Uptake and Usage Patterns of Biosimilar Infliximab in the Medicare Population

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INTRODUCTION

Biological products are high-cost, complex therapeutics used to treat severe and chronic conditions. The Biologics Price Competition and Innovation Act created an abbreviated approval pathway for US biosimilar and interchangeable biological products in 2010. This abbreviated approval pathway allows for extrapolation of the conclusion of biosimilarity across clinical indications based on the totality of evidence from a data package that may include data for only one clinical indication, with sufficient scientific justification. As of December 9, 2019, twenty-six biosimilars were approved by the US Food and Drug Administration (FDA), including four biosimilars for infliximab.

Information on the uptake of biosimilars over time and the demographics of users are important for measuring the success of the biosimilar approval pathway and for identifying potential areas that warrant further research or education. Investigating prescribing patterns such as prescriber specialty and indication is of particular interest for the infliximab biosimilar because several approved gastrointestinal indications were not directly examined via clinical study in the original application, but rather were extrapolated from the conclusion of biosimilarity through key clinical studies exploring rheumatoid arthritis outcomes.^{1, 2}

METHODS

Our primary analysis compared usage of infliximab-dyyb (Inflectra, approved April 2016) to the reference infliximab (Remicade) in the Medicare fee-for-service (FFS) population from July 1, 2016, to December 31, 2018. We examined infliximab product user demographics, uptake, and usage patterns. All beneficiaries who received an infliximab administration during the study period and were enrolled in Medicare FFS for

6 months prior (to allow for evaluation of past infliximab usage) were included in the beneficiary-level analysis. Cohort entrance was defined by the first eligible infliximab administration. All beneficiary-level characteristics are reported as counts and percentages, with accompanying standardized mean differences (SMD)³ and *p* values, for ease of identifying differences across cohorts.

RESULTS

The demographics of beneficiaries using the biosimilar infliximab-dyyb were broadly similar to those using the reference product (Table 1), with some differences in geographic distribution (SMD > 0.1, *p* < 0.001 for all region categories). Overall uptake of the infliximab biosimilar gradually increased over time, but as of December 2018, infliximab-dyyb still only accounted for < 10% of the monthly administrations of infliximab products.

There were some notable differences in prescribing and usage patterns between the biosimilar and reference products overall. Gastrointestinal indications (ulcerative colitis and Crohn's disease) accounted for a smaller proportion of administrations of the biosimilar as compared with the reference product (22.5% versus 25.9%, respectively, SMD 0.08, *p* < 0.001). Additionally, gastroenterologists prescribed a smaller proportion of administrations of the biosimilar as compared with the reference product (14.0% versus 17.7%, respectively, SMD 0.10, *p* < 0.001), while oncologists prescribed a larger proportion (10.5% versus 5.5%, respectively, SMD > 0.10, *p* < 0.001).

Of the approximately 70% of beneficiaries who used at least one type of infliximab product in the 6 months prior to index date, the vast majority used only one unique type of infliximab product, with < 1% using two or three unique types of infliximab products. Both cohorts were more likely to have prior usage of the reference product than of the biosimilar, which indicates that some beneficiaries are switching from the reference product to the biosimilar.

The dose distributions of infliximab-dyyb and the reference infliximab were similar across indications (Fig. 1). For Crohn's disease, the label for each product specifies that increasing the dose to 10 mg/kg may benefit patients who have lost their response.⁴ The biosimilar and

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Table 1 Study Population Demographics and Characteristics of Infliximab Usage for Beneficiaries Meeting Study Qualifications From July 2016 Through December 2018

Demographic variables ^a	Demographic counts (% of eligible population)				Standard mean differences	<i>p</i> value
	Infliximab (Remicade)		Infliximab-dyyb (Inflectra)		Infl vs. Remi	Infl vs. Remi
Eligible population	74,472		6799			
Age summary						
Mean	67.67		68.67		0.09	-
SD	11.64		11.38		-	-
Median	69.00		70		-	-
IQR	(65, 75)		(65, 75)		-	-
Gender						
Male	25,000	33.57%	2275	33.46%	0.00	0.856
Female	49,472	66.43%	4524	66.54%	0.00	0.856
Regions						
Northeast	13,333	17.90%	707	10.40%	0.22	< 0.001
Midwest	18,440	24.76%	2101	30.90%	0.14	< 0.001
West	14,662	19.69%	1815	26.70%	0.17	< 0.001
South or other ^b	28,037	37.65%	2176	32.00%	0.12	< 0.001
Indication ^c						
Ankylosing spondylitis	3047	4.09%	265	3.90%	0.01	0.439
Crohn's disease	12,980	17.43%	1039	15.28%	0.06	< 0.001
Plaque psoriasis	998	1.34%	101	1.49%	0.01	0.320
Psoriatic arthritis	8768	11.77%	858	12.62%	0.03	0.039
Rheumatoid arthritis	38,907	52.24%	3741	55.02%	0.06	< 0.001
Ulcerative colitis	6305	8.47%	491	7.22%	0.05	< 0.001
Combined GI indications	19,285	25.90%	1530	22.50%	0.08	< 0.001
No labeled indication	3467	4.66%	304	4.47%	0.01	0.490
Prescribing clinician specialty						
Rheumatology	44,569	59.85%	3954	58.16%	0.03	0.007
Gastroenterology	13,173	17.69%	955	14.05%	0.10	< 0.001
Oncology ^d	4125	5.54%	716	10.53%	0.18	< 0.001
General ^e	9273	12.45%	923	13.58%	0.03	0.007
Dermatology	497	0.67%	38	0.56%	0.01	0.290
Other specialty ^f	2753	3.70%	196	2.88%	0.05	< 0.001
Missing specialty	82	0.11%	17	0.25%	0.03	0.002
Number of unique prior infliximab product(s) used ^g						
0	21,326	28.64%	1877	27.61%	0.02	0.072
1	53,010	71.18%	4700	69.13%	0.04	< 0.001
2	109	0.15%	157	2.31%	0.20	< 0.001
3	27	0.04%	65	0.96%	0.13	< 0.001
Type of prior infliximab product(s) used ^h						
Infliximab (Remicade)	52,983	71.14%	4708	69.25%	0.04	< 0.001
Infliximab-dyyb (Inflectra)	189	0.25%	300	4.41%	0.28	< 0.001
Infliximab-abda (Renflexis)	137	0.18%	201	2.96%	0.22	< 0.001

^aMedicare includes patients over 65 and patients under 65 with disabilities. There were no notable differences in race (SMDs < 0.05)

^bSouth and other region categories were combined due to small cell sizes; "other region" accounts for < 1% of the combined category within each cohort

^cFor PB claims, the line diagnosis corresponding to the line item of the infliximab administration was used; for OP claims, the indication was defined by the earliest diagnosis position on the claim with a code that corresponded to one of the indication definitions

^dIncludes hematology oncology, medical oncology, radiation oncology, and gynecological oncology specialties

^eIncludes general practice, family practice, internal medicine, pediatric medicine, geriatric medicine, nurse practitioner, and physician assistant

^fDefined as all specialties not included under rheumatology, gastroenterology, oncology, dermatology, or general specialty

^gCount of unique product types used in the 6 months prior to index date (includes Remicade, Inflectra, and Renflexis)

^hAll unique infliximab product types used in the 6 months prior to index date are included. Beneficiaries may appear in more than one category

reference infliximab had similar dose distributions for Crohn's disease, suggesting the biosimilar has not required more dose escalation than the reference product.

DISCUSSION

The overall uptake of biosimilar infliximab has been much slower than that of the biosimilar filgrastim, the first biosimilar product to enter the US market.⁵ These findings demonstrate use of biosimilar infliximab for

extrapolated gastrointestinal indications; however, the proportion of biosimilar usage for gastrointestinal indications was somewhat lower, and a smaller proportion of the biosimilar product was prescribed by gastroenterologists as compared with the reference product. There may still be some reservations among certain patients or providers regarding usage of the product for indications extrapolated from the overall conclusion of biosimilarity. This study did not explore prescriber rationale for product choice. Additional research, education, and

Figure 1 Infliximab dose distribution: counts of administrations from July 2016 through December 2018. Administrations with a dose > 1200 mg accounted for <1% of administrations of either product and are excluded from this figure.

experience should further encourage acceptance of biosimilars and improve access to important biological therapeutics.

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