substances during the acute and chronic phases.
- Providers must review the Controlled Substances Reporting System (CSRS) pertaining to the employee for the 12-month period preceding the first prescription and document the review of any potential contraindications found in the CSRS.
- Health care providers prescribing targeted controlled substances must consider co-prescribing opioid antagonists under specific situations.
- Health care providers may, if they believe in their medical opinion that an injured worker may benefit, refer the injured worker to another health care provider specializing in discontinuation or tapering of a targeted controlled substance or treating substance use disorder.

## Ohio

Effective May 1, 2018, Ohio has adopted amendments to the Professional Provider Medical Services Fee Schedule, Rule 4123-6-08, the Outpatient Medication Formulary, Rule 4123-6-21.3, the Outpatient Hospital Fee Schedule, Rule 4123-6-37.2, and the Ambulatory Surgical Center Fee Schedule, Rule 4123-6-37.3. The rules address Managed Care Organizations (MCOs) certified under the Health Partnership Program (HPP), Qualified Health Plans (QHPs), and self-insured employers. The Outpatient Medication Formulary is required for use for state fund claims. Self-insured employers may utilize the formulary, but are not required to do so. Changes include, but are not limited to, the following:

- Establishes the 2018 Professional Provider Medical Services Fee Schedule
- Revises the Outpatient Medication Formulary Rule by developing a new formulary
- Specifies rates for covered orthopedic procedures, pain management services, and device-intensive services

## Oklahoma

SB 1446 regarding opioid prescribing limitations was signed into law by Oklahoma Governor Mary Fallin on May 2, 2018, with an effective date of November 1, 2018. The rule provides various definitions, documentation requirements, subsequent prescription rules and requires that practitioners must not prescribe an initial prescription for an opioid to treat acute pain exceeding a seven-day supply.

## Oregon

Oregon has adopted OAR 333-023-0825 regarding requirements to register with the Prescription Drug Monitoring Program (PDMP). No later than July 21, 2018, practitioners meeting specified criteria must register with the PDMP in accordance with Oregon regulations in order to have access to the PDMP's electronic system. This rule was published by the Oregon Health Authority on April 5, 2018, and is effective April 5, 2018 through September 15, 2018.

Oregon has also adopted OAR 436-009, -010, -015 regarding medical fees and payments, interpreter services, treatment guidelines, and MCOs. There are several changes to the rule, including, but not limited to, updates to various fee schedules, guidelines, and reference manuals. The rule was published by the Department of Consumer and Business Services, Workers' Compensation Division on March 16, 2018, and became effective April 1, 2018.

## Texas

Effective July 1, 2018 Texas will adopt changes to the Texas Closed Formulary for network and non-network claims. Changes include compound exclusions and preauthorization requirement updates to the closed formulary. Changes to the closed formulary were published on April 13, 2018, and include amendments to Title 28 Texas Administrative Code (TAC) §§134.500, 134.530, and 134.540.

## West Virginia

Senate Bill 273 regarding opioid prescribing limitations was adopted on March 27, 2018 with an effective date of June 7, 2018. Significant changes in the bill include, but are not limited to, the new definitions of "acute pain," "chronic pain," and "health care practitioner;" new practitioner rules, and the establishment of opioid prescribing limitations.

**Coventry's Regulatory and Legislative Affairs (RLA) group will continue to monitor further discussion on these topics. If you have questions regarding these changes, please contact your First Script Account Manager.**