Biosimilar Use in the United States: An Analysis of Filgrastim and Infliximab

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Background

- The Biologics Price Competition and Innovation Act of 2009 created an approval pathway for biosimilars in the U.S.
- To date, 21 biosimilars referencing 9 biologics have been approved in the U.S.[1]
- As more biosimilars are approved, accurate identification of biologics and biosimilars and understanding of use patterns and patient characteristics are fundamental needs for conducting future post-marketing studies.

Objective

To identify users of filgrastim and infliximab, the first products with biosimilars approved in the U.S, and describe their use patterns and patient characteristics

Table 1. Biologic products included in the analysis

Product family	Non-proprietary name	Proprietary name	U.S. Approval
filgrastim	filgrastim (reference)	Neupogen	February 20, 1991
	tbo-filgrastim*	Granix	August 29, 2012
	filgrastim-sndz	Zarxio	March 6, 2015
infliximab	infliximab (reference)	Remicade	August 24, 1998
	infliximab-dyyb	Inflectra	April 5, 2016
	infliximab-abda	Renflexis	April 21, 2017

*Tbo-filgrastim was approved prior to the abbreviated biosimilars pathway established in the BPCIA

Methods

Data Source: Sentinel Distributed Database, 17 Data Partners from January 2015-August 2018

Exposures: Reference biologic and biosimilar filgrastim and infliximab products (**Table 1**)

- Products were identified via administrations in healthcare encounters [Healthcare Common Procedure Coding System (HCPCS) codes] and outpatient pharmacy dispensings [National Drug Codes (NDCs)]

Analyses: We characterized use of filgrastim and infliximab in three ways:

1. We calculated the proportion of use by code type and assessed uptake over time
   - We included all drug use episodes, defined as unique administrations or dispensings, where the patient had medical and drug coverage
   - To evaluate trends over time, we report the overall number of filgrastim and infliximab episodes, and the proportion of each unique product as a proportion of all products with the same clinically active component, by month and year
2. We described baseline patient characteristics and treatment indications for users of each reference biologic and biosimilars
   - Patients were required to be continuously enrolled in a health plan with medical and drug coverage for ≥183 days prior to their first qualifying code (index date), and each patient's first index date was included. Patients could be included in >1 exposure cohort if they used multiple products of interest during the study period.
3. Among patients with >1 exposure episode, we characterized the gap, in days, between each exposure episode, and report the median and interquartile range (IQR)

Results

Product Coding and Uptake

- Use was identified primarily via HCPCS codes (filgrastim: 86.4%-97.7%; infliximab: 87.8%-100%)
- Dispensings (NDCs) identified 2.3% (tbo-filgrastim) to 13.6% (filgrastim-sndz) of filgrastim episodes and 0% (infliximab-abda) to 12.2% (infliximab-dyyb) of infliximab episodes
- Among the subset of Data Partners that include NDCs in the Sentinel Common Data Model Procedure Table, 27% to 40% of filgrastim episodes and <1% to 46% of infliximab episodes had an NDC from a clinical encounter
  - >98% were in combination with a HCPCS code
- Filgrastim reference product use declined from 89.4% in January 2015 to 30.3% in June 2018, with corresponding increases in filgrastim-sndz (0% to 49.3%) and tbo-filgrastim (10.6% to 20.4%) (**Figure 1a**)
- Uptake of all infliximab biosimilars reached 9.7% in June 2018 (**Figure 1b**)

Figure 1a. Number and proportion of filgrastim episodes over time

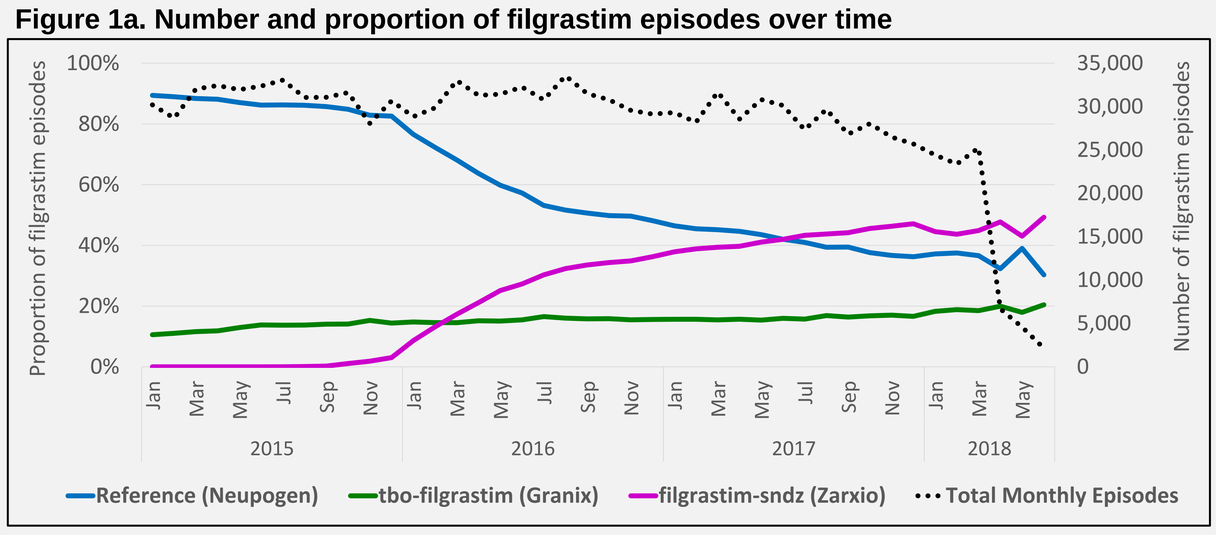

Figure 1b. Number and proportion of infliximab episodes over time

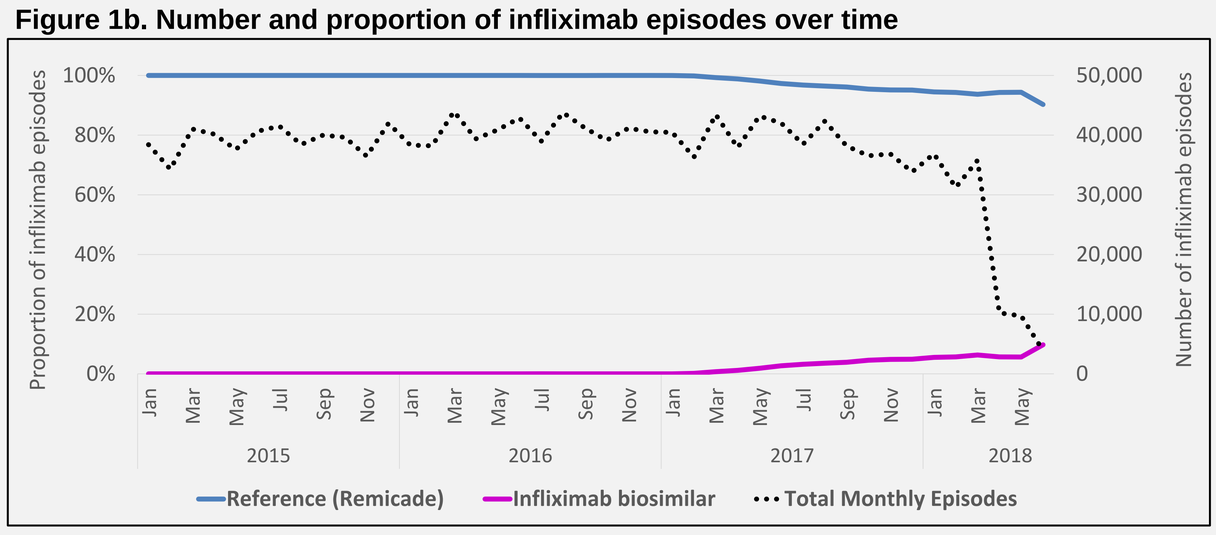

Table 2. Patient characteristics for filgrastim users

	Reference Product (Neupogen)	Tbo-filgrastim (Granix)	Filgrastim-sndz (Zarxio)
N	94,846	27,143	38,264
Age, years (mean, SD)	66.3 (12.6)	67.7 (11.0)	66.6 (11.3)
Female sex (%)	57.2	56.8	59.5
Race (%)			
White	64.8	68.5	68.2
Black or African American	8.5	8.3	7.8
Other[a]	2.9	2.1	5.4
Unknown	23.8	21.1	18.6
Combined comorbidity score (mean, SD)	6.2 (3.6)	6.8 (3.7)	6.4 (3.6)
Evidence of Indication (%)			
Bone marrow transplantation	<0.1	0.1	0.1
Malignancy/myelosuppressive chemo	60.2	62.6	55.9
AML receiving chemo	0.2	0.2	0.1
Bone marrow harvest	<0.1	<0.1	<0.1
Neutropenia	10.1	10.0	8.8
No labeled indication observed	29.4	27.1	35.1

Table 3. Patient characteristics for infliximab users

	Reference Product (Remicade)	Infliximab-dyyb (Inflectra)	Infliximab-abda (Renflexis)	Infliximab biosimilar
N	125,412	1,034	49	4,855
Age, years (mean, SD)	57.1 (14.7)	52.1 (17.7)	54.2 (20.8)	64.5 (13.6)
Female sex (%)	62.6	57.6	51.0	64.7
Race (%)				
White	56.8	59.3	77.6	78.2
Black or African American	5.4	3.5	2.0	6.3
Other[a]	1.2	3.7	0.0	2.7
Unknown	36.6	33.6	20.4	12.7
Combined comorbidity score (mean, SD)	1.8	1.7	1.8	2.1
Evidence of Indication (%)				
GI[b]	37.9	47.6	40.8	26.7
Non-GI[c]	55.2	44.3	42.9	67.1
Both GI and non-GI	4.1	3.6	6.1	3.4
No labeled indication observed	2.9	4.5	10.2	2.8

[a] Other includes: American Indian/Alaska Native, Asian, Native Hawaiian/Pacific Islander
[b] GI: Ulcerative colitis, Crohn's disease
[c] non-GI: Rheumatoid arthritis, Ankylosing spondylitis, Psoriatic arthritis, Psoriasis
Infliximab-dyyb: Defined using infliximab-dyyb NDCs and HCPCS (Q5103)
Infliximab-abda : Defined using infliximab-abda NDCs and HCPCS (Q5104)
Infliximab biosimilar: Defined using the infliximab biosimilar HCPCS code (Q5102)

Patient Characteristics

- Users of filgrastim products were similar in terms of age, sex, and race (**Table 2**)
- Most filgrastim users had evidence of receiving chemotherapy for a nonmyeloid malignancy, although the proportion with this indication was lower among filgrastim-sndz users than among users of filgrastim reference product or tbo-filgrastim
- Users of an infliximab biosimilar were older and a higher proportion were of white race compared to users of infliximab reference product (**Table 3**)
- A higher proportion of infliximab reference product users had evidence of a non-GI indication compared to users of infliximab-dyyb and infliximab-abda, although not for users of an undetermined infliximab biosimilar

Patterns of Use

- Among those with >1 filgrastim episode, the median gap ranged from 1-3 (IQR: 0-20) days across the reference biologic and biosimilars
- Among those with >1 infliximab episode, the median gap ranged from 47-50 (IQR: 38-55) days across the reference biologic and biosimilars

Conclusions

- Use of biosimilar filgrastim has increased in the U.S., but uptake of infliximab biosimilars remains low
- Consistent with their use in a clinical setting, use of filgrastim and infliximab was identified primarily via HCPCS codes although a substantial proportion of use was identified via NDC-based dispensings, indicating both code types should be used to identify complete exposure in future studies of these products
- Patients receiving filgrastim products were largely similar, but differences in age, sex, and indication were observed across infliximab product users, suggesting the importance of confounding control in future inferential studies
- Observed gaps between episodes represent patient use patterns and can inform the creation of exposure episodes in drug safety studies of biosimilars

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