DRIVING Rx DRUG COSTS DOWN VIA BIOSIMILARS

NATIONAL COUNCIL OF INSURANCE LEGISLATORS

July 12, 2019

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Biosimilars

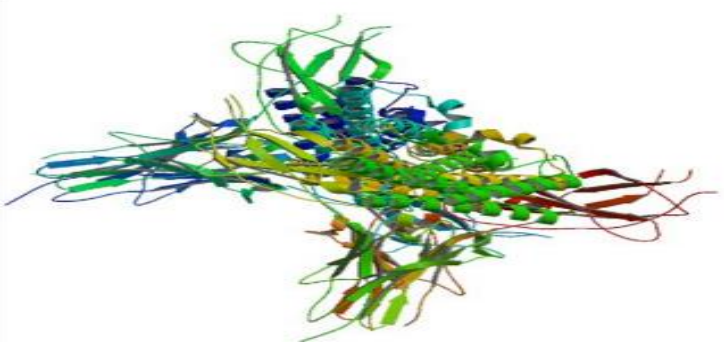
- **Generic drugs** are copies of brand-name drugs, have the same active ingredient, and are the same as those brand name drugs in dosage form, safety, strength, route of administration, quality, performance characteristics and intended use. That means the brand-name and the generic are bioequivalent.

- **Biosimilars** are made from living organisms and are highly similar to the reference product they were compared to. Biosimilars cannot be exactly reproduced due to natural variation but also have no clinically meaningful differences in terms of safety, purity, and potency from the reference product.

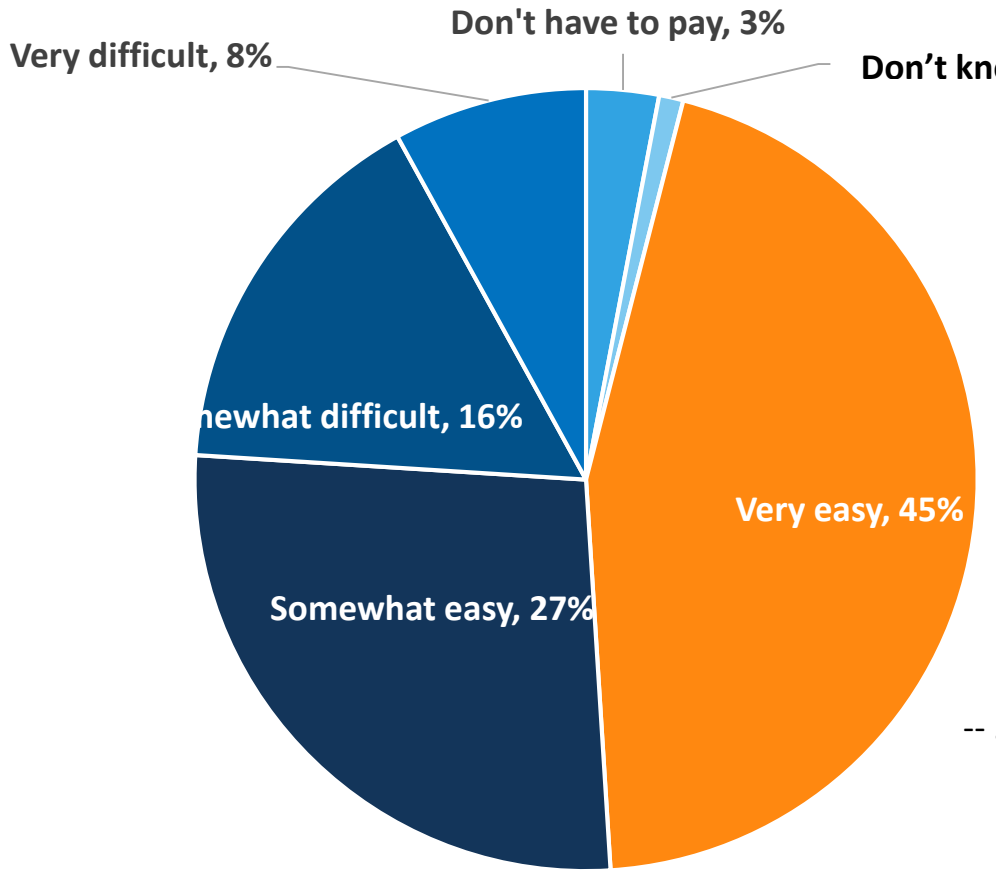
Small Molecule vs. Biologics

Small molecule: Lisinopril
Molecular weight: 441.52

Large molecule: filgrastim
Molecular weight: 18,802.80



What problem are we trying to solve?
1 in 4 people have a difficult time affording their medicine



Prescription drug prices comprise **15.9%** of total health care spending for a family of four, up from **13.2%** in 2001

-- 2015 Milliman Medical Index

Source: Kaiser Family Foundation Health Tracking Poll (conducted Aug 6-11, 2015)

RAND CORPORATION

Perspective

Expert insights on a timely policy issue

Biosimilar Cost Savings in the United States

Initial Experience and Future Potential

Andrew W. Mulcahy, Jakub P. Hlávka, and Spencer R. Case

The Biologics Price Competition and Innovation Act (BPCIA), enacted as part of the 2010 Patient Protection and Affordable Care Act (ACA), authorized the U.S. Food and Drug Administration (FDA) to create a new regulatory approval pathway for biosimilars, which are biologic drugs that are very similar to already approved "reference" biologics in terms of potency, safety, and efficacy, but manufactured by different companies. In the seven years since the ACA, many drug manufac- ers, leading estimates p States, sum biosimilar i surroundin to a reducti from 2017 spending ov

The New York Times

Humira's Best-Selling Drug Formula: Start at a High Price. Go Higher.

By DANNY HAKIM JAN. 6, 2018

Date	% Increase	Months Between Increases
1/18/2017	8.4%	6.9
6/23/2016	7.9%	5.1
1/21/2016	9.9%	4.8
8/28/2015	7.9%	4.9
4/1/2015	9.9%	4.5
11/14/2014	7.9%	4.5

8.6% increase every 5 months
64% increase over 2.6 years

Oct 2017:
"We estimate that biosimilars will lead to a **reduction of $54 billion in direct spending on biologic drugs from 2017 to 2026**…"
(range $24 to $150 billion)

21 Approved Biosimilar Medicines in the U.S. Only 6 Currently Available for Patient Use

Drug Name	Approval Date
Zirabev (bevacizumab-bvzr)	June, 2019
Kanjinti (trastuzumab-anns)	June, 2019
Eticovo (etanercept-ykro)	April, 2019
Trazimera (trastuzumab-qyyp)	March, 2019
Ontruzant (trastuzumab-dttb)	January, 2019
Herzuma (trastuzumab-pkrb)	December, 2018
Truxima (rituximab-abbs)	November, 2018
Udenyca (pegfilgrastim-cbqv)	November, 2018
Hyrimoz (adalimumab-adaz)	October, 2018
Nivestym (filgrastim-aafi)	July, 2018
Fulphila (pegfilgrastim-jmdb)	June, 2018

Drug Name	Approval Date
Retacrit (epoetin alfa-epbx)	May, 2018
Ixifi (infliximab-qbtx)	December, 2017
Ogivri (trastuzumab-dkst)	December, 2017
Mvasi (Bevacizumab-awwb)	September, 2016
Cyltezo (Adalimumab-adbm)	August, 2016
Renflexis (Infliximab-abda)	May, 2017
Amjevita (Adalimumab -atto)	September, 2016
Erelzi (Etanercept-szzs)	August, 2016
Inflectra (Infliximab-dyyb)	April, 2016
Zarxio (Filgrastim-sndz)	March, 2015

Patent Litigation Delaying Biosimilar Competition

Janssen vs. Pfizer (infliximab-dyyb, Inflectra)

Pfizer launched at risk Nov 2016

Abbie vs. Amgen (adalimumab-atto, Amjevita)

Settlement delays U.S. launch until 2023

Abbie vs. Boehringer Ingelheim (adalimumab-adbm, Cyltezo)

U.S. launch likely delayed until 2023+ given Amgen settlement

Amgen vs. Sandoz (etanercept-szzs, Erelzi)

Sandoz expects launch delayed until 2018+

- **Amgen vs. Hospira**(biosimilar epoetin alfa)
- **Amgen vs. Sandoz** (biosimilar pegfilgrastim)
- **Amgen vs. Apotex** (biosimilar pegfilgrastim and filgrastim)
- **Amgen vs. Mylan** (biosimilar pegfilgrastim)

53 EU Authorised* Biosimilars for 15 reference products

Active substance	Reference product	Biosimilar medicines
Adalimumab (8)	Humira®	Amgevita®, Solymbic®, Cytelzo®, Imraldi®, Halimatoz®, Hyrimoz®, Hefiya®, Hulio®
Bevacizumab (1)	Avastin®	Mvasi®
Enoxaparin sodium (2)	Lovenox®	Inhixa®, Thorinane®
Epoetin (5)	Erypo®/Eprex®	Abseamed®, Binocrit®, Epoetin Alfa Hexal®, Retacrit®, Silapo®
Etanercept (2)	Enbrel®	Benepali®, Erelzi®
Filgrastim (7)	Neupogen®	Accofil®, Filgrastim Hexal®, Grastofil®, Nivestim®, Ratiograstim®, Tevagrastim, Zarzio®
Follitropin alfa (2)	Gonal-f®	Bemfola®, Ovaleap®
Infliximab (4)	Remicade®	Flixabi®, Inflectra®, Remsima®, Zessly®
Insulin glargine (3)	Lantus®	Abasaglar®, Lusduna®, Semglee®
Insulin Lispro (1)	Humalog®	Insulin Lispro Sanofi®
Pegfilgrastim (5)	Neulasta®	Fulphila®, Pelgraz®, Pelmeg®, Udenyca®, Ziextenzo®
Rituximab (6)	MabThera®	Blitzima®, Ritemvia®, Rituzena®, Rixathon®, Riximyo®, Truxima®
Somatropin (1)	Genotropin®	Omnitrope®
Teriparatide (2)	Forsteo®	Movymia®, Terrosa®
Trastuzumab (4)	Herceptin®	Ontruzant®, Herzuma®, Kanjinti®, Trazimera®

Source: European Medicines Agency (September 2018) - *positive recommendation from EMA, EC decision might be pending

The Impact Of Biosimilar Competition In Europe

	Price per TD 2016 / Year before Biosimilar entrance
EPO	Total market
Portugal	-66%
Slovakia	-53%
Norway	-51%
HGH	
Finland	-52%
Poland	-42%
Norway	-37%
Fertility	
Denmark	-24%
Spain	-14%
Sweden	-10%

	Price per TD 2016 / Year before Biosimilar entrance
G-CSF	Total market
Romania	-62%
Slovakia	-61%
Slovenia	-57%
Anti-TNF	
Sweden	-39%
Norway	-32%
Denmark	-24%
Insulins	
Finland	-18%
France	-5%
Ireland	-3%

	Volume TD 2016/ Year before Biosimilar entrance
Anti-TNF	
Bulgaria	190%
Slovakia	93%
Sweden	74%
Portugal	63%
Czech	59%
EPO	
Poland	237%
Greece	196%
Italy	39%
Czech	36%
Bulgaria	36%

The entrance of biosimilars increases price competition

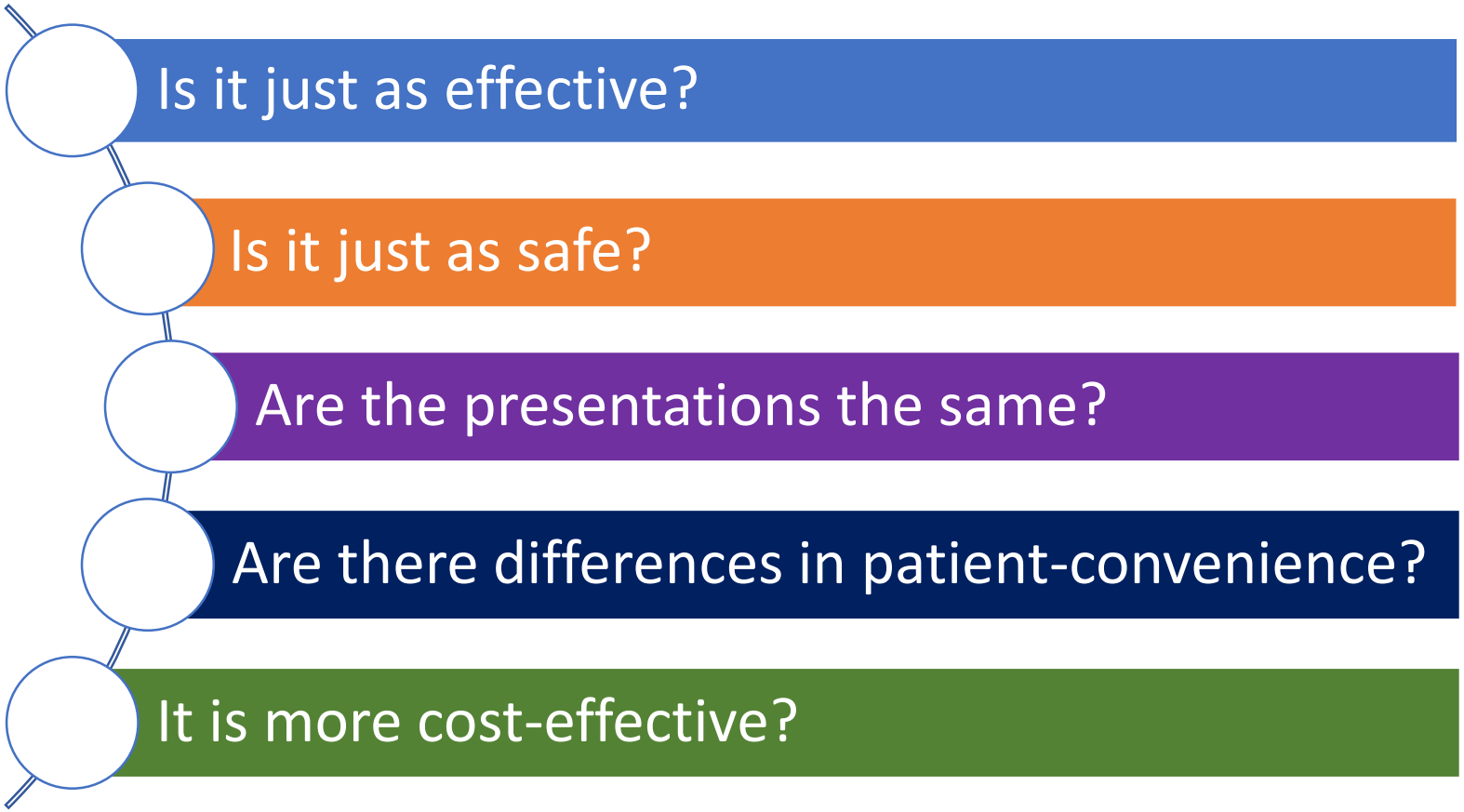
Competition drives down price

Lower prices increase patient access

[The Impact of Biosimilar Competition in Europe - European Commission]

https://ec.europa.eu/docsroom/documents/23102/attachments/1/translations/en/.../pdf
May 8, 2017

What do clinicians & patients want to know about biosimilars?



Zarxio: Febrile Neutropenia Rates

- Compared Neupogen patients in 1st quarter 2015 vs Zarxio patients in 1st quarter 2016.
- 860 Neupogen patients, 701 Zarxio patients
- Overall FN rate (all cycles) per patient was decreased with Zarxio vs Neupogen (4.2% vs 8.3%).
- The FN rate with Zarxio was numerically lower than Neupogen for cycle 1 of chemotherapy (5.7% vs 9.5%).
- Statistically, both were non-inferior in regards to FN rate.

Data from Kaiser Permanente Program

Zarxio Pull Through!

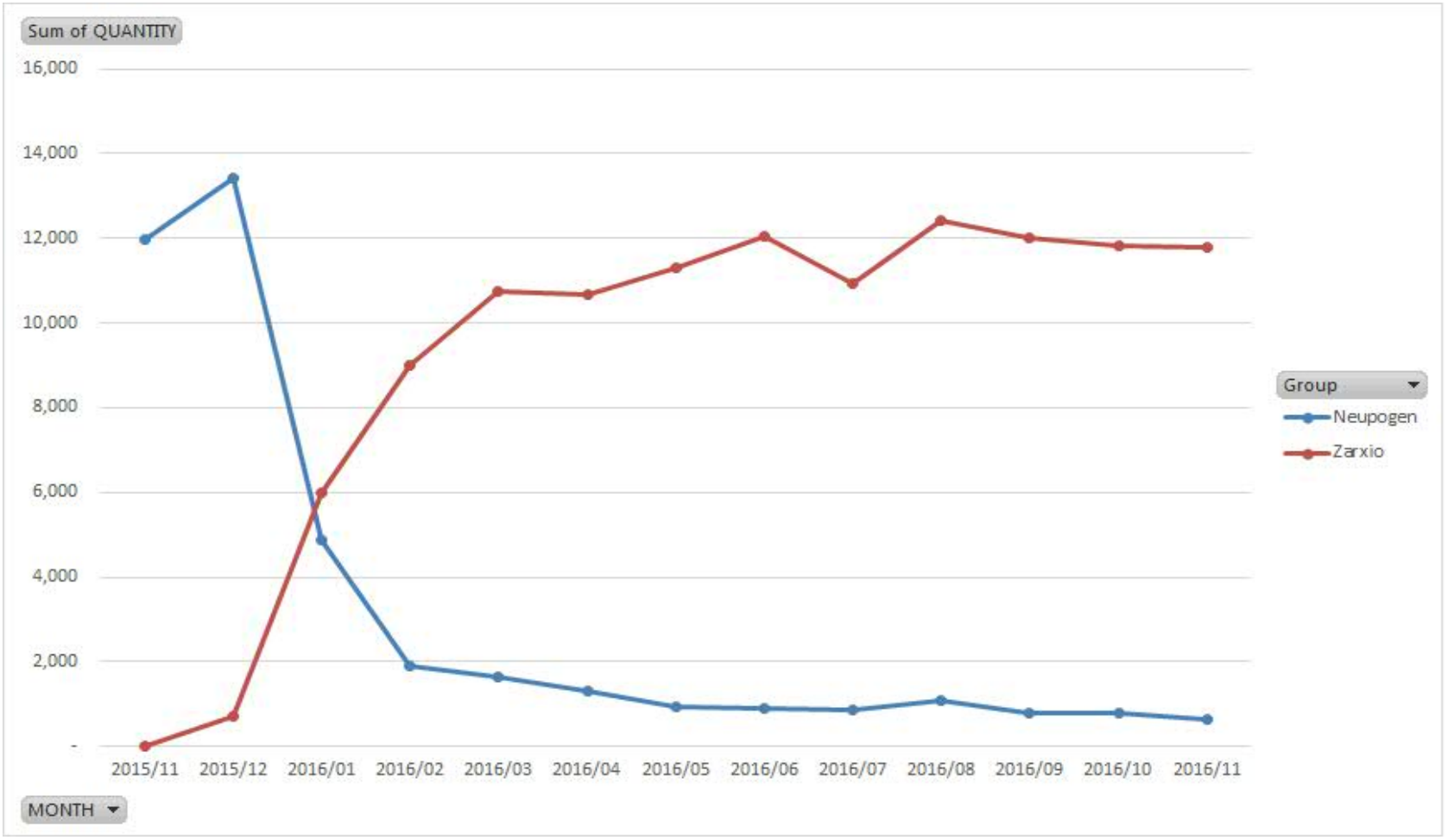


Chart data from KP Program

Biosimilars: Remicade to Inflectra
Kaiser Permanente 2017 Market Share 80% vs. National Market Share 2.3%

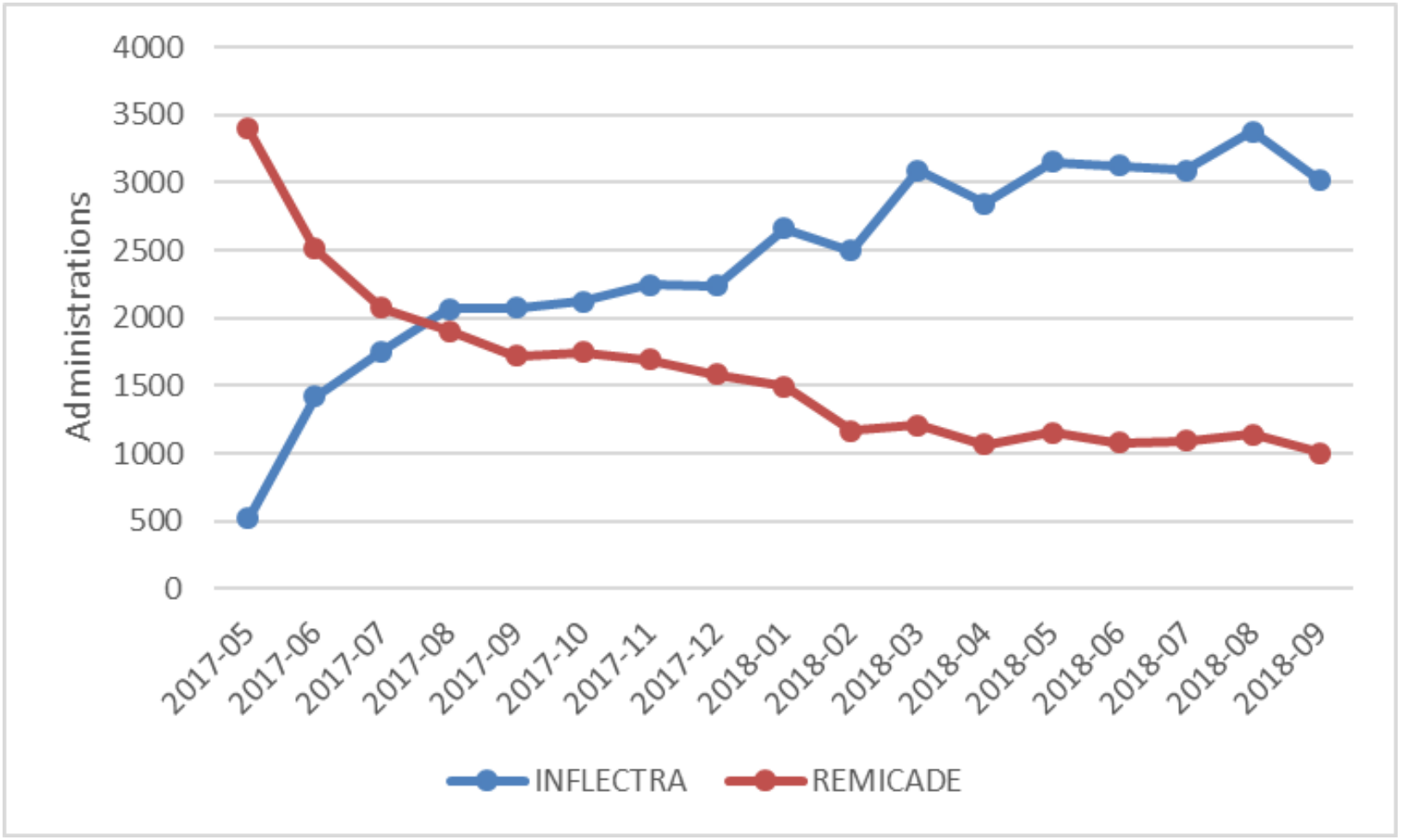


Chart data from KP Program

Key Discussion Points

- The US Biosimilars Market is at a “critical juncture” as uptake has failed to materialize compared to Europe due to patent litigation amongst pharmaceutical companies, pay for delay, restricted access by PBMs/insurers, lack of physician and patient education regarding availability and efficacy
- This is despite the fact that there are substantial financial savings to be gained through the use of biosimilars and improved access for patients to these medications
- Biosimilar adoption provides a solution to the drug pricing and spending debate like generics did for brand name drugs
- Additional policies should be considered to help uptake and viability of the biosimilars market in the U.S.