Drug Utilization Review (DUR) Newsletter

COLORADO
Department of Health Care Policy & Financing

Select HCPF Medication Use Policy Updates

WINTER 2022

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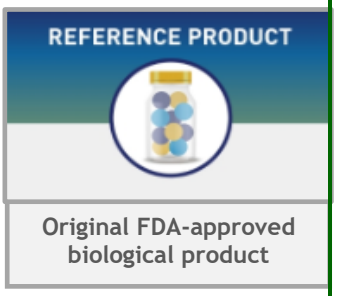
The Nuts and Bolts of Biologics and Biosimilars

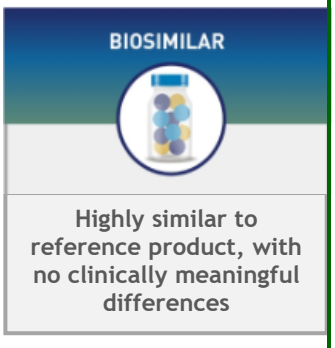
Biological drug products, or *biologics*, are generally complex molecules made from living organisms such as bacteria, yeast, and animal cells. Because biologics come from living organisms they are often more complicated to purify, process and manufacture than smaller, simpler drug molecules that can be synthetically produced. Therefore, biologics inherently contain many slight variations from batch to batch.[1]

Since the approval of recombinant insulin in 1982, there has been an expansive growth in the types and numbers of biologic products.[2] Biologic products now have FDA approved indications for the treatment of a wide range of disease states, including cancer, Crohn's disease, plaque psoriasis, several forms of arthritis, asthma, and other forms of autoimmune disease. The biologics also include vaccines, blood components, and gene therapies.[3]

What is a *biosimilar* product?

While biologics are impossible to exactly duplicate, legitimate copies (biosimilars) can be created through reverse-engineering to produce a drug that is *highly similar* to the complex molecule of the originator, or reference, product. To receive FDA approval, a biosimilar must be rigorously tested to demonstrate similarity in terms of structure, binding characteristics, pharmacokinetics, safety, efficacy, immunogenicity, and quality.[4] Biosimilars have the same route of administration, strength and dosage form, and potential side effects as their originator products. They are as safe and effective as the reference product they were compared to in order to be approved.[1,3]





Are biosimilar products considered generic drugs?

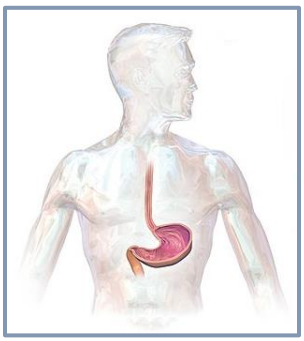
No. Since it is not possible to make an exact duplicate of an originator biologic product, biosimilars cannot be considered generic drugs.[4] Of note, biosimilars are not automatically interchangeable with originator products without undergoing additional studies and obtaining specific FDA interchangeability approval. As with generic drugs, biosimilars can improve patient access and offer more affordable treatment options for Health First Colorado members.

Where can I learn more?

The FDA provides additional information about biosimilars for patients and health care professionals at https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/biosimilars

Deprescribing Proton Pump Inhibitors: Who, Why, and How

Robert L Page II, PharmD, MSPH

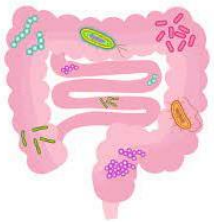


Proton pump inhibitors (PPIs) have been used to treat gastric ulcer, duodenal ulcer, and reflux esophagitis; to suppress recurrence of gastric or duodenal ulcer when low-dose aspirin or a nonsteroidal anti-inflammatory drug is administered; and to eradicate *Helicobacter pylori* (*H. pylori*). Furthermore, a PPI is used to treat not only mucosal damage such as reflux esophagitis and ulcer, but also non-erosive gastroesophageal reflux disease (GERD) and functional dyspepsia in which the goal of therapy is symptom control.[1,2] Therefore, it is possible to discontinue PPI treatment if symptoms improve or resolve by PPI treatment. In addition, mild esophagitis with Los Angeles grade A or B does not progress to severe esophagitis in 90% of the cases; therefore, it is known that treatment does not need to be continued if there are no symptoms.[3,4]

Although PPIs are effective and necessary long-term therapies for certain rare conditions, such as Zollinger-Ellison syndrome, most common indications for PPIs, such as GERD, require only short-term use of the drugs and little evidence supports their long-term use. However, unnecessary off-label long-term use of PPIs is prevalent, with up to 65% of patients receiving PPI therapy in the United States having no documented ongoing indication, raising concerns about inappropriate polypharmacy and its risks.[4]

In recent years, potential side effects associated with PPI use have been reported. Long-term PPI use may affect nutrient absorption, including calcium, magnesium, and vitamin B_{12} malabsorption resulting in an increase in the risk of fracture.[5,6] PPI use may increase the risk of enteric infections such as with *Clostridium difficile* and *Campylobacter*, and community-acquired pneumonia.[7]

The gut microbiota plays an important role in host resistance against colonization by exogenous enteric microbes and overgrowth of indigenous commensals. Two large cohort studies found that PPIs altered the composition of the gut microbiota which in turn lead to the increased risk of enteric infections in PPI users caused by the influence of PPI on the gut microbiota.[7,8] Moreover, intestinal bacterial overgrowth promotes bacterial translocation. Therefore, PPIs may cause bacterial translocation.[9-12] Finally, prolonged use of these medicines has been associated kidney disease, injury and failure, as well as gastric cancer.[13] Therefore, it is necessary to discontinue PPI use in patients who have been taking PPI for a long period of time if a PPI is not necessary. However, sudden discontinuation may cause symptoms to recur, and discontinuation may be unsuccessful, which leads to a clinical conundrum.



Unfortunately, specific guidelines regarding deprescribing or de-escalation of PPIs are scant. In 2017, using the GRADE framework for guideline development, Farrell et al developed deprescribing evidence-based guidelines considerations for PPI.[14] Per their evaluation of the literature, the writing committee recommended deprescribing PPIs (reducing dose, stopping, or using "on-demand" dosing) in adults who have completed a minimum of four weeks of PPI treatment for heartburn or mild to moderate gastroesophageal reflux disease or esophagitis, and whose symptoms are resolved. However, these recommendations do not apply to those who have or have had Barrett's esophagus, severe esophagitis grade C or D, or documented history of bleeding gastrointestinal ulcers.

While no evidence exists that one PPI tapering approach is better than another, the committee suggested applying one of the following:

- Lowering the PPI dose from twice daily to once daily
- Halving the dose or taking a dose every second day
- Stopping the PPI and using it on demand

Consideration can also be given to step down therapy, which involves abrupt discontinuation or tapering of the PPI followed by prescription of a histamine H2-receptor antagonist. The authors provide a step-by-step PPI deprescribing algorithm available at:
https://deprescribing.org/wp-content/uploads/2018/08/ppideprescribing-algorithm_2018_En.pdf

Recently, the American Gatroenterology Association (AGA) published their expert review on deprescribing of PPIs. Within this clinical statement, the AGA provided their top ten best practice statements addressing who to consider deprescribing and the specific indications for PPI use (Tables 1 and 2).[15] Of note, the AGA specifically stated "prescribers should not use concern about unproven complications of PPI use as a justification for PPI deprescribing if there remain ongoing valid indications for PPI use."[15]

Nonetheless, the decisions about PPI discontinuation are complex and nuanced, and consequences for inappropriate or poorly considered discontinuation can be significant. Conversely, the unchecked use of PPIs in situations when indications are absent or murky is a major contributor to health care costs, and even a small risk of medical harm is significant in the complete absence of benefit. While a "one size fits all" strategy does not exist, PPI discontinuation requires a systematic approach as well as shared decision making between patient and provider, taking into account both the specific PPI indication and duration of use.

Table 1. Ten Best Practices for Deprescribing PPIs per the AGA[14]

1	All patients taking a PPI should have a regular review of the ongoing indications for use and documentation of that indication. This review should be the responsibility of the patient's primary care provider
2	All patients without a definitive indication for chronic PPI should be considered for trial of deprescribing.
3	Most patients with an indication for chronic PPI use who take twice-daily dosing should be considered for step down to once-daily PPI.
4	Patients with complicated GERD, such as those with a history of severe erosive esophagitis, esophageal ulcer, or peptic stricture, should generally not be considered for PPI discontinuation.
5	Patients with known Barrett's esophagus, eosinophilic esophagitis, or idiopathic pulmonary fibrosis should generally not be considered for a trial of deprescribing.
6	PPI users should be assessed for upper gastrointestinal bleeding risk using an evidence-based strategy before deprescribing
7	Patients at high risk for upper gastrointestinal bleeding should not be considered for PPI deprescribing.
8	Patients who discontinue long-term PPI therapy should be advised that they may develop transient upper gastrointestinal symptoms due to rebound acid hypersecretion.
9	When deprescribing PPIs, either dose tapering or abrupt discontinuation can be considered.
10	The decision to discontinue PPIs should be based solely on the lack of an indication for PPI use, and not because of concern for PAAEs. The presence of a PAAE or a history of a PAAE in a current PPI user is not an independent indication for PPI withdrawal. Similarly, the presence of underlying risk factors for the development of an adverse event associated with PPI use should also not be an independent indication for PPI withdrawal.

AGA: American Gastroenterological Association, GERD: Gastrointestinal Esophageal Reflex Disease, PPI: Proton Pump Inhibitor, PAAE: PPI-associated adverse events

Table 2. Indications and Duration of Use of PPIs per the AGA[14]

PPI Indications					
Definitely **indicated for long-term use (>8 weeks)**	***Conditionally*** **indicated for long-term use**	***Not*** **indicated for long-term use**	***Definitely*** **indicated for acute/short-term use (≤8 weeks)**	***Conditionally*** **indicated for acute/ short-term use**	***Not*** **indicated for acute/ short-term use**
Barrett's esophagus Clinically significant (LA Classification grade C/D) erosive esophagitis Esophageal strictures from GERD (i.e., peptic strictures) Zollinger-Ellison syndrome Eosinophilic esophagitis Gastroprotection in users of ASA/NSAID therapy at high risk for GI bleeding Prevention of progression of idiopathic pulmonary fibrosis	PPI-responsive endoscopy negative reflux disease, with recurrence on PPI cessation PPI-responsive functional dyspepsia, with recurrence on PPI cessation PPI-responsive upper airway symptoms ascribed to laryngopharyngeal reflux with recurrence on PPI cessation Refractory steatorrhea in chronic pancreatic insufficiency with enzyme replacement Secondary prevention of gastric and duodenal peptic ulcers with no concomitant antiplatelet drug	Symptoms of nonerosive reflux disease with no sustained response to high-dose PPI therapy Functional dyspepsia with no sustained response to PPI therapy Steroid therapy in the absence of ASA/NSAID therapy Prevention of recurrent upper GI bleeding from causes other than PUD, including gastric and duodenal erosions and erosive esophagitis	*Helicobacter pylori* eradication Stress ulcer prophylaxis for ICU patients with risk factors Uninvestigated GERD/dyspepsia Treatment of NSAID-related gastric and duodenal peptic ulcers	Initial or on-demand treatment of endoscopy negative reflux disease Initial treatment of functional dyspepsia Uninvestigated dyspepsia Ulcer prevention after sclerotherapy or band ligation treatment of esophageal varices Prevention of rebleeding from Mallory-Weiss tears	Empiric treatment of laryngopharyngeal symptomatology Acute undifferentiated abdominal pain Acute nausea and vomiting not believed to be related to GERD/esophagitis Any isolated lower GI symptomatology

AGA: American Gastroenterological Association, ASA: aspirin, GERD: Gastrointestinal Esophageal Reflex Disease, ICU: intensive care unit, LA, Los Angeles, NSAID: Non-steroidal Anti-inflammatory Drug, PPI: Proton Pump Inhibitor, PUD: Peptic Ulcer Disease

DUR Board Member Spotlight

By Mandy Li
PharmD Candidate
DUR Intern

Ingrid Pan, PharmD

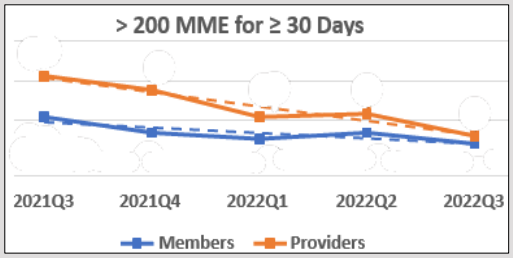
Dr. Ingrid Pan is a Clinical Pharmacy Specialist in Rheumatology at Children's Hospital Colorado. She ensures that patients, particularly patients who have limited access to healthcare, are well educated and have access to specialty medications. She facilitates interprofessional relationships between inpatient and outpatient departments. Dr. Pan engages in the rheumatology fellowship and residency program and conducts her own clinical research. She is Secretary-Treasurer of the national American College of Clinical Pharmacy Pediatrics Practice and Research Network (PRN) and serves as a Lexicomp pediatric monograph consultant.

Dr. Pan's pharmacy journey began in high school where she shadowed a clinical pharmacist. After attending the University of Pittsburgh's accelerated program, she started pharmacy school at the University of Pittsburgh School of Pharmacy. A year prior to pharmacy school, Dr. Pan began an internship at the University of Pittsburgh Medical Center. Dr. Pan built interest in pediatrics and valued the relationships she made with her patients. After receiving her PharmD, she entered into a PGY1 practice residency in Adult Medicine at Palmetto Health Richland Hospital in Columbia, SC. This experience solidified her passion for pediatrics and led her to complete a PGY2 practice residency at the University of Chicago Medicine Comer Children's Hospital in Chicago, IL.

Dr. Pan loves to travel and she sets a goal to travel internationally every year. This year she took a trip to Spain. She is also a Yelp elite! To help alleviate stress during her pharmacy school years, Dr. Pan tried all sorts of food and coffee shops and wrote reviews. She continues to be a top food reviewer for the Denver Metro area.

Dr. Pan strives to be a model for pharmacy students and residents to inspire bright individuals to pursue pediatric pharmacy. She has a high interest in transitions of care from pediatrics to adulthood and wants to continue to conduct research in this area.

The number of Colorado Medicaid members with Rx claims totaling a morphine milligram equivalent (MME) >200 continues to decline



November 2022
DUR Board PDL Drug Classes Reviewed

- Hepatitis C Virus Treatments
  - Direct Acting Antivirals
  - Other Agents
  - Ribavirin
- HIV Treatments
- Intranasal Rhinitis Agents
- Targeted Immune Modulators
  - Rheumatoid Arthritis
  - Polyarticular Course JIA
  - Ankylosing Spondylitis
  - Psoriatic Arthritis
  - Plaque Psoriasis
  - Crohn's Disease
  - Ulcerative Colitis
  - Asthma
  - Atopic Dermatitis
  - Other indications
- Newer Hereditary Angioedema Products
- Inhaled Antibiotics
- Oral and Topical Antiherpetic Agents
- Oral Fluoroquinolones
- Immune Globulins
- Antihistamines
- Newer Antihistamines/Decongestants
- Leukotriene Modifiers
- Methotrexate Products
- Epinephrine Products
- Respiratory Agents
  - Inhaled Anticholinergics
  - Inhaled Beta2 Agonists
  - Inhaled Corticosteroids
  - Phosphodiesterase Inhibitors

The January 1, 2023 Colorado Preferred Drug List (PDL)

is available at

https://www.colorado.gov/hcpf/pharmacy-resources#PDL

Hepatitis C Therapy Update

Effective January 1, 2023, prior authorization will **no longer be required** for first-line preferred products* prescribed for initial treatment of Hepatitis C. Additionally, first-line preferred products will be eligible for up to a 90-day supply fill for the initial treatment regimen. Prior Authorizations will continue to be required for non-preferred drugs or retreatment regimens.

***First-Line Preferred Products Effective 1/1/23:** EPCLUSA (sofosbuvir/velpatasvir) 200 mg -50 mg, 150 mg-37.5 mg tablet, pellet pack; HARVONI (ledipasvir/sofosbuvir) 45mg-200mg tablet, pellet pack; Ledipasvir/Sofosbuvir 90 mg-400 mg tablet (Asequa only); MAVYRET (glecaprevir/pibrentasvir) tablet, pellet pack; Sofosbuvir/Velpatasvir 400mg-100mg (Asequa only).

Are you interested in observing a virtual Colorado DUR Board Meeting?

Board meetings are held quarterly

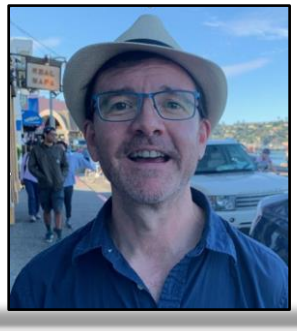
- FEBRUARY
- MAY
- AUGUST
- NOVEMBER

Meeting dates & times, agendas, minutes, a newsletter library, and other information can be found on the DUR Board web page at https://hcpf.colorado.gov/drug-utilization-review-board

Zoom meeting information for public attendees is posted on the same web page a few days prior to each meeting

DUR Board Member Spotlight

by Tracy Van
PharmD Candidate
DUR Intern



Ken MacIntyre, DO

Dr. Ken MacIntyre is a psychiatrist at Wellpower in Denver, Colorado. Having been at this unique mental health center for eight years, his role involves working in clinics that encompass high intensity and acuity care and case management needs. His passion to care for patients and the community strongly align with Wellpower's commitment and mission to truly help the underserved. Dr. MacIntyre notes that one of his favorite things about work is getting to connect with some of the most challenging patients and help them achieve wellness.

Though he has had many years of experience in his specialty thus far, Dr. MacIntyre did not have what some may call a traditional journey in medicine. He was a mortgage banker for just over 20 years and then was involved in local Denver theatre for a little over 5 years. It was after these two professional experiences that he then obtained his medical degree from Touro University of California, College of Osteopathic Medicine. With psychiatry striking an interest and coming naturally to him, Dr. MacIntyre then completed his four-year residency at Temple University in Philadelphia, Pennsylvania.

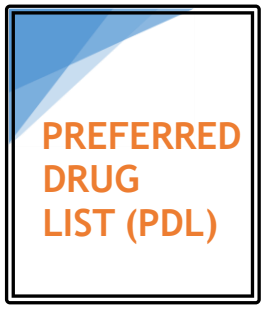
Outside of work, Dr. MacIntyre is an avid disc golfer, and he plays at least once a week. When not at the course, he enjoys hanging out with his friends, often at cultural events. He was also recently able to restore his piano and is starting to play again. When he was younger he both played and composed piano music.

Regarding his general outlook, Dr. MacIntyre wisely notes that, as humans, we need to be able to have a sense of humor with what we do, so as to not take ourselves too seriously in order to flexibly deal with the absurdities of life. Through his professional practice, he hopes to continue being a passionate voice for marginalized communities and continue to help break down barriers to treatment.

Our mission is to improve health care equity, access and outcomes for the people we serve while saving Coloradans money on health care and driving value for Colorado.
https://hcpf.colorado.gov

Colorado Drug Utilization Criteria Resources

The Department manages 3 types of prior authorization criteria maintained on separate online documents



Preferred Drug List (PDL)

https://hcpf.colorado.gov/pharmacy-resources#PDL

- The preferred drug list (PDL) is a list of therapeutic drug classes (groups of categorically similar drug products) where individual drugs included in a class are managed with preferred and non-preferred designations
- Medication is covered by the **pharmacy benefit**
- Prior Authorization (PA) criteria and other coverage policies for specific drugs and drug classes are also available within this document

Appendix P

https://hcpf.colorado.gov/pharmacy-resources#PDLP

- Medication is covered by the **pharmacy benefit** and billed in the point-of-sale system
- Appendix P includes all other drugs, or groups of drugs, that are non-PDL drugs managed with coverage limitations or PA criteria (essentially any pharmacy benefit "managed" drugs that are not included on the PDL/in PDL drug classes)
- All pharmacy benefit physician administered drugs (PADs) are subject to the PAD Policy on Appendix P that limits coverage to cases where the drug is administered by a healthcare professional in the member's home or a long term care facility (LTCF)
- Some pharmacy benefit PADs also have other PA criteria and coverage limitations listed for the specific drug on Appendix P

Appendix Y

https://hcpf.colorado.gov/physician-administered-drugs

- Medication is covered by the **medical benefit** and billed on a professional claim
- PAD** medications (such as injections, IV infusions, and implants) must be administered in an office or clinic under medical supervision
- Providers must ensure that an approved PA is on file **prior to PAD administration**
- Retroactive authorizations are not allowed, with few exceptions due to extenuating circumstances

** Physician Administered drugs (PADs) include any medication or medication formulation that requires administration by a healthcare professional, including cases where FDA package labeling for a medication specifies that administration should be performed by or under the direct supervision of a healthcare professional.

References

The Nuts and Bolts of Biologics and Biosimilars

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Deprescribing Proton Pump Inhibitors: Who, Why, and How

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Images

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