

Supplemental Table 1. FDA- and EMA-Approved Biosimilars for Originator Adalimumab, Etanercept, and Infliximab as of February 14, 2018.

Originator (Brand Name)	Biosimilar Name	INN and Suffix ^a	Regulatory Authority (Approval Year)	Biosimilar Brand Name	Manufacturer	Marketing Authorization Holder	Approved Indication Extrapolation
Adalimumab (Humira [1,2])^b	ABP 501	Adalimumab	EMA (2017)	Amgevita [3]	Amgen	Amgen	Partial ^c
		Adalimumab	EMA (2017)	Solymbic [4]	Amgen	Amgen	Partial ^c
		Adalimumab-atta	US FDA (2016)	Amjevita [5]	Amgen	Amgen	Partial ^c
	SB5	Adalimumab	EMA (2017)	Imraldi [6]	Biogen	Samsung Bioepis	Partial ^c
	BI 695501	Adalimumab	EMA (2017)	Cyltezo [7]	Boehringer Ingelheim	Boehringer Ingelheim	Partial ^c
		Adalimumab-adbm	US FDA (2017)	Cyltezo [8]	Boehringer Ingelheim	Boehringer Ingelheim	Partial ^c
Etanercept (Enbrel [9,10])^d	SB4	Etanercept	EMA (2016)	Benepali [11]	Biogen	Samsung Bioepis	Full
	GP2015	Etanercept	EMA (2017)	Erelzi [12]	Sandoz	Sandoz	Full
		Etanercept-szsz	US FDA (2016)	Erelzi [13]	Sandoz	Sandoz	Partial ^e
Infliximab (Remicade [14,15])^f	CT-P13	Infliximab	EMA (2013)	Remsima [16]	Celltrion	Celltrion	Full
		Infliximab	EMA (2013)	Inflectra [17]	Celltrion	Hospira	Full
		Infliximab-dyyb	US FDA (2016)	Inflectra [18]	Celltrion	Pfizer	Partial ^g
	SB2	Infliximab	EMA (2016)	Flixabi [19]	Samsung Bioepis	Samsung Bioepis	Full
		Infliximab-abda	US FDA (2017)	Renflexis [20]	Samsung Bioepis	Merck	Partial ^g
	PF-06438179	Infliximab-qbtx	US FDA (2017)	Ixifi [21]	Pfizer	Pfizer	Partial ^g

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AS, ankylosing spondylitis; CD, Crohn's disease; EOA, extended oligoarthritis; EMA, European Medicines Agency; ERA, enthesitis-related arthritis; FDA, US Food and Drug Administration; HS, hidradenitis suppurativa; INN, international non-proprietary name; JIA, juvenile idiopathic arthritis; nr-AxSpA, nonradiographic axial spondyloarthritis; PA, polyarthritis; Ps, psoriasis; PsA, psoriatic arthritis; RA, rheumatoid arthritis; UC, ulcerative colitis.

^aSuffixes are only adopted in the United States (US FDA recommendations for nomenclature).

^bIn the United States, Humira [1] is approved for RA, polyarticular JIA (age ≥ 2 y), PsA, AS, CD, pediatric CD (age ≥ 6 y), UC, Ps, HS, and UV. In the European Union, Humira [2] is approved for RA, JIA (polyarticular, age ≥ 2 y; ERA, age ≥ 6 y), AS, nr-axSpA, PsA, Ps, pediatric Ps (age ≥ 4 y), HS, adolescent HS (age ≥ 12 y), CD, pediatric CD (age ≥ 6 y), UC, UV, and pediatric UV (age ≥ 2 y).

^cAmgevita is not approved in the European Union for adolescent HS or pediatric UV; Solymbic is not approved in the European Union for polyarticular JIA, adolescent HS, or pediatric UV. Amjevita and Cytelzo are not approved in the United States for JIA in patients < 4 y, pediatric CD, HS, or UV. Imraldi and Cytelzo are not approved in the European Union for pediatric UV.

^dIn the United States, Enbrel [9] is approved for RA, polyarticular JIA (age ≥ 2 y), PsA, AS, Ps, pediatric Ps (age ≥ 4 y). In the European Union, Enbrel [10] is approved for RA, JIA (ERA, age ≥ 2 y; PsA, PA, and EOA, age ≥ 12 y), PsA, AS, nr-axSpA, Ps, pediatric Ps (age ≥ 6 y).

^eErelzi is not approved for PsA, Ps, or pediatric Ps.

^fIn the United States [14] and the European Union [15], Remicade is approved for RA, PsA, AS, CD, pediatric CD (age ≥ 6 y), UC, pediatric UC (age ≥ 6 y), and Ps.

^gInflectra, Renflexis, and Ixifi are not approved in the United States for pediatric UC.

References

1. HUMIRA (adalimumab). Full Prescribing Information, AbbVie Inc., North Chicago, IL, USA, 2017.
2. HUMIRA (adalimumab). Summary of Product Characteristics, AbbVie Ltd, Maidenhead, UK, 2018.
3. AMGEVITA (adalimumab). Summary of Product Characteristics, Amgen Europe B.V., Breda, The Netherlands, 2018.
4. SOLYMBIC (adalimumab). Summary of Product Characteristics, Amgen Europe B.V., Breda, The Netherlands, 2018.
5. AMJEVITA (adalimumab). Full Prescribing Information, Amgen Inc, Thousand Oaks, CA, USA, 2016.
6. IMRALDI (adalimumab). Summary of Product Characteristics, Samsung Bioepis UK Limited, Brentford, UK, 2018.
7. CYLTEZO (adalimumab). Summary of Product Characteristics, Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany, 2018.
8. CYLTEZO (adalimumab). Full Prescribing Information, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA, 2017.
9. ENBREL (etanercept). Full Prescribing Information, Amgen Inc., Thousand Oaks, CA, USA, 2017.
10. ENBREL (etanercept). Summary of Product Characteristics, Pfizer Limited, Sandwich, UK, 2018.
11. BENEPALI (etanercept). Summary of Product Characteristics, Samsung Bioepis UK Limited, Brentford, UK, 2018.
12. ERELZI (etanercept). Summary of Product Characteristics, Sandoz GmbH, Kundl, Austria, 2018.
13. ERELZI (etanercept). Full Prescribing Information, Sandoz Inc., Princeton, NJ, USA, 2018.
14. REMICADE (infliximab). Full Prescribing Information, Janssen Biotech, Inc., Horsham, PA, USA, 2017.

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15. REMICADE (infliximab). Summary of Product Characteristics, Janssen Biologics B.V., Leiden, The Netherlands, 2018.
16. REMSIMA (infliximab). Summary of Product Characteristics, Celltrion Healthcare Hungary Kft., Budapest, Hungary, 2018.
17. INFLECTRA (infliximab). Summary of Product Characteristics, Hospira UK Limited, Maidenhead, UK, 2018.
18. INFLECTRA (infliximab). Full Prescribing Information, Hospira, a Pfizer Company, Lake Forest, IL, 2016.
19. FLIXABI (infliximab). Summary of Product Characteristics, Samsung Bioepis UK Limited, Brentford, UK, 2018.
20. RENFLEXIS (infliximab). Full Prescribing Information, Merck Sharp & Dohme Corp., Kenilworth, NJ, USA, 2017.
21. IXIFI (infliximab). Full Prescribing Information, Pfizer Inc., New York, NY, USA, 2017.

Supplemental Table 2. Search Strategy.

Set#	Searched for
S1	Ti,ab(biosimilar OR biogeneric OR “subsequent entry biologic” OR sbe or “follow on biologic” OR “GP 2015” or gp2015 OR “CT P13” or ctp13 OR SB2 OR SB4 OR Remsima OR Flixabi OR Benepali OR Brenzys OR Inflectra)
S2	ti,ab(humira or adalimumab or remicade or infliximab or Enbrel or etanercept or simponi or golimumab or cimzia or certolizumab)
S3	ti,ab(interchange* OR switch* OR transition* OR substitute* OR exchang[*4] OR replac[*4] or crossover OR alternat* or conversion or convert[*3])
S4	MESH.EXACT.EXPLODE("Drug Substitution") OR EMB.EXACT.EXPLODE("drug substitution") OR su("drug substitution")
S5	ti,ab(nocebo or "non immunogenic*" or nonimmunogenic* or nonmedical or "non medical")
S6	ti,ab(humira or adalimumab or remicade or infliximab or Enbrel or etanercept or simponi or golimumab or cimzia or certolizumab)
S7	ti,ab (“tum*r necrosis factor blocker” or “tnf alpha blockade” or “anti tnf agent**”)
S8	ti,ab(“tnf alpha antagonist**” or “anti tnf alpha” or “anti tnf” or “tnf alpha inhibitor**” or “tnf alpha antibod**”) and (therapy or therapies or treatment* or therapeutic* or medication* or agent* OR drug*)
S9	ti,ab(tnf near/3 (antagonist* or inhibitor* or blocker*)) and (therapy or therapies or treatment* or therapeutic* or medication* or agent* OR drug*)
S10	ti,ab(“tum*r necrosis factor antagonist**” or “tumour necrosis factor antagonist**” or “tumor necrosis factor inhibitor**” or “tumour necrosis factor inhibitor**”) and (therapy or therapies or treatment* or therapeutic* or medication* or agent* OR drug*)
S11	ti,ab(“anti tnf” or “anti tumor necrosis factor” or “anti tumour necrosis factor”) near/4 (therapy or therapies or treatment* or therapeutic* or medication* or agent* OR drug*)
S12	Ti,ab((biosimilar OR biogeneric OR “subsequent entry biologic” OR sbe or “follow on biologic” OR “GP 2015” or gp2015 OR “CT P13” or ctp13 OR SB2 OR SB4 OR Remsima OR Flixabi OR Benepali OR Brenzys OR Inflectra) n/3 (interchange* OR switch* OR transition* OR substitute* OR exchang[*9] OR replac[*4] or crossover OR alternat* or conversion or convert[*3]))

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S13	Ti,ab((biosimilar OR biogeneric OR “subsequent entry biologic” OR sbe or “follow on biologic” OR “GP 2015” OR gp2015 or “CT P13” or ctp13 OR SB2 OR SB4 OR Remsima OR Flixabi OR Benepali OR Brenzys OR Inflectra) n/5 (interchange* OR switch* OR substitute* OR crossover OR alternat* OR transition*) n/3 (reference OR innovator* OR originator*))
S14	ti,ab((juvenile OR jia) NEAR/5 (arthritis OR arthropathy OR polyarthritis OR arthritides OR rheumatoid) OR (chauffard OR stiel OR still[*1]) PRE/0 (disease OR syndrome))
S15	ti,ab((arthritis OR nodul[*4] OR vasculitis) NEAR/5 (rheumatoid OR RA) OR (felty[*1] OR sjogren[*1] OR caplan[*1] OR still[*1] OR beauvais[*1]) NEAR/5 (syndrome OR disease))
S16	ti,ab((colitis or coloproctitis or proctocolitis) NEAR/3 (ulcerativ[*1] or ulcerosa or mucosal or ulcerous or ulceration) OR "Colitis Gravis" OR "Idiopathic Proctocolitis")
S17	ti,ab(psoriasis OR "psoriatic patient*" OR "psoriatic condition*")
S18	tio,ab("Psoriatic arthritis" OR "alibert bazin disease" OR "arthritis psoriatica" OR "psoriasis arthritis" OR "arthropathic psoriasis" OR "psoriatic arthropath[*3]" OR "psoriatic polyarthritis" OR "psoriasis arthropathica" OR "psoriasis pustulosa arthropathica" OR "arthritis psoriasis" OR "psoriatic rheumatism" OR "psoriatic rheumatoid arthritis" OR "Arthritic Psoriasis")
S19	ti,ab((ankylating OR ankylopoietic OR ankylos* OR ankylotic) N/3 (spondylitis OR spondylarthritis OR spine OR sponsylarthrosis OR spinal OR vertebral)) OR ((bechterew OR bekhtereve) P/1 (disease OR morbus)) OR (“spondylarthritis ankylopoietica” OR “spondylitis ankylopo*etica”)
S20	tio,ab((Hidradenitis OR Hidradenitides) NEAR/2 (suppurativa OR Suppurative) OR "acne inversa")
S21	ti,ab(crohn OR crohns OR (colitis OR enteritis OR enterocolitis) n/5 (granulomatous OR regional OR regionalis) OR ileitis n/5 (regional OR terminal) OR Ileocolitis or "inflammatory bowel disease" or uveitis)
S22	s6 or s7 or s8 or s9 or s10 or s11
S23	s14 or s15 or s16 or s17 or s18 or s19 or s20 or s21
S24	(s22 or s23) and s12

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S25	(s22 or s23) and s5
S26	s1 s2 s4
S27	s1 s2 s3
S28	s1 s5
S29	s1 s4
S30	s1 s3 s4
S31	s12 s5
S32	s12 or s13 or s24 or s25 or s26 or s27 or s28 or s29 or s30 or s31
S33	Tio,ab,su((clinical OR multicenter[*2] OR multicentre[*2] OR "multi center[*2]" OR "multi centre[*2]" OR controlled OR randomized OR randomised OR masked OR blind[*3] OR "open label[*2]" OR equipoise OR compar[*6] OR crossover OR "cross over") and (trial[*1] OR study OR studies OR volunteer[*1] OR placebo[*1] OR postmarket[*4] OR "post market[*4]" OR "meta analys[*4]" OR "phase I" OR "phase II" OR "phase III" OR "phase IV"))
S34	tio,ab,su((clinical OR multicenter[*2] OR multicentre[*2] OR "multi center[*2]" OR "multi centre[*2]" OR controlled OR randomized OR randomised OR masked OR blind[*3] OR "open label[*2]" OR equipoise OR compar[*6] OR crossover OR "cross over") NEAR/8 (trial[*1] OR study OR studies OR volunteer[*1] OR placebo[*1] OR postmarket[*4] OR "post market[*4]" OR "meta analys[*4]" OR "phase I" OR "phase II" OR "phase III" OR "phase IV"))
S35	tio,ab,su((Controlled or randomized or clinical or blind or multicenter or "open label*" or masked or compar* or crossover or "cross over" or placebo or "post market" or postmarket or "meta analysis" or "head to head") p/2 (study or trial) or phase p/1 (0 or 1 or 2 or 3 or 4 or I or ii or iii or iv))
S36	tio,ab,su("clinical trial[*1]" or (single or double or treble or triple) n/5 blind[*2] or (mask[*2] or placebo[*5] or random[*5] or prospective or clinical or control[*5] or volunteer[*3] or case or major or multicent[*3]) n/5 (stud[*5] or trial[*4]))
S37	tio,ab,su("head to head")

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S38	tio,ab(direct[*2] n/3 (compare or compared or comparing or compares or comparison[*1] or comparative[*2] or comparabl[*2]))
S39	DTYPE("CLINICAL TRIAL*" OR "CONTROLLED CLINICAL TRIAL" OR "MULTICENTER STUDY" OR "RANDOMIZED CONTROLLED TRIAL")
S40	MESH.EXACT.EXPLODE("CLINICAL TRIALS AS TOPIC") or EMB.EXACT.EXPLODE("clinical study") OR EMB.EXACT.EXPLODE("CLINICAL TRIAL") or EMB.EXACT.EXPLODE("major clinical study") or EMB.EXACT.EXPLODE("CLINICAL TRIAL (TOPIC)") or EMB.EXACT.EXPLODE("CLINICAL TRIAL*")
S41	SU.exact("Clin.trial") OR su("Clinical Trial") OR su("clinical study") OR su("major clinical study")
S42	s33 or s34 or s35 or s36 or s37 or s38 or s39 or s40 or s41
S43	s32 s42
S44	s43 and pd(>2011) and la(English)
S45	s44 AND (tio,ab(patient*) OR Mesh.exact("humans") or Emb.exact("human") or Su(human or humans))