Mountain-Pacific Quality Health

# DUR PROGRAM NEWS

**SPRING 2016**


Lisa Sather, RPh
DUR Coordinator
Mountain-Pacific
Quality Health
3404 Cooney Drive
Helena, MT 59602
406-457-5818


The Drug Utilization Reveiw (DUR) Program, administered by Mountain-Pacific through a contract with the Allied Health Services Bureau of the Montana Department of Public Health and Human Services, is the quality assurance body seeking to assure the quality of pharmaceutical care and to help provide rational, cost-effective medication therapy for Montana's Medicaid recipients.

## Biosimilars: A basic primer

In March, the FDA approved Zarxio® (filgrastim-sndz), which is the first biosimilar approved in the United States. Zarxio® is considered a biosimilar to the reference product Neupogen® (filgrastim), although it is not directly interchangeable. Biosimilars may cost less than the reference product in specific situations. So what is a biosimilar, and how does it differ from a *generic* product?

### *First things first. What is a biologic?*

A biologic product is one which is derived from a ***natural source***, such as human, animal, or microbiological origin. Examples include Neupogen®, Remicade® and Humira®.

- Neupogen®- produced by Escherichia coli bacteria into which has been inserted the human granulocyte colony-stimulating factor gene.
- Remicade®- a chimeric (composed of human and murine variable regions) monoclonal antibody produced by a recombinant cell line.
- Humira®- produced by recombinant DNA technology in a mammalian cell expression system using phage display technology.

### *A biosimilar is a biologic that has been shown to be highly similar to its FDA-approved reference product.*

- Why just *highly similar and not identical?* Each manufacturer owns its own unique cell lines which produce a specific biologic (each with its own genetic makeup), therefore is not possible to produce an **exact** copy of the original product.
- This is in contrast to generic medications for chemical-based drugs (like esomeprazole magnesium, the generic version of Nexium®) that are created through a set of *reproducible chemical reactions*.

### *No clinical meaningful differences in safety and efficacy are allowed between a biosimilar and the reference product.*

- Only **minor** differences in clinically **inactive** components may be present.
- Safety, purity, potency and efficacy must be equivalent to the reference product.

### *Biosimilars are approved under a different pathway than generic drugs.*

- Expedited approval for biosimilars is allowed through the "The Biologics Price Competition and Innovation Act of 2009" (BCPI Act), which was passed as part of the 2010 Affordable Care Act. This is in contrast to generic drug approval, which is through the abbreviated new drug application (ANDA) pathway.

**For drug-specific prior authorization information, please contact the Medicaid Drug Prior Authorization Unit @ Mountain-Pacific 1-800-395-7961**

- Biosimilarity and/or interchangeability between the proposed biosimilar and the reference product must be established, but not separate safety and efficacy of the biosimilar compared to the reference product.
- Requirements for FDA biosimilar approval include:
  - » Same mechanism of action, route of administration, dosage form, and strength as reference drug,
  - » Same (or fewer) indications than approved for the reference product,
  - » Manufacturing facilities must meet FDA standards,
  - » Analytical studies demonstrating the biosimilar is "highly similar" except for inactive components, animal studies (assessing toxicity) and clinical studies sufficient to demonstrate safety/purity/potency.

***A biosimilar must meet additional FDA standards to also be considered interchangeable with the reference product.***

- A manufacturer may choose not to seek a designation of interchangeability with the reference product (i.e. Zarxio® is not interchangeable with Neupogen®)
- If interchangeability is sought, specific data/information must be provided:
  - » to support the biosimilar is expected to produce the same clinical result as the reference product in *any* patient,
  - » to demonstrate there is no difference in safety/efficacy if the patient is switched between the reference product and the biosimilar.
- The **Purple Book** (similar to the **Orange Book** for generics) lists licensed biological products and biosimilar ("B") and/or interchangeable ("I") status with the reference product.
  Available at:
  http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm411418.htm).

Draft guidance for industry issued by the FDA suggests naming a biosimilar with a 4-letter suffix derived from the name of the license holder.

i.e.,filgrastim-sndz, after the manufacturer, Sandoz, for Zarxio®

**References:**

1. **Neupogen [package insert]. Available at** http://pi.amgen.com/united_states/neupogen/neupogen_pi_hcp_english.pdf . Accessed 3/8/2016.
2. **Humira [package insert].** Available at http://www.rxabbvie.com/pdf/humira.pdf. Accessed 3/8/2016.
3. http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm411424.htm. **Accessed 3/8/2106.**
4. http://www.zarxio.com/info/hcp/pioneer.jsp?utm_medium=cpc&utm_term=neupogen&utm_content=Neupogen&utm_source=bing&utm_campaign=IE - Zarxio - HCP Competitive#. **Accessed 3/10/2016.**
5. PL Detail-Document, FAQs About Biosimilars, Pharmacists Letter/Prescriber's Letter. October 2015.
6. Remicade [package insert]. Available at http://www.remicade.com/shared/product/remicade/prescribing-information.pdf. **Accessed 3/8/2016.**


## MONTANA MEDICAID PRIOR AUTHORIZATION CRITERIA UPDATES

Rexulti®- Brexpiprazole (Rexulti®) is an atypical antipsychotic agent indicated as adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD), and also for the treatment of schizophrenia. Its mechanism of action is combination partial agonist activity at serotonin 5-$HT_{1a}$ and dopamine $D_2$ receptors, and antagonism at serotonin 5-$HT_{2a}$ receptors. Due to the availability of numerous other therapeutic alternative agents for these indications, the Montana Medicaid Drug Utilization Review Board (DURB) unanimously recommended implementation of the following clinical criteria for this brand-name medication:

- Patient must be 18 years of age or older
- Covered diagnoses are MDD and schizophrenia

Continued ›

(Rexulti® criteria continued)

- MDD adjunctive treatment:
  - » Patient must have an inadequate response, after at least four weeks of therapy, to ***at least two*** preferred antidepressant agents **AND**
  - » Patient must have had an inadequate response or contraindication to aripiprazole and quetiapine as add-on therapy **AND**
  - » Patient is concurrently using an antidepressant.
  - » Dosing limitation of 1 tablet daily, up to maximum of 3 mg daily.
- Schizophrenia:
  - » Patient must have had an inadequate response, after at least six weeks of therapy, to ***at least two*** preferred FDA-approved medications for schizophrenia
  - » Dosing limitation of 1 tablet daily, up to maximum of 4 mg daily.

**Of note:**

- » **No current published studies exist comparing aripiprazole and brexpiprazole, and therefore it is difficult to predict if any meaningful clinical differences exist.**
- » **In 2015, the first generic formulation of Abilify® (aripiprazole) was FDA approved.**
- » **Rexulti® is manufactured by Otsuka, the same manufacturer as Abilify®. Both medications have similar mechanisms of action.**

Invega Trinza®-Paliperidone palmitate (Invega Trinza®) is an every 3-month injectable antipsychotic indicated for the treatment of schizophrenia in patients after they have been adequately treated with Invega Sustenna® (a once-monthly paliperidone palmitate injection) for at least four months. Like all other available injectable atypical antipsychotic medications, it is administered by a health-care professional. Due to the extremely long half-life once administered (~3-4 months depending on injection site) and the FDA-requirement for first establishing compliance on Invega Sustenna®, the DURB has recommended implementation of the following clinical criteria:

- Patient must meet Medicaid criteria for all long-acting atypical injectables: compliance issue with oral medication and tolerability must be established with corresponding oral molecule,
- Patient must be 18 years of age or older,
- Must have a diagnosis of schizophrenia,
- Patient must have been compliant w/treatment using Invega Sustenna® for at least **6 months**. This requirement is to ensure tolerability/effectiveness due to the time required for elimination once the medication is injected,
- Approval will be granted with compelling clinical rationale (non-compliance alone will not warrant coverage).

Aristada®- Aripiprazole lauroxil (Aristada®) is a long-acting (once monthly or once very 6 weeks, depending on dose) atypical antipsychotic injection indicated for the treatment of schizophrenia. ***Abilify Maintena®, a once-monthly aripiprazole injection, is currently the preferred long-acting injectable aripiprazole product.***

- » **Aristada® is available in higher dosages (up to 882 mg) vs a maximum 400 mg for Abilify Maintena®.**
- » **Place in therapy may be in clinical situations warranting higher dose than is available with the current preferred product, Abilify Maintena®.**

The DURB has recommended implementation of the following clinical criteria:

- Patient must meet Medicaid criteria for long-acting atypical injectable: compliance issue with oral medication, tolerability established with corresponding oral molecule,
- Patient must be 18 years of age or older,
- Patient must have a diagnosis of schizophrenia,
- Compelling clinical rationale explaining why the preferred agent Abilify Maintena® cannot be prescribed. Example: Patient is not adequately controlled on 400mg Abilify Maintena® and requires higher dose,
- Concurrent oral aripiprazole is approved for 21 days per FDA labeling.

## Sampling policy update:

Prior to 2016, patients sampled on atypical antipsychotics were allowed to continue under the Medicaid grandfathering (stable-therapy) policy on a non-preferred agent. This policy was implemented when few agents were available. After review of the numerous available preferred agents, the DUR board recommended to discontinue this policy. Samples will no longer qualify for grandfathering purposes for atypical antipsychotic agents. No other classes allow samples for grandfathering purposes.

## Montana Medicaid Top 20 Drugs for YTD 2016 by Generic Name

| Drug Name | By Dollars | # of Patients | Drug Name | By Rx Count |
|---|---|---|---|---|
| Aripiprazole | $567,032 | 670 | Hydrocodone/Acetaminophen | 2,670 |
| Methylphenidate | $270,269 | 1,397 | Albuterol | 2,425 |
| Lurasidone | $182,456 | 200 | Amoxicillin | 2,085 |
| Atomoxetine | $166,398 | 382 | Methylphenidate | 1,672 |
| Lisdexamphetamine | $162,803 | 712 | Omeprazole | 1,518 |
| Dextroamphetamine/amphet | $157,626 | 943 | Gabapentin | 1,453 |
| Duloxetine | $151,509 | 665 | Levothyroxine | 1,376 |
| Insulin aspart | $143,794 | 276 | Azithromycin | 1,340 |
| Paliperidone palmitate | $143,472 | 76 | Fluoxetine | 1,304 |
| Fluticasone/salmeterol | $140,690 | 410 | Sertraline | 1,151 |
| Albuterol | $138,624 | 2,265 | Dextroamphetamine/amphet | 1,079 |
| Pregabalin | $133,812 | 337 | Quetiapine | 996 |
| Insulin glargine | $120,579 | 306 | Clonazepam | 987 |
| Ledipasvir/sofosbuvir | $96,390 | 3 | Lamotrigine | 976 |
| Dornase alfa | $90,161 | 21 | Montelukast | 939 |
| Lumacaftor/ivacaftor | $87,100 | 5 | Lisinopril | 938 |
| Quetiapine | $86,598 | 828 | Bupropion | 917 |
| Sofosbuvir | $85,680 | 3 | Oxycodone | 890 |
| Oxycodone | $78,929 | 733 | Trazodone | 845 |
| Dexmethylphenidate | $75,753 | 246 | Citalopram | 781 |

*excludes injectable drugs except insulins (dollars are pre-rebate)

Mountain-Pacific Quality Health
3404 Cooney Drive
Helena, MT 59602