

Factors Associated with Biosimilar Exclusions and Step Therapy Restrictions among U.S. Commercial Health Plans

Journal: BioDrugs

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ESM 1. Treatment duration estimates and WAC price update dates for biosimilar-indication pairs identified in the SPEC Database

Reference brand name	Biosimilar brand name	Biosimilar generic name	WAC price date in Redbook	Indication	Duration	Source
Avastin	Mvasi	bevacizumab-awwb	08/18/2021	Cervical cancer - Persistent/Recurrent/Metastatic	6 months	Assumption
Avastin	Mvasi	bevacizumab-awwb	08/18/2021	Colorectal cancer - Metastatic	6 months	Assumption
Avastin	Mvasi	bevacizumab-awwb	08/18/2021	Glioblastoma	6 months	Assumption
Avastin	Mvasi	bevacizumab-awwb	08/18/2021	Non-small cell lung cancer - Nonsquamous	6 months	Assumption
Avastin	Mvasi	bevacizumab-awwb	08/18/2021	Renal cell carcinoma - Metastatic	6 months	Assumption
Avastin	Zirabev	bevacizumab-bvzr	12/31/2019	Cervical cancer - Persistent/Recurrent/Metastatic	6 months	Assumption
Avastin	Zirabev	bevacizumab-bvzr	12/31/2019	Colorectal cancer - Metastatic	6 months	Assumption
Avastin	Zirabev	bevacizumab-bvzr	12/31/2019	Glioblastoma	6 months	Assumption
Avastin	Zirabev	bevacizumab-bvzr	12/31/2019	Non-small cell lung cancer - Nonsquamous	6 months	Assumption
Avastin	Zirabev	bevacizumab-bvzr	12/31/2019	Renal cell carcinoma - Metastatic	6 months	Assumption
Herceptin	Herzuma	trastuzumab-pkrb	03/16/2020	Breast cancer - Adjuvant treatment	12 months	Earl et al., 2019
Herceptin	Herzuma	trastuzumab-pkrb	03/16/2020	Breast cancer - Metastatic	6 months	Assumption
Herceptin	Herzuma	trastuzumab-pkrb	03/16/2020	Gastric cancer - Metastatic	6 months	Assumption
Herceptin	Kanjinti	trastuzumab-anns	08/18/2021	Breast cancer - Adjuvant treatment	12 months	Earl et al., 2019
Herceptin	Kanjinti	trastuzumab-anns	08/18/2021	Breast cancer - Metastatic	6 months	Assumption
Herceptin	Kanjinti	trastuzumab-anns	08/18/2021	Gastric cancer - Metastatic	6 months	Assumption
Herceptin	Ogivri	trastuzumab-dkst	11/29/2019	Breast cancer - Adjuvant treatment	12 months	Earl et al., 2019
Herceptin	Ogivri	trastuzumab-dkst	11/29/2019	Breast cancer - Metastatic	6 months	Assumption
Herceptin	Ogivri	trastuzumab-dkst	11/29/2019	Gastric cancer - Metastatic	6 months	Assumption
Herceptin	Ontruzant	trastuzumab-dttb	04/15/2020	Breast cancer - Adjuvant treatment	12 months	Earl et al., 2019
Herceptin	Ontruzant	trastuzumab-dttb	04/15/2020	Breast cancer - Metastatic	6 months	Assumption
Herceptin	Ontruzant	trastuzumab-dttb	04/15/2020	Gastric cancer - Metastatic	6 months	Assumption
Herceptin	Trazimera	trastuzumab-qyyp	02/18/2020	Breast cancer - Adjuvant treatment	12 months	Earl et al., 2019
Herceptin	Trazimera	trastuzumab-qyyp	02/18/2020	Breast cancer - Metastatic	6 months	Assumption
Herceptin	Trazimera	trastuzumab-qyyp	02/18/2020	Gastric cancer - Metastatic	6 months	Assumption
Neulasta	Fulphila	pegfilgrastim-jmdb	07/09/2018	Neutropenia - Myelosuppressive chemotherapy	6 months	Assumption
Neulasta	Udenyca	pegfilgrastim-cbqv	01/03/2019	Neutropenia - Myelosuppressive chemotherapy	6 months	Assumption
Neulasta	Ziextenzo	pegfilgrastim-bmez	11/07/2019	Neutropenia - Myelosuppressive chemotherapy	6 months	Assumption
Neupogen	Nivestym	filgrastim-aafi	09/05/2018	Neutropenia - Acute myeloid leukemia	28 days	Heil et al., 1997
Neupogen	Nivestym	filgrastim-aafi	09/05/2018	Neutropenia - Bone marrow transplantation	30 days	Othman et al., 2018
Neupogen	Nivestym	filgrastim-aafi	09/05/2018	Neutropenia - Chronic	5 months	Dale et al., 1993
Neupogen	Nivestym	filgrastim-aafi	09/05/2018	Neutropenia - Myelosuppressive chemotherapy	14 days	Waller et al., 2010
Neupogen	Nivestym	filgrastim-aafi	09/05/2018	Peripheral blood progenitor cell collection and therapy	7 days	FDA Label
Neupogen	Zarxio	filgrastim-sndz	09/03/2015	Neutropenia - Acute myeloid leukemia	28 days	Heil et al., 1997
Neupogen	Zarxio	filgrastim-sndz	09/03/2015	Neutropenia - Bone marrow transplantation	30 days	Othman et al., 2018
Neupogen	Zarxio	filgrastim-sndz	09/03/2015	Neutropenia - Chronic	5 months	Dale et al., 1993

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Neupogen	Zarxio	filgrastim-sndz	09/03/2015	Neutropenia - Myelosuppressive chemotherapy	14 days	Waller et al., 2010
Neupogen	Zarxio	filgrastim-sndz	09/03/2015	Peripheral blood progenitor cell collection and therapy	7 days	FDA Label
Procrit/Epogen	Retacrit	epoetin alfa-epbx	05/22/2018	Anemia - Chemotherapy	6 months	Assumption
Procrit/Epogen	Retacrit	epoetin alfa-epbx	05/22/2018	Anemia - Chronic kidney disease	12 weeks	Provenzano et al., 2004
Procrit/Epogen	Retacrit	epoetin alfa-epbx	05/22/2018	Anemia - HIV	12 weeks	Volberding et al., 2004
Procrit/Epogen	Retacrit	epoetin alfa-epbx	05/22/2018	Reduction of blood cell transfusions	15 days	Migeotte et al., 2021
Remicade	Avsola	infliximab-axxq	05/26/2020	Ankylosing spondylitis	12 weeks	Webers et al., 2020
Remicade	Avsola	infliximab-axxq	05/26/2020	Crohn's disease	12 weeks	Lepp et al., 2020
Remicade	Avsola	infliximab-axxq	05/26/2020	Crohn's disease - Pediatric	34 weeks	Xu et al., 2021
Remicade	Avsola	infliximab-axxq	05/26/2020	Psoriasis	46 weeks	Kleyn and Griffiths, 2006
Remicade	Avsola	infliximab-axxq	05/26/2020	Psoriatic arthritis	1 year	Papoutsaki et al., 2013
Remicade	Avsola	infliximab-axxq	05/26/2020	Rheumatoid arthritis	1 year	Hanrahan and Lee, 2021
Remicade	Avsola	infliximab-axxq	05/26/2020	Ulcerative colitis	46 weeks	Wilhelm et al., 2008
Remicade	Avsola	infliximab-axxq	05/26/2020	Ulcerative colitis - Pediatric	46 weeks	Bradley and Oliva-Hemker, 2012
Remicade	Inflectra	infliximab-dyyb	10/17/2016	Ankylosing spondylitis	12 weeks	Webers et al., 2020
Remicade	Inflectra	infliximab-dyyb	10/17/2016	Crohn's disease	12 weeks	Lepp et al., 2020
Remicade	Inflectra	infliximab-dyyb	10/17/2016	Crohn's disease - Pediatric	34 weeks	Xu et al., 2021
Remicade	Inflectra	infliximab-dyyb	10/17/2016	Psoriasis	46 weeks	Kleyn and Griffiths, 2006
Remicade	Inflectra	infliximab-dyyb	10/17/2016	Psoriatic arthritis	1 year	Papoutsaki et al., 2013
Remicade	Inflectra	infliximab-dyyb	10/17/2016	Rheumatoid arthritis	1 year	Hanrahan and Lee, 2021
Remicade	Inflectra	infliximab-dyyb	10/17/2016	Ulcerative colitis	46 weeks	Wilhelm et al., 2008
Remicade	Inflectra	infliximab-dyyb	10/17/2016	Ulcerative colitis - Pediatric	46 weeks	Bradley and Oliva-Hemker, 2012
Remicade	Renflexis	infliximab-abda	07/25/2017	Ankylosing spondylitis	12 weeks	Webers et al., 2020
Remicade	Renflexis	infliximab-abda	07/25/2017	Crohn's disease	12 weeks	Lepp et al., 2020
Remicade	Renflexis	infliximab-abda	07/25/2017	Crohn's disease - Pediatric	34 weeks	Xu et al., 2021
Remicade	Renflexis	infliximab-abda	07/25/2017	Psoriasis	46 weeks	Kleyn and Griffiths, 2006

Reference brand name	Biosimilar brand name	Biosimilar generic name	WAC price date in Redbook	Indication	Duration	Source
Remicade	Renflexis	infliximab-abda	07/25/2017	Psoriatic arthritis	> 1 year	Papoutsaki et al., 2013
Remicade	Renflexis	infliximab-abda	07/25/2017	Rheumatoid arthritis	> 1 year	Hanrahan and Lee, 2021
Remicade	Renflexis	infliximab-abda	07/25/2017	Ulcerative colitis	46 weeks	Wilhelm et al., 2008
Remicade	Renflexis	infliximab-abda	07/25/2017	Ulcerative colitis - Pediatric	46 weeks	Bradley and Oliva-Hemker, 2012
Rituxan	Riabni	rituximab-arrx	01/01/2021	Chronic lymphocytic leukemia	By # of doses	Label
Rituxan	Riabni	rituximab-arrx	01/01/2021	Granulomatosis with Polyangiitis & Microscopic Polyangiitis	By # of doses	Label
Rituxan	Riabni	rituximab-arrx	01/01/2021	Non-Hodgkin's lymphoma	By # of doses	Label
Rituxan	Ruxience	rituximab-pvvr	01/23/2020	Chronic lymphocytic leukemia	By # of doses	Label
Rituxan	Ruxience	rituximab-pvvr	01/23/2020	Granulomatosis with Polyangiitis & Microscopic Polyangiitis	By # of doses	Label
Rituxan	Ruxience	rituximab-pvvr	01/23/2020	Non-Hodgkin's lymphoma	By # of doses	Label
Rituxan	Truxima	rituximab-abbs	11/09/2019	Chronic lymphocytic leukemia	By # of doses	Label
Rituxan	Truxima	rituximab-abbs	11/09/2019	Granulomatosis with Polyangiitis & Microscopic Polyangiitis	By # of doses	Label
Rituxan	Truxima	rituximab-abbs	11/09/2019	Non-Hodgkin's lymphoma	By # of doses	Label
Rituxan	Truxima	rituximab-abbs	11/09/2019	Rheumatoid arthritis	By # of doses	Label

ESM 2. Model diagnostics for model specification in the main text

We followed [Chambers et al, 2022](#)¹ to conduct model diagnostics. We assessed the model's goodness-of-fit by plotting the receiver operating characteristics (ROC) curve and calculating the area under the curve (AUC). The model had an AUC of 0.92, suggesting a good level of discrimination. We also assessed the goodness-of-fit using the Hosmer–Lemeshow's test. This test indicated a good fit, given a p value > 0.05. We tested for multicollinearity by evaluating the correlation among estimated coefficients. There was no correlation higher than 0.8 between any pairs of coefficients.

¹ Chambers, J.D., Margaretos, N.M., Enright, D.E. et al. Is an Orphan Drug's Cost-Effectiveness Associated with US Health Plan Coverage Restrictiveness?. *PharmacoEconomics* 40, 225–232 (2022). <https://doi.org/10.1007/s40273-021-01096-5>

ESM 3. Alternative model specifications

	Odds Ratio (95% CI)			
	(1)	(2)	(3)	(4)
Total, N	1,181	1,181	1,181	1,181
McFadden's Adjusted R ²	0.400	0.379	0.397	0.398
Log likelihood	-320.26	-334.93	-326.14	-323.59
Characteristics				
Cancer treatment	0.019** (0.008-0.041)	0.056** (0.030-0.102)	0.027** (0.013-0.054)	0.020** (0.009-0.043)
Pediatric population	11.558** (3.906-34.203)	1.235 (0.676-2.255)	4.567** (2.105-9.908)	10.247** (3.512-29.892)
FDA line of therapy				
1	Reference	Reference	Reference	Reference
2	0.521 (0.270-1.007)	0.415** (0.218-0.791)	0.509* (0.266-0.974)	0.522 (0.271-1.008)
First biosimilar	0.225** (0.118-0.429)	0.216** (0.114-0.407)	0.260** (0.148-0.458)	0.228** (0.120-0.432)
Years since market launch	0.823 (0.659-1.028)	1.085 (0.902-1.305)	1.008 (0.855-1.189)	0.826 (0.662-1.030)
No. of competitors				
1	Reference	Reference	Reference	Reference
2	0.060* (0.006-0.586)	0.017** (0.002-0.158)	0.038** (0.004-0.348)	0.061* (0.007-0.561)
3+	3.194 (0.462-22.082)	1.351 (0.203-8.985)	1.148 (0.186-7.070)	2.937 (0.453-19.027)
Disease prevalence				
< 200,000	Reference	Reference	Reference	Reference
200,000 – 1,000,000	2.000 (0.854-4.685)	2.950* (1.297-6.710)	1.674 (0.736-3.808)	1.992 (0.853-4.652)
> 1,000,000	2.067* (1.060-4.029)	3.095** (1.622-5.904)	1.326 (0.732-2.403)	2.044* (1.056-3.958)
Annual savings per patient				
< \$5,000	Reference	Reference	-	Reference
\$5,000 - \$9,999	0.534 (0.273-1.046)	0.416** (0.217-0.797)	-	0.537 (0.275-1.047)
\$10,000 - \$15,000	0.474 (0.213-1.055)	0.627 (0.293-1.344)	-	0.478 (0.216-1.056)
> \$15,000	0.171** (0.057-0.514)	0.477 (0.186-1.224)	-	0.174** (0.059-0.518)
Coverage of reference product relative to FDA label				
Not more restrictive	Reference	Reference	Reference	Reference
More restrictive	0.065** (0.038-0.109)	0.067** (0.040-0.111)	0.069** (0.042-0.115)	0.065** (0.038-0.109)
Cost-effectiveness measure availability of the reference product				
Available	Reference	-	Reference	Reference
Not available	0.066** (0.023-0.186)	-	0.122** (0.052-0.286)	0.074** (0.027-0.207)
Plan size				
National	Reference	Reference	Reference	Reference

	Odds Ratio (95% CI)			
	(1)	(2)	(3)	(4)
Regional Pharmacy benefit manager	1.511 (0.981-2.329)	1.808* (1.185-2.758)	1.599* (1.044-2.448)	1.489 (0.969-2.288)
Big three ^a	Reference	Reference	Reference	-
Other	1.683* (1.129-2.507)	1.543* (1.185-2.758)	1.670* (1.125-2.478)	-

* p < 0.05, ** p < 0.01

^a Big three included CVS Caremark, Express Scripts, and OptumRx.

CI: Confidence Interval

- (1) Model specification presented in the main text
- (2) (1) – Cost-effectiveness measure availability of the reference product
- (3) (1) – Annual savings per patient
- (4) (1) – Pharmacy benefit manager type