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Table A1 Substitution catalogue: reference product & biosimilar (2016-2021)

ATC	Reference Product			Biosimilar			
	medication	Dose (mg) / unit	cost (in CHF)	medication	Reimburment date	Dose (mg) / unit	cost (in CHF)
<i>Low-molecular-weight heparins</i>							
B01	Clexane	20 / 10	41	Inhixa	01.08.2020	20 / 10	38.55
B01	Clexane	20 / 50	139.55	Inhixa	01.08.2020	20 / 50	127.25
B01	Clexane	40 / 2	17.35	Inhixa	01.08.2020	40 / 2	16.45
B01	Clexane	40 / 10	62.45	Inhixa	01.08.2020	40 / 10	57.85
B01	Clexane	40 / 50	246.75	Inhixa	01.08.2020	40 / 50	223.7
B01	Clexane	60 / 10	76.65	Inhixa	01.08.2020	60 / 10	70.6
B01	Clexane	80 / 10	102.3	Inhixa	01.08.2020	80 / 10	93.7
B01	Clexane	100 / 10	123.75	Inhixa	01.08.2020	100 / 10	113
B01	Clexane	120 / 10	134.9	Inhixa	01.08.2020	120 / 10	123.05
B01	Clexane	150 / 10	161.3	Inhixa	01.08.2020	150 / 10	146.8
B01	Clexane	300 / 1	41.3	Inhixa	01.08.2020	300 / 1	38.8
<i>Growth factors</i>							
L03	Neupogen	0.3 / 5	531.1	Accofil	01.11.2019	0.3 / 5	479.65
				Filgrastim-Teva	01.03.2010	0.3 / 5	479.65
				Zarzio	01.05.2010	0.3 / 5	479.65
L03	Neupogen	0.48 / 5	740.9	Accofil	01.11.2019	0.48 / 5	668.45
				Filgrastim-Teva	01.03.2010	0.48 / 5	668.45
				Zarzio	01.05.2010	0.48 / 5	668.45
L03	Neulasta	6 / 1	1668.75	Grasustek	01.09.2021	6 / 1	1266.95
				Pelgraz	01.11.2019	6 / 1	1266.85
				Pelgraz	01.11.2019	6 / 1	1266.85
				Pelmeg	01.01.2020	6 / 1	857.55
				Ziextenzo	01.03.2020	6 / 1	1266.95
				Fulphila	01.06.2020	6 / 1	1266.85
B03	Epex	0.008 / 6	71.5	Binocrit	01.10.2009	0.008 / 6	66.15
B03	Epex	0.017 / 6	126.55	Binocrit	01.10.2009	0.017 / 6	115.7
B03	Epex	0.025 / 6	181.65	Binocrit	01.10.2009	0.025 / 6	165.25
B03	Epex	0.037 / 6	236.75	Binocrit	01.10.2009	0.037 / 6	214.7
B03	Epex	0.046 / 6	291.8	Binocrit	01.10.2009	0.046 / 6	264.5
B03	Epex	0.092 / 6	567.2	Binocrit	01.10.2009	0.092 / 6	512.1
<i>Hormones</i>							
A10	Lantus	10.9 / 5	81.85	Abasaglar	01.09.2015	10.9 / 5	68.4
G03	GONAL-F	0.022 / 1	156.4	Ovaleap	01.11.2018	0.022 / 1	122.05
G03	GONAL-F	0.033 / 1	226.45	Ovaleap	01.11.2018	0.033 / 1	174.95

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G03	GONAL-F	0.066 / 1	430.65	Ovaleap	01.11.2018	0.066 / 1	329.1
H01	Genotropin	5 / 1	221.65	Omnitrope	01.11.2010	5 / 1	201.1
H01	Genotropin	5 / 5	1041.9	Omnitrope	01.11.2010	5 / 5	940
H05	Forsteo	0.25 / 1	412.75	Movymia	01.09.2019	0.25 / 1	340.75
				Terrosa	01.09.2019	0.25 / 1	340.75
				Terrosa	01.09.2019	0.25 / 1	340.75
<i>Fusion proteins</i>							
L01	MabThera	100 / 2	627.3	Rixathon	01.09.2018	100 / 2	505.5
				Truxima	01.01.2019	100 / 2	505.5
L01	MabThera	500 / 1	1515.65	Rixathon	01.09.2018	500 / 1	1225.7
				Truxima	01.01.2019	500 / 1	1225.7
L01	Herceptin	150 / 1	686.4	Herzuma	01.12.2021	150 / 1	562.45
				Trazimera	01.10.2019	150 / 1	562.45
				Kanjinti	01.02.2020	150 / 1	562.45
				Ogivri	01.09.2020	150 / 1	562.45
L01	Herceptin	440 / 1	1932.85	Herzuma	01.12.2021	150 / 1	1586.75
				Trazimera	01.10.2019	150 / 1	1586.75
				Kanjinti	01.02.2020	150 / 1	1586.75
				Ogivri	01.09.2020	150 / 1	1586.75
L01	Avastin	100 / 1	410.65	Oyavas	01.08.2021	100 / 1	312.1
				Bevacizumab-Teva	01.07.2021	100 / 1	312.1
				MVASI	01.07.2020	100 / 1	312.1
				Zirabev	01.08.2020	100 / 1	312.1
L01	Avastin	400 / 1	1469.5	Oyavas	01.08.2021	400 / 1	1117.5
				Bevacizumab-Teva	01.07.2021	400 / 1	1117.5
				MVASI	01.07.2020	400 / 1	1117.5
				Zirabev	01.08.2020	400 / 1	1117.5
L04	Enbrel	25 / 4	682.35	Benepali	01.04.2019	25 / 4	515.8
				Erelzi	01.07.2018	25 / 4	515.8
L04	Enbrel	50 / 2	669.05	Benepali	01.04.2019	50 / 2	504.3
				Erelzi	01.07.2018	50 / 2	505.9
L04	Remicade	100 / 1	695.75	Inflectra	01.08.2016	100 / 1	627.25
				Remsima	01.01.2016	100 / 1	627.25
L04	Humira	20 / 2	661.8	Hyrimoz	01.11.2019	20 / 2	500.45
L04	Humira	40 / 1	661.8	Abirilada	01.06.2021	40 / 1	500.45
				Amgevita	01.11.2019	40 / 1	500.45
				Hyrimoz	01.11.2019	40 / 1	500.45
				Idacio	01.08.2020	40 / 1	500.45
				Imraldi	01.07.2020	40 / 1	498.55
				Hulio	01.08.2020	40 / 1	500.45

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Table A2 First Prescriptions: Reference Products (active substance)

Active substance	total	2016	2017	2018	2019	2020	2021
n	14'987	433 (2.9%)	394 (2.6%)	501 (3.3%)	861 (5.7%)	4'525 (30.2%)	8'273 (55.2%)
Adalimumab	369 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	24 (2.8%)	182 (4.0%)	163 (2.0%)
Bevacizumab	267 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	96 (2.1%)	171 (2.1%)
Enoxaparin	9'785 (65.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3'047 (67.3%)	6'738 (81.4%)
Epoetin alfa	136 (0.9%)	20 (4.6%)	30 (7.6%)	19 (3.8%)	23 (2.7%)	24 (0.5%)	20 (0.2%)
Etanercept	176 (1.2%)	0 (0.0%)	0 (0.0%)	37 (7.4%)	55 (6.4%)	38 (0.8%)	46 (0.6%)
Filgrastim	658 (4.4%)	158 (36.5%)	134 (34.0%)	107 (21.4%)	85 (9.9%)	104 (2.3%)	70 (0.8%)
Follitropin alfa	747 (5.0%)	0 (0.0%)	0 (0.0%)	41 (8.2%)	182 (21.1%)	226 (5.0%)	298 (3.6%)
Infliximab	530 (3.5%)	141 (32.6%)	103 (26.1%)	74 (14.8%)	68 (7.9%)	68 (1.5%)	76 (0.9%)
Insulin glargin	640 (4.3%)	113 (26.1%)	127 (32.2%)	126 (25.1%)	102 (11.8%)	88 (1.9%)	84 (1.0%)
Pegfilgrastim	457 (3.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	35 (4.1%)	225 (5.0%)	197 (2.4%)
Rituximab	661 (4.4%)	0 (0.0%)	0 (0.0%)	97 (19.4%)	203 (23.6%)	178 (3.9%)	183 (2.2%)
Somatropin	5 (0.0%)	1 (0.2%)	0 (0.0%)	0 (0.0%)	2 (0.2%)	2 (0.0%)	0 (0.0%)
Teriparatid	304 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	55 (6.4%)	134 (3.0%)	115 (1.4%)
Trastuzumab	252 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	27 (3.1%)	113 (2.5%)	112 (1.4%)

Table A3 First Prescriptions: Biosimilars (active substance)

Active substance	total	2016	2017	2018	2019	2020	2021
n	3'489	261 (7.5%)	344 (9.9%)	393 (11.3%)	616 (17.7%)	809 (23.2%)	1'066 (30.6%)
Adalimumab	165 (4.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (1.1%)	63 (7.8%)	95 (8.9%)
Bevacizumab	28 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (0.6%)	23 (2.2%)
Enoxaparin	76 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (0.9%)	69 (6.5%)
Epoetin alfa	34 (1.0%)	8 (3.1%)	2 (0.6%)	7 (1.8%)	9 (1.5%)	3 (0.4%)	5 (0.5%)
Etanercept	185 (5.3%)	0 (0.0%)	0 (0.0%)	10 (2.5%)	49 (8.0%)	69 (8.5%)	57 (5.3%)
Filgrastim	1'854 (53.1%)	243 (93.1%)	271 (78.8%)	295 (75.1%)	342 (55.5%)	336 (41.5%)	367 (34.4%)
Follitropin alfa	219 (6.3%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	40 (6.5%)	71 (8.8%)	107 (10.0%)
Infliximab	281 (8.1%)	7 (2.7%)	31 (9.0%)	49 (12.5%)	54 (8.8%)	61 (7.5%)	79 (7.4%)
Insulin glargin	141 (4.0%)	0 (0.0%)	39 (11.3%)	29 (7.4%)	33 (5.4%)	21 (2.6%)	19 (1.8%)
Pegfilgrastim	129 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	32 (4.0%)	97 (9.1%)
Rituximab	318 (9.1%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	78 (12.7%)	120 (14.8%)	119 (11.2%)
Somatropin	5 (0.1%)	3 (1.1%)	1 (0.3%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Teriparatid	47 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (0.6%)	20 (2.5%)	23 (2.2%)
Trastuzumab	7 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	6 (0.6%)

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Table A4 Rest prescriptions: Reference Products (active substance)

Active substance	total	2016	2017	2018	2019	2020	2021
n	33'958	1'293 (3.8%)	1'645 (4.8%)	1'736 (5.1%)	3'662 (10.8%)	9'939 (29.3%)	15'683 (46.2%)
Adalimumab	3'070 (9.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	41 (1.1%)	1'354 (13.6%)	1'675 (10.7%)
Bevacizumab	2'109 (6.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	481 (4.8%)	1'628 (10.4%)
Enoxaparin	8'669 (25.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2'343 (23.6%)	6'326 (40.3%)
Epoetin alfa	2'052 (6.0%)	234 (18.1%)	385 (23.4%)	408 (23.5%)	200 (5.5%)	422 (4.2%)	403 (2.6%)
Etanercept	791 (2.3%)	0 (0.0%)	0 (0.0%)	90 (5.2%)	310 (8.5%)	198 (2.0%)	193 (1.2%)
Filgrastim	2'252 (6.6%)	408 (31.6%)	428 (26.0%)	403 (23.2%)	275 (7.5%)	403 (4.1%)	335 (2.1%)
Follitropin alfa	1'914 (5.6%)	0 (0.0%)	0 (0.0%)	19 (1.1%)	502 (13.7%)	561 (5.6%)	832 (5.3%)
Infliximab	2'973 (8.8%)	543 (42.0%)	660 (40.1%)	424 (24.4%)	434 (11.9%)	435 (4.4%)	477 (3.0%)
Insulin glargin	1'036 (3.1%)	108 (8.4%)	170 (10.3%)	134 (7.7%)	443 (12.1%)	112 (1.1%)	69 (0.4%)
Pegfilgrastim	1'426 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	78 (2.1%)	699 (7.0%)	649 (4.1%)
Rituximab	3'148 (9.3%)	0 (0.0%)	0 (0.0%)	258 (14.9%)	1'177 (32.1%)	814 (8.2%)	899 (5.7%)
Somatropin	7 (0.0%)	0 (0.0%)	2 (0.1%)	0 (0.0%)	2 (0.1%)	3 (0.0%)	0 (0.0%)
Teriparatid	1'791 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	79 (2.2%)	856 (8.6%)	856 (5.5%)
Trastuzumab	2'720 (8.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	121 (3.3%)	1'258 (12.7%)	1'341 (8.6%)

Table A5 Rest prescriptions: Biosimilars (active substance)

Active substance	total	2016	2017	2018	2019	2020	2021
n	16'293	754 (4.6%)	1'071 (6.6%)	1'578 (9.7%)	2'644 (16.2%)	4'349 (26.7%)	5'897 (36.2%)
Adalimumab	3'100 (19.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	64 (2.4%)	1'256 (28.9%)	1'780 (30.2%)
Bevacizumab	306 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	21 (0.5%)	285 (4.8%)
Enoxaparin	41 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (0.1%)	38 (0.6%)
Epoetin alfa	844 (5.2%)	32 (4.2%)	114 (10.6%)	257 (16.3%)	369 (14.0%)	55 (1.3%)	17 (0.3%)
Etanercept	930 (5.7%)	0 (0.0%)	0 (0.0%)	23 (1.5%)	247 (9.3%)	377 (8.7%)	283 (4.8%)
Filgrastim	5'894 (36.2%)	695 (92.2%)	752 (70.2%)	897 (56.8%)	1'110 (42.0%)	1'142 (26.3%)	1'298 (22.0%)
Follitropin alfa	583 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	74 (2.8%)	210 (4.8%)	299 (5.1%)
Infliximab	1'507 (9.2%)	23 (3.1%)	115 (10.7%)	274 (17.4%)	278 (10.5%)	374 (8.6%)	443 (7.5%)
Insulin glargin	509 (3.1%)	0 (0.0%)	80 (7.5%)	126 (8.0%)	143 (5.4%)	98 (2.3%)	62 (1.1%)
Pegfilgrastim	406 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	125 (2.9%)	281 (4.8%)
Rituximab	1'763 (10.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	356 (13.5%)	564 (13.0%)	843 (14.3%)
Somatropin	16 (0.1%)	4 (0.5%)	10 (0.9%)	1 (0.1%)	1 (0.0%)	0 (0.0%)	0 (0.0%)
Teriparatid	297 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.1%)	114 (2.6%)	181 (3.1%)
Trastuzumab	97 (0.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	10 (0.2%)	87 (1.5%)

Table A6 Biosimilars quota by active substance

Active substance	Avg. relative Price difference	Biosimilars quota (IP+RP)					
		2016	2017	2018	2019	2020	2021
Adalimumab	24.63	-	-	-	52.21	46.2	50.5
Bevacizumab	23.98	-	-	-	-	4.31	14.62
Enoxaparin	7.77	-	-	-	-	<1	<1
Epoetin alfa	8.91	3.1	21.85	38.21	62.9	11.51	4.94
Etanercept	24.52	-	-	20.63	44.78	65.4	58.72

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Filgrastim	9.73	62.37	64.54	70.04	80.13	74.46	80.43
Follitropin alfa	22.76	-	-	1.64	14.29	26.31	26.43
Infliximab	9.85	4.2	15.53	39.34	39.81	46.38	48.56
Insulin glargin	16.43	-	33.62	37.35	24.41	37.3	34.62
Pegfilgrastim	48.61	-	-	-	-	14.52	30.88
Rituximab	19.27	-	-	<1	23.93	40.81	47.06
Somatropin	9.53	87.5	84.62	100	20	0	-
Teriparatid	17.44	-	-	-	4.29	11.84	17.36
Trastuzumab	17.98	-	-	-	-	<1	6.02

Table A7 Frequency of medication switches by active substance

Category	Active substance	Proportion to all switches (%)			
		RP to RP	RP to B	B to B	B to RP
Fusion proteins	Etanercept	0.27	4.4	0.29	1.59
Hormones	Follitropin alfa	9.41	5.35	8.1	5.84
Hormones	Insulin glargin	0.27	2.95	0.17	2.72
Hormones	Somatropin	0.02	0.07	0	0
Hormones	Teriparatid	0.21	1.42	1.34	2.51
Monoclonal antibodies	Adalimumab	4.52	4.04	1.75	4.63
Monoclonal antibodies	Bevacizumab	11.38	1.67	4.31	5.98
Monoclonal antibodies	Infliximab	1.86	8.95	2.33	6.4
Monoclonal antibodies	Rituximab	21.81	11.75	31.24	13.05
Monoclonal antibodies	Trastuzumab	6.94	1.02	1.52	7.89
Low-molecular-weight heparins	Enoxaparin	25.57	0.65	0.06	30.88
Growth factors	Epoetin alfa	14.22	1.16	24.94	1.17
Growth factors	Filgrastim	2.4	50.75	21.5	8.07
Growth factors	Pegfilgrastim	1.13	5.82	2.45	9.27

Table A8 Three models (A-C) assessing determinants of biosimilar first prescription (logistic regression)

Variables	Model A: sociodemographic variables	Model B: Model A + medication variables	Model C: Model B + provider variables
	OR [95%CI]	OR [95%CI]	OR [95%CI]
Intercept	0.429 [0.355, 0.518]	0.831 [0.49, 1.402]	0.706 [0.399, 1.241]
Year:			
2016 (reference)			
2017	1.381 [1.129, 1.692]	1.602 [1.246, 2.062]	1.594 [1.233, 2.064]
2018	1.354 [1.113, 1.648]	1.983 [1.551, 2.539]	1.934 [1.503, 2.492]
2019	1.493 [1.246, 1.793]	2.64 [2.094, 3.332]	2.602 [2.054, 3.302]
2020	0.42 [0.356, 0.497]	2.203 [1.755, 2.769]	2.232 [1.769, 2.819]
2021	0.302 [0.256, 0.355]	3.077 [2.452, 3.867]	3.012 [2.388, 3.806]
Sex:			
Female (reference)			
Male	0.998 [0.922, 1.081]	1.137 [1.02, 1.267]	1.132 [1.014, 1.263]

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Age:			
<50 (reference)			
50-64	1.302 [1.169, 1.452]	1.005 [0.867, 1.164]	1.022 [0.881, 1.185]
65-74	1.571 [1.401, 1.761]	1.044 [0.889, 1.227]	1.044 [0.887, 1.228]
>74	0.961 [0.849, 1.086]	0.825 [0.694, 0.98]	0.864 [0.725, 1.03]
Language region			
German (reference)			
French	0.578 [0.521, 0.64]	0.582 [0.51, 0.664]	0.611 [0.532, 0.7]
Italian	0.467 [0.397, 0.546]	0.744 [0.601, 0.918]	0.761 [0.612, 0.942]
Number of comorbidity:			
0 (reference)			
1	1.054 [0.932, 1.191]	0.934 [0.796, 1.094]	0.95 [0.81, 1.115]
2	1.095 [0.963, 1.244]	1.041 [0.88, 1.23]	1.05 [0.886, 1.243]
>2	0.938 [0.837, 1.051]	1.05 [0.904, 1.22]	1.08 [0.928, 1.256]
Deductible:			
Low (reference)			
High	1.067 [0.954, 1.192]	1.005 [0.868, 1.163]	0.998 [0.861, 1.155]
Managed care	1.029 [0.949, 1.116]	1.103 [0.992, 1.226]	1.095 [0.984, 1.22]
Category:			
Fusion proteins (reference)			
Hormones		1.297 [0.816, 2.081]	1.281 [0.803, 2.06]
Monoclonal antibodies		0.152 [0.116, 0.199]	0.115 [0.087, 0.152]
Low-molecular-weight heparins		0.001 [0.001, 0.001]	0.001 [0, 0.001]
Growth factors		0.235 [0.168, 0.327]	0.158 [0.112, 0.222]
Multiple package size		4.551 [3.808, 5.461]	4.64 [3.876, 5.575]
Cost per package of reference product (in CHF)			
<100			
100-599		0.254 [0.185, 0.349]	0.202 [0.145, 0.28]
>600		0.853 [0.592, 1.236]	0.657 [0.453, 0.957]
Relative price difference (%)			
<10			
10-19		0.091 [0.072, 0.115]	0.076 [0.059, 0.096]
>20		0.067 [0.053, 0.084]	0.067 [0.054, 0.084]
Number of available imitator drug:			
1 (reference)			
2		2.15 [1.671, 2.785]	2.363 [1.819, 3.093]
>2		8.143 [6.502, 10.248]	9.649 [7.614, 12.303]
Suppl			
General practitioner (reference)			
Outpatient hospital			2.477 [1.887, 3.28]
Specialist			1.417 [1.075, 1.884]
Traditional pharmacy			1.207 [0.911, 1.611]
Rest			0.998 [0.609, 1.606]
Observations	18'953	18'953	18'953
AIC	16'588	9'868	9'735
BIC	16'722	10'088	9'986