



Adult Medicine PRN

Fall Newsletter

Edited by Andrew Miesner, PharmD, BCPS & Beth Resman-Targoff, PharmD, FCCP

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A Message From The Chair

Kurt Wargo, PharmD, FCCP, BCPS (AQ-ID)



It was once said, "The more reflective you are, the more effective you are." As I reflect upon this past year as the Chair of the Adult Medicine PRN, I cannot be more proud of all that you have accomplished together. I must give special thanks to our Chair-Elect, Leigh Anne Gravatt, Secretary/Treasurer Andrew Miesner, and past Chair Sarah Anderson, for all of their hard work and assistance throughout the year. This past year we had such an outstanding response to the call to join committees that we added vice-chair roles to each of them. Therefore, I would also like to thank the committee chairs and vice-chairs, Leigh Anne Gravatt, Antoine Jenkins, Ryan Owens, Ryan D'Angelo, Yulia Murray, Kristina Shvets, Andrew Miesner, Beth Resman-Targoff, Sarah Anderson, Andy Woods, Branden Nemecek, Rachel Flurie, Jennifer Twilla, and Jessica Wallace. There are many successful projects that the various committees have worked on, and this would not be possible without the dedication of our members. Thank you!

One of our top priorities of 2016-2017 was to increase our engagement of members within the PRN. With a membership of nearly 1250, it is easy to get lost in the shuffle or to be inactive within the PRN. The addition of new committees has allowed for increased presence of the PRN and engagement of a broader base of members through social media channels and resident journal club presentations. We hope you have found these endeavors to be helpful! This fall, I challenge each of you to sign up for committees when the call is made. There is no better way to stay engaged and become an active member of ACCP than through the committees of our PRN. Whatever your interest/expertise, you are sure to find a committee that you will be able to serve.

2017 AMED PRN Award Winners

The following AMED PRN members have been selected to receive awards from the PRN at the 2017 ACCP Annual Meeting. Come congratulate them during the AMED Business Meeting and Networking Forum on October 9th.

AMED PRN Mentoring Award: Joel Marrs, PharmD, FCCP, FASHP, FNLA, BCPS-AQ Cardiology, BCACP, CLS (University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences)

Clinical Practice Award: Jennifer Twilla, PharmD, BCPS (University of Tennessee Health Science Center)

Practitioner Registration Award: Jennie Jarrett, PharmD, BCPS, MMedEd (University of Illinois at Chicago)

Resident Travel Award: Nichole Szczerbowski, PharmD (University of Tennessee Medical Center)

Student Travel Award: Lauren Moore, PharmD candidate (University of South Carolina College of Pharmacy)

Save the Date...

2017 ACCP Annual Meeting
Sheraton Grand Phoenix, Phoenix, AZ
October 7-10, 2017

- **October 8 @ 4PM (MST)**
AMED PRN Focus Session - *Feeling the Burn of Proton Pump Inhibitor Therapy: When Do Risks Outweigh the Benefits?*
- **October 9 @ 6:30PM (MST)**
AMED PRN Business Meeting and Networking Forum
- **October 9 @ 8:30PM (MST).**
AMED PRN Social Hour at The Park

Upcoming AMED PRN Online Journal Clubs:
-October 18, 2017 -January 17, 2018
-November 15, 2017 -February 21, 2018
-December 13, 2017 -March 28, 2018

Message from the Chair, continued

I want to offer congratulations to our incoming officers, Chair Leigh Anne Gravatt; Chair-Elect Andrew Miesner and Secretary/Treasurer Ryan Owens. I personally challenge each of them with the task of continuing to find new ways to engage you, our members, so that you can be proud of the PRN we are becoming.

On behalf of the Adult Medicine PRN, I would like to offer special Congratulations to two of our PRN members for being amongst the newest Fellows of ACCP, Sarah Anderson and Jason Lancaster. This is a terrific accomplishment and we thank you for all the years of service to the profession and to ACCP. The PRN would also like to offer special congratulations to Diana M. Sobieraj for being selected by ACCP as the recipient of the 2017 New Investigator Award. Diana is well deserving of the award as her research and scholarly pipeline are impeccable!

If you are coming to the Annual Meeting in Phoenix, we would like to invite you to the Adult Medicine PRN Focus Session at the meeting entitled "Feeling the Burn of Proton Pump Inhibitor Therapy: When Do the Risks Outweigh the Benefits?" on Sunday, Oct. 8th from 4:00 PM to 5:30 at the Phoenix Convention Center North Building Street Level, Meeting Room 121. We have Drs. Lindsay Saum, Carolyn Brackett, and Gregory Hughes preparing an engaging presentation for all of you. We hope to see you at the PRN business meeting on Monday, Oct. 9th beginning at 6:30 PM at the Sheraton Grand Phoenix Third Level, Phoenix Ballroom A. We have planned a social event for immediately following the business meeting - we welcome you to head over to The Park Street Food Bar and Beer Garden for some networking and socializing, so please sign up to join us!

Thank all of you for the opportunity you have given me to Chair this amazing PRN! I look forward to continuing to help out in any way possible!

Sincerely,

Kurt

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Recent Accomplishments from our PRN Members

Promotions:

- **Anastasia L. Armbruster:** Associate Professor, St. Louis College of Pharmacy
- **Ayesha M. Khan:** Interim Assistant Dean of Student Affairs, Chicago State University College of Pharmacy
- **Ifeanyi Onor:** Clinical Associate Professor of Pharmacy, Xavier University of Louisiana College of Pharmacy
- **Katie B. Tellor:** Associate Professor, St. Louis College of Pharmacy
- **Abigail M. Yancey:** Professor, St. Louis College of Pharmacy
- **Nancy Yunker:** Associate Professor, VCU School of Pharmacy

Grants:

- **Ayesha M. Khan:** Khan AM. Chicago Schweitzer Fellows For Life Seed Grant; \$2140.00
- **Sarah Petite** and **Julie Murphy:** Petite SE, Murphy JA. The impact of the implementation of a pharmacist-driven COPD management program. ASHP Foundation New Investigator Award. \$20,000

Awards:

- **Sarah L. Anderson:** Finalist; Next-Generation Pharmacist: Health-System Pharmacist award
- **Denise Kelley:** University of Florida New Inpatient Preceptor of the Year Award and Florida Society of Health-System Pharmacists New Practitioner Award
- **Ayesha M. Khan:** Chicago State 2017 P3 Class Teacher of the Year
- **Donny More:** Carolinas HealthCare System Key Engagement Award
- **Mate M. Soric:** Class of 2017 Commencement Hooder

Congratulations to these AMED PRN members who have been recognized by ACCP for their accomplishments!

2017 ACCP Fellows

- **Sarah L. Anderson PharmD, BCPS, BCACP, FCCP**
Associate Professor; University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences; Denver, Colorado
- **Jason W. Lancaster, PharmD, MEd, BCPS, FCCP**
Associate Clinical Professor; Northeastern University; Boston, MA

New ACCP fellows will be introduced at the Annual Meeting during the Awards and Recognition Ceremony on October 8.

2017 ACCP New Investigator Award

- **Diana M. Sobieraj, PharmD**
Assistant Professor of Pharmacy Practice; University of Connecticut School of Pharmacy; Storrs, CT



Dr. Sobieraj will deliver the New Investigator Award Lecture at the ACCP Annual Meeting on October 8.

Other Notable Achievements:

- **Emily J. Christenberry:** 2017 ACCP MeRIT Program Participant
- **Jaime A. Foushee:** Presbyterian College School of Pharmacy 2016-2017 Teacher of the Year
- **Caitlin Gibson:** University of North Texas System College of Pharmacy Pharmacotherapy Faculty of the Year Teaching Award
- **Jennie Jarrett:** Completed the ACCP Research Institute's Focused Investigator Training (FIT) Program
- **Heather Kehr:** Distinguished Service Award
- **Denise Kelley:** Installed as a Florida Society of Health-System Pharmacists Board of Director
- **Ifeanyi Onor:** appointed Fellow of the National Kidney Foundation
- **Angela Pegram:** Distinguished Service Award
- **Beth H. Resman-Targoff:** Delivered an invited talk on Ask the Experts: Inside Musculoskeletal Diseases at the APhA Annual Meeting in San Francisco and Appointed to the Association of Rheumatology Health Professionals Membership & Nominations Committee.
- **Katie B. Tellor, Anastasia L. Armbruster, and Abigail M. Yancey:** ACCP Virtual Symposium, Best Poster Award. Evaluation of Warfarin Requirements in Hospitalized, Obese Patients Admitted with a Therapeutic INR
- **Jennifer Twilla:** Residency program director for the Tennessee Society of Health-System Pharmacy 2017 Residency Program of the Year

Recent Publications from Our PRN Members

- **Sarah Anderson**

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- **Melissa Butler**

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- **Craig Cox**

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- **Jennie Jarrett**

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- **Jason Lancaster**

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- **Christina Miele**

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- **Andrew Miesner**

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- **Diana M. Sobieraj**

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- **Mate Soric**

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- **Jennifer Twilla**

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- **Tramaine Young**

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to listen to our authors bring you additional insights on their articles!



Delafloxacin: A Novel Fluoroquinolone for Acute Bacterial Skin and Skin Structure Infections

Stanley Luc, PharmD and Maegan M. Whitworth, PharmD, BCPS

Approved on June 19, 2017, delafloxacin (Baxdela™) is a fluoroquinolone antibiotic for the treatment of acute bacterial skin and skin structure infections (ABSSSI).¹ This is the first U.S. Food and Drug Administration (FDA)-approved antibacterial since ceftazidime-avibactam (Avycaz®) in 2015. In addition, delafloxacin is the first antibiotic approved for ABSSSI since oritavancin (Orbactiv®) in 2014, and the first with an oral dosage form since tedizolid (Sivextro®) in 2014.² Under the FDA, it was designated as a Qualified Infectious Disease Product (QIDP) thus expediting its review.³ Dosing for delafloxacin in ABSSSI is 300 mg IV twice daily or 450 mg PO twice daily for a total of five to fourteen days.¹ Despite no renal adjustment for the oral tablet, a dose reduction is indicated for the intravenous formulation in patients with eGFR less than 30 mL/min/1.73m². Use in patients with eGFR < 15 mL/min/1.73m² or on hemodialysis is not recommended due to insufficient clinical data in this population and potential accumulation of sulfobutylether-β-cyclodextrin for the IV formulation. Furthermore, delafloxacin possesses the same boxed warnings as other fluoroquinolones including: serious adverse effects (e.g. tendinitis and tendon rupture, peripheral neuropathy, CNS effects) and exacerbation of myasthenia gravis.

When compared to other fluoroquinolones, delafloxacin is perceived to have enhanced antibacterial activity against gram-positive organisms with a few potential improvements in safety. First, it exhibits substantially greater activity against methicillin-resistant *Staphylococcus aureus* (MRSA).⁴ When U.S. MRSA isolates from 2014 were tested *in vitro*, 30% were considered susceptible to levofloxacin, while over 85% were considered susceptible to delafloxacin using the listed breakpoints in its labeling.^{1,4} Its effectiveness also extends to isolates of *S. aureus* that are non-susceptible to levofloxacin in *in vitro* and Phase 3 studies.⁵ *In vitro* and clinical data indicate its spectrum of activity also includes multiple *Streptococcus* species, *E. faecalis*, *E. coli*, *K. pneumoniae*, *E. cloacae*, and *P. aeruginosa*.^{1,4} For these pathogens, delafloxacin appears to have *in vitro* activity comparable to levofloxacin; however, despite its FDA indication in treating ABSSSI with susceptible isolates of these bacteria, less than 15% of the clinically identified isolates in Phase 3 trials were gram-negative pathogens.^{1,4}

Unlike ciprofloxacin and levofloxacin, delafloxacin does not appear to have any clinically significant CYP-mediated drug interaction potential despite weak inhibition of CYP3A4 in *in vitro* studies.^{1,6} However, delafloxacin still possesses metal chelating properties, similar to that of other fluoroquinolones.¹ No clinically meaningful QTc prolongation (defined as ≥ 10 ms) was detected after a single supratherapeutic dose of 900 mg IV in healthy subjects.⁷ Although the fluoroquinolone class is notorious for relatively increasing the risk for *Clostridium difficile*-associated diarrhea (CDAD), no published data exist directly comparing the CDAD risk for delafloxacin versus other fluoroquinolones.

A Phase 2 randomized trial (n = 256) evaluated delafloxacin, linezolid, and vancomycin in ABSSSI with the option to add aztreonam to the comparator drugs for proven or suspected gram-negative infection (treatment duration 5 to 14 days).⁸ Delafloxacin demonstrated higher clinical cure rates (i.e., improvement or resolution of baseline signs and symptoms) than vancomycin (70.4% vs. 54.1%, P=0.031), and this difference was even larger in obese patients (78.8% vs. 48.8%, P=0.009). However, delafloxacin had similar cure rates to linezolid (70.4% vs. 64.9%, P=0.496). For safety, nausea, vomiting, and diarrhea occurred more frequently in the delafloxacin group. Subsequently, two Phase 3 randomized trials (Trial 1: n = 660; Trial 2: n = 850) compared delafloxacin with the combination of vancomycin and aztreonam for treatment of ABSSSI.¹ For both studies, the objective clinical responses (defined as a ≥ 20% decrease in lesion size without any reasons for failure) at 48-72 hours were similar between delafloxacin and comparator groups: Trial 1, 78.2% vs. 80.9%, and Trial 2, 83.7% vs. 80.6%, respectively. Investigator-assessed clinical cure rates were also similar between groups for both studies. Similarly, composite results indicate nausea and diarrhea occurred more frequently in the delafloxacin group. This can possibly be attributed to the administration of an oral formulation of delafloxacin in Trial 2, whereas the comparator group was randomized to receive only IV antibiotic therapy in both trials.

Overall, clinical trials suggest delafloxacin is a viable option in the treatment of ABSSSI as it demonstrates adequate activity against MRSA and no significant safety concerns relative to one of the standards of care, vancomycin.^{1,8} Its oral formulation is also a welcome addition to the currently limited arsenal of oral antibiotics providing MRSA coverage. Nevertheless, the fact that it is a fluoroquinolone may spur some unease in clinicians. Over the years, fluoroquinolones have been associated with numerous safety concerns, and it can be argued that the clinical trials for delafloxacin were not powered to detect significant differences in safety. Therefore, the verdict is not finalized for its safety. Furthermore, sole availability as a brand-only product will likely make affordability an issue. Currently, delafloxacin is being evaluated in Phase 3 trials for community-acquired bacterial pneumonia (CABP) and Phase 2 for complicated urinary tract infection (cUTI).³ Its potential use in pneumonia is particularly of interest since it covers common CABP pathogens and MRSA while having excellent lung penetration.⁹ This essentially consolidates the combination of levofloxacin and vancomycin into one therapeutic option for treating pneumonia, theoretically decreasing the risk of nephrotoxicity with vancomycin and established safety problems with levofloxacin (e.g. QTc prolongation, CDAD risk). At this time, the current place in therapy for delafloxacin (Baxdela™) is not fully determined as it is expected to become commercially available in Fall 2017.¹⁰ Pharmacy clinicians must be ready to evaluate the known and unknown risks and benefits when considering the appropriate utilization of delafloxacin.

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Bevyxxa® (betrixaban): The new factor Xa inhibitor on the market

Jaclyn D. Cole, PharmD, BCPS and Melissa J. Ruble, PharmD, BCPS

Introduction

Venous thromboembolism (VTE), which includes both deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common preventable cause of hospital mortality and morbidity.¹ Thromboprophylaxis in patients at risk for VTE can reduce the incidence by 30-65%. It is estimated that hospitalization for acute medical illnesses such as stroke, heart failure, and pneumonia are associated with an eightfold increased risk of VTE.² Other identifiable risk factors for VTE in hospitalized patients include prolonged immobilization, age greater than 75, cancer, recent surgery, and history of VTE. There is a variety of medications currently approved for the prevention of VTE in hospitalized patients, including vitamin K antagonists (warfarin), low molecular weight heparins (enoxaparin, dalteparin), and unfractionated heparin.³ Select direct oral anticoagulants (apixaban, rivaroxaban, and dabigatran) are used in hospitalized patients for thromboprophylaxis, but are only approved for postoperative hip and/or knee replacement surgeries as opposed to the medically ill population.⁴ With many to choose from, physicians and other healthcare providers must take into consideration patient-specific factors when selecting the best agent for their patients.

Bevyxxa® (betrixaban) is the newest factor Xa inhibitor, indicated for VTE prophylaxis in adult patients hospitalized for an acute medical illness.⁵ It is marketed for patients at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE. This medication was approved June 23, 2017 and is available in both 40 mg and 80 mg capsules. The recommended dosing for betrixaban is an initial single dose of 160 mg, followed by 80 mg by mouth once daily, taken at the same time each day with food. The caveat with this medication is that it is approved for extended prophylaxis and should be continued for 35 to 42 days since risk for VTE remains elevated for at least one month post-discharge.⁶ Betrixaban requires dose adjustments in patients with severe renal impairment and in patients taking medications that are P-glycoprotein (P-gp) inhibitors.

Drug Review

In phase II trials, betrixaban was evaluated for orthopedic and atrial fibrillation (AFib) thromboprophylaxis.⁷ The EXPERT trial evaluated two doses of betrixaban (15 mg or 40 mg PO BID) for 10-14 days compared to Lovenox® (enoxaparin) 30 mg subcutaneously BID for 10-14 days in patients undergoing elective total knee replacement (TKR).⁸ The primary outcome of incidence of DVT was 20% for betrixaban 15 mg (95% CI: 11-31%), 15% for betrixaban 40 mg (95% CI: 8-27%), and 10% for enoxaparin (95% CI: 3-24%). Bleeding rates were not increased with betrixaban 15 mg or 40 mg (0% major and 2.4% non-major bleeds respectively) compared to enoxaparin (2.3% major bleeds, 4.6% non-major bleeds).

The EXPLORE-Xa trial studied three betrixaban doses (40 mg, 60 mg, and 80 mg daily) in comparison to warfarin (INR titrated to goal of 2 to 3) for patients with AFib and at least one risk factor for stroke according to the CHADS₂ scoring system (average score 2.2).⁹ Although all three doses of betrixaban had lower incidence of major or clinically relevant non-major bleeding (0.78%, 3.94%, and 3.94%) compared to warfarin (5.51%), the primary outcome of major or clinically relevant non-major bleeding was only statistically significant with the 40 mg dosing (HR=0.14, p=0.04). Although all three doses suppressed D-dimer and thrombin generation, suppression at a level similar to therapeutic warfarin was only observed with the 80 mg dose.

The Phase III APEX study was a randomized, double-blind, multinational superiority trial that evaluated betrixaban for extended VTE prophylaxis in medically ill patients.³ Hospitalized patients received either betrixaban 160 mg oral loading dose followed by 80 mg daily for 35 to 42 days or enoxaparin 40 mg subcutaneously daily for 10±4 days; a concomitant placebo was provided for each group for the 35 to 42 days of treatment. In patients with severe renal

insufficiency, defined as CrCl between 15 and < 30 ml/min, doses were changed to betrixaban load 80 mg then 40 mg daily or enoxaparin 20 mg daily. It should be noted that the enoxaparin dosing chosen was unusual as the approved prophylactic dose in medical patients with severe renal impairment is 30 mg daily in the United States. Doses were also adjusted for patients receiving concomitant P-gp inhibitors, who received a reduced dose of betrixaban 40 mg daily. Patients with hepatic impairment or those who had both renal insufficiency and concomitant P-gp inhibitors were excluded. The primary efficacy outcome included asymptomatic DVT between days 32 and 47, and/or symptomatic VTE between days 1 and 42. The safety outcome was major bleeding at any point up until 7 days after medication discontinuation.

Two cohorts were used for statistical analysis; patients with an elevated D-dimer (cohort 1) and those with an elevated D-dimer or age $\geq$ 75 years (cohort 2). Baseline characteristics for the 7513 patients were comparable between treatment groups, reporting an average hospital stay of 10 days, 45% male, 93% white, and average age 76 years. Severe renal impairment was reported in 4.6% of the betrixaban group and 4% of the enoxaparin group, and concomitant P-gp inhibitor use was reported in 18% and 17.3% of each treatment group, respectively.

The primary outcome for cohort 1 (n=3870) was 6.9% in the betrixaban group and 8.5% in the enoxaparin group (RR=0.81, 95%CI: 0.65 to 1.00; P=0.054). The primary outcomes for Cohort 2 (n=5735) were 5.6% treatment group compared to 7.1% in the control group (RR=0.80, 95% CI: 0.66 to 0.98, p=0.03), while the overall population (n=6286) showed 5.3% in the treatment group versus 7.0% in the control group (RR=0.76, 95% CI: 0.63 to 0.92, p=0.006). However, the outcomes for cohort 2 and the overall population are considered exploratory since significance was not met in analysis of cohort 1 per the trial design. Major bleeding in the overall population was similar between groups, with occurrence of 0.7% of the betrixaban group and 0.6% of the enoxaparin group (RR=1.19; 95% CI:0.67 to 2.12; P=0.55). The study concluded there was no significant difference in the efficacy outcome between extended-duration betrixaban and a standard regimen of enoxaparin in patients with an elevated D-dimer alone, although exploratory data suggests possible benefit with betrixaban in patients with an elevated D-dimer or patients 75 or older.

Place in therapy

With the increased number of anticoagulants approved for VTE prophylaxis, it is important to appreciate where to utilize betrixaban. As with the other factor Xa inhibitors, betrixaban is not approved for use in patients with prosthetic heart valves. Evidence supports the use of VTE prophylaxis in acutely ill medical patients at risk, but the duration of therapy has not been clearly determined.¹ Several studies have evaluated this idea of extended thromboprophylaxis with agents such as enoxaparin, apixaban, and rivaroxaban.³ These trials were unable to show a statistically significant benefit, but did have an increased risk of bleeding. Betrixaban's use in this setting showed up to a 1.7% absolute reduction in VTE without increased incidence of major bleeding; however, there was significantly more non-major bleeding in this group.³ Previous evidence suggests that although the risk for VTE is highest in the first 9 days of admission, this risk remains elevated for at least one month after discharge in medically ill patients.⁶ The lack of evidence for use of other agents in this setting allows betrixaban to have a unique place in therapy. Currently the Phase III Mariner trial is underway, which will evaluate the extended use of rivaroxaban in acute medically ill patients with VTE risk.¹⁰ If this study is able to show efficacy, betrixaban may have competition for extended use anticoagulation.

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Biosimilars for Beginners

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An emerging area of pharmaceuticals and pharmacy practice involves biological products known as biosimilars and interchangeables. This rapidly developing field of specialty pharmacy is often met with confusion and unfamiliarity from prescribers and pharmacists. Pharmacists should be aware of new biosimilar approvals and be able to provide education to healthcare providers and patients.

Over the past several years, patents on FDA-approved biological originator products, or reference products, have expired and several more will expire in the years to come. This opens the door for pharmaceutical companies to enter the biologic market by creating biosimilars and interchangeables. Biological products have a more complex structure and contain larger molecules, or mixture of molecules, that are difficult to completely identify or confirm compared to conventional drugs. Because there is no guarantee that these biological drugs are chemically identical, as is the case with conventional generic and brand name drugs, the theory of and term biosimilars was born. A “biosimilar” is defined as a biological product that is “highly similar” to an FDA-approved reference product. The biosimilar must not have any clinically meaningful differences in terms of safety and efficacy from the reference product.^{1,2}

Although the first biosimilar was approved in the United States in 2015, these products have been approved for use in Europe since the mid-2000s. In 2009, the Affordable Care Act amended the Public Health Service Act to create an abbreviated licensing process for biosimilars; similar to the Abbreviated New Drug Application (ANDA) process for generic medications. Biosimilars do not go through the traditional Biologic License Application (BLA) process for a biologic. Instead, they are approved through an abbreviated process enacted by the Biologics Price Competition and Innovation Act (BPCI Act).¹⁻³

To seek approval for a biosimilar, a company files a 351(k) application with the FDA. The application must include data from three types of studies: analytical studies, animal studies, and clinical studies. Analytical studies must demonstrate that the product is “highly similar” to the reference product. Animal studies must be completed to assess toxicity and clinical studies must assess pharmacokinetics, pharmacodynamics, safety, purity, and potency of the biosimilar.⁴⁻⁶ All pieces of the application are designed to establish that the biosimilar:

- Has the same mechanism of action (but only to the extent that the mechanism is known for the reference product)
- Has data to support use for at least one of the same indications labeled for the reference product
- Has the same dosage form and strength
- Is manufactured, processed, packed, and held in a facility that meets good manufacturing process standards⁴⁻⁶

Biologic products may also be classified as interchangeable with their reference product. The designation of “interchangeable” allows a pharmacist to substitute the interchangeable product for the reference product without an intervention by the prescriber, where state laws allow for pharmacist product substitution. A biosimilar product is not automatically granted interchangeability when it is approved. It has to meet additional standards set forth by the FDA. In January 2017, the FDA released draft guidance describing processes and expectations for interchangeability. In this document, the FDA states that an interchangeable product must be expected to produce the same clinical result as the reference product. For a product to be interchangeable, the sponsor must prove that there is no impact on efficacy or safety when switching from the reference product to the interchangeable product and back to the reference product. Once a product has met the requirements for interchangeability for at least one indication, the data can be extrapolated to additional uses approved for the reference product.^{6,7}

As of September 2017, there are seven biosimilar products approved by the FDA. Whether a new product is a biosimilar or interchangeable can be found in the Purple Book; a similar reference to the Orange Book used for non-biologic bioequivalent product substitutions. Table 1 displays the seven biosimilars that are approved in the US. None of these products is approved to be interchangeable with their reference products. Interestingly, almost all of these products were approved within the last year. It is important to recognize that approval by the FDA does not mean that a product will be immediately available on the market.

It is also important to note the nomenclature of these products. Biosimilars are named using the core name that reflects the product's chemical structure and pharmacological properties, similar to the generic name of a conventional drug. However, with biosimilars, this core name is accompanied by a suffix of four randomly chosen letters devoid of any meaning. This naming process was established to link a specific product to the manufacturer, to provide product specific pharmacovigilance when assessing for adverse drug reactions, and insuring the correct product is being prescribed and dispensed. Utilizing one of the products in Table 1 as an example, *infliximab* is the core name and *-dyyb* is the suffix that links that product to Celltrion/Pfizer and *-abda* represents the product made by Samsung Bioepis/Merck. Since there are currently no products available that are interchangeable, the FDA has yet to provide guidance for naming interchangeable products.⁶⁻⁹

There are biosimilar applications pending before the FDA for the following originator products. They are projected to be approved by 2018:

- Pegfilgrastim (Neulasta®)
- Insulin glargine (Lantus®)
- Trastuzumab (Herceptin®)
- Rituximab (Rituxan®)

Biosimilar pharmaceuticals are a rapidly developing class of medications. As the FDA plans to approve several more products in 2017, it is imperative that pharmacists are able to recognize and provide education to practitioners and patients on the safety and efficacy of these products and their interchangeability.

Table 1: FDA Approved Biosimilars⁸

Biosimilar	Reference Product	Manufacturer	FDA Approval Date
Zarxio (filgrastim-sndz)	Neupogen®	Sandoz	March 6, 2015
Inflectra (infliximab-dyyb)	Remicade®	Celltrion/Pfizer	April 2016
Renflexis (infliximab-abda)	Remicade®	Samsung Bioepis/Merck	April 2016
Erelzi (etanercept-szzs)	Enbrel®	Sandoz	August 2016
Amjevita (adalimumab-atto)	Humira®	Amgen	September 2016
Cyltezo (adalimumab-adbm)	Humira®	Boehringer Ingelheim	August 2017
Mvasi (bevacizumab-awwb)	Avastin®	Amgen	September 2017

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