

Treatment Group	Selection criteria
Severe	Yearly factor consumption > 100,000 IU, or ≥ 1 prescription of Emicizumab w/o a diagnosis of inhibitor status (Excl., pts. w/ current evidence of inhibitors)
Non-Severe	Yearly factor consumption ≤ 100,000 IU, or ≥ 1 prescription of desmopressin or tranexamic acid (Excl., pts. w/ current evidence of inhibitors)
Inhibitors	≥ 1 prescription of a bypassing agent or ≥ 1 prescription of Emicizumab in combination with a diagnosis of inhibitor status

Supplemental Table 1 Classification algorithm Hemophilia A

Product category	Subcategory	ATC Code	ATC Name	Products
Factor replacement therapy - standard half-life (SHL)	Plasma factor products	B02BD02	Coagulation factor VIII	Beriate; Intersero; Haemoctin; Octanate;
		B02BD06	von Willebrand factor and coagulation factor VIII in combination	Fanhdi; Haemate; Immunate; Voncento; Wilate; Optivate
	Recombinant Factor – standard half-life (recSHL)	B02BD15	Octocog alfa	Advate; Kovaltry;
		B02BD16	Turoctocog alfa	NovoEight
		B02BD17	Simoctocog alfa	Nuwiq; Vihuma
		B02BD31	Moroctocog alfa	Refacto
		B02BD35	Lonoctocog alfa	Afstyla
Factor replacement therapy - extended half-life (EHL)	Recombinant Factor – Extended half-life	B02BD32	Efmoroctocog alfa	Elocta
		B02BD38	Rurioctocog alfa pegol	Adynovi
		B02BD39	Damoctocog alfa pegol	Jivi
		B02BD41	Turoctocog alfa pegol	Esperoct
Bypassing agents	Recombinant Factor VIIa	B02BD37	Eptacog alfa (aktiviert)	Novoseven
	Activated prothrombin complex	B02BD03	factor VIII inhibitor bypassing activity	Feiba
Non factor replacement therapy	Bispecific human monoclonal antibody	B02BX06	Emizicumab	Hemlibra
Non specific therapy		H01BA02	Desmopressin	
		B02AA02	tranexamic acid	Exacyl; Spotof

Supplemental Table 2 Hemophilia A related medication

Treatment Group	Selection criteria
Severe	Yearly factor consumption > 80,000 IU, OR >40,000, if ≥1 EHL prescription (Excl., pts. w/ current evidence of inhibitors)
Non-Severe	Yearly factor consumption ≤ 80,000 IU, OR ≤40,000, if ≥1 EHL prescription, OR ≥ 1 prescription of tranexamic acid (if no factor prescription) (Excl., pts. w/ current evidence of inhibitors)
Inhibitors	≥ 1 prescription of a bypassing agent

Supplemental Table 3 Classification algorithm Hemophilia B

Product category	Subcategory	ATC Code	ATC Name	Products
Factor replacement therapy - standard half-life (SHL)	Plasma factor products	B02BD04	coagulation factor IX	AlphaNine; Haemonine; Immunine; Mononine; Octanine;
	Recombinant Factor – standard half-life (recSHL)	B02BD09	Nonacog alfa	Benefix
		B02BD29	Nonacog gamma	Rixubis
Factor replacement therapy - extended half-life (EHL)	Recombinant Factor – Extended half-life	B02BD33	Albutrepenonacog alfa	Idelvion
		B02BD34	Eftrenonacog alfa	Alprolix
		B02BD36	Nonacog beta pegol	Refixia
Bypassing agents	Recombinant Factor VIIa	B02BD37	Eptacog alfa (aktiviert)	Novoseven
Non specific therapy		B02AA02	tranexamic acid	Exacyl; Spotof

Supplemental Table 4 Hemophilia B related medication

Selection step	2016	2017	2018	2019	2020	2021
1) Persons in the InGef database ▼	4,171,377	4,201,273	4,278,020	4,284,818	4,282,793	4,321,057
2) Persons fully insured in resp. baseline and analysis year ▼	3,990,293	4,000,856	3,946,476	3,911,267	3,896,796	3,721,474
3) Diagnosis M2Q D66 ▼	856	909	905	964	1019	993
4) Age 12 yrs or older ▼	784	836	833	901	950	924
5a) Treatment group 'Severe'	55	58	62	66	71	63
5b) Treatment group 'Non-severe'	72	74	68	57	74	75
5c) Treatment group 'Inhibitors'	<5	<5	<5	<5	6	<5
▼ 5) Overall treated study population	129	135	131	125	151	142

Supplemental Table 5 Patient flow in InGef Database – Hemophilia A. M2Q – Minimum two quarters; yrs – years.

Selection step	2016	2017	2018	2019	2020	2021
1) Persons in the InGef database ▼	4,171,377	4,201,273	4,278,020	4,284,818	4,282,793	4,321,057
2) Persons fully insured in resp. baseline and analysis year ▼	3,990,293	4,000,856	3,946,476	3,911,267	3,896,796	3,721,474
3) Diagnosis M2Q D67 ▼	149	151	153	150	149	141
4) Age 12 yrs or older ▼	134	134	137	138	132	128
5a) Treatment group "Severe"	12	12	13	12	17	19
5b) Treatment group "Non-severe"	18	15	13	17	13	15
5c) Treatment group "Inhibitors"	0	0	0	0	<5	<5
▼ 5) Overall treated study population	30	27	26	29	31	35

Supplemental Table 6 Patient flow in InGef Database - Hemophilia B. M2Q – Minimum two quarters; yrs – years.

		2016		2017		2018		2019		2020		2021	
Overall	Total	N = 129	(100)	N = 135	(100)	N = 131	(100)	N = 125	(100)	N = 151	(100)	N = 142	(100)
	pdSHL	23	(17.8)	26	(19.3)	28	(21.4)	24	(19.2)	30	(19.9)	25	(17.6)
	recSHL	78	(60.5)	79	(58.5)	71	(54.2)	56	(44.8)	61	(40.4)	51	(35.9)
	All SHL	101	(78.3)	103	(76.3)	98	(74.8)	80	(64.0)	90	(59.6)	76	(53.5)
	recEHL	<5	(NA)	<5	(NA)	10	(7.6)	26	(20.8)	28	(18.5)	34	(23.9)
	Emici- zumab	0	(0)	0	(0)	1	(0.8)	3	(2.4)	8	(5.3)	12	(8.5)
Severe	Total	N = 55	(100)	N = 58	(100)	N = 62	(100)	N = 66	(100)	N = 71	(100)	N = 63	(100)
	pdSHL	9	(16.4)	11	(19.0)	11	(17.7)	14	(21.2)	16	(22.5)	13	(20.6)
	recSHL	46	(83.6)	47	(81.0)	48	(77.4)	38	(57.6)	36	(50.7)	27	(42.9)
	All SHL	55	(100)	56	(96.6)	58	(93.6)	52	(78.8)	51	(71.8)	40	(63.5)
	recEHL	<5	(NA)	<5	(NA)	10	(16.1)	22	(33.3)	23	(32.4)	22	(34.9)
	Emicizum ab	0	(0)	0	(0)	0	(0)	<5	(NA)	6	(8.5)	11	(17.5)
Non- Severe	Total	N = 72	(100)	N = 74	(100)	N = 68	(100)	N = 57	(100)	N = 74	(100)	N = 75	(100)
	pdSHL	14	(19.4)	14	(18.9)	16	(23.5)	10	(17.5)	14	(18.9)	12	(16)
	recSHL	32	(44.4)	32	(43.2)	23	(33.8)	18	(31.6)	25	(33.8)	24	(32.0)
	All SHL	46	(63.9)	46	(62.2)	39	(57.4)	28	(49.1)	39	(52.7)	36	(48.0)
	recEHL	0	(0)	0	(0)	0	(0)	<5	(NA)	5	(6.8)	12	(16.0)
	Emicizum ab	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)

Supplemental Table 7 Number of Hemophilia A patients, with factor replacement prescriptions; by treatment group and product category, n patients with prescriptions from the product category (% of total patients)
pdSHL – plasma-derived standard half-life factor; recSHL – recombinant standard half-life factor; recEHL – recombinant extended half-life factor; NA – Not available

		2016		2017		2018		2019		2020		2021	
Overall	Total	N = 30	(100)	N = 27	(100)	N = 26	(100)	N = 29	(100)	N = 31	(100)	N = 35	(100)
	pdSHL	13	(43,3)	10	(37,0)	7	(26,9)	5	(17,2)	<5	NA	5	(14,3)
	recSHL	12	(40,0)	8	(29,6)	8	(30,8)	8	(27,6)	<5	NA	5	(14,3)
	Total SHL	24	(80,0)	18	(66,7)	15	(57,7)	13	(44,8)	8	(25,8)	10	(28,6)
	recEHL	5	(16,7)	7	(25,9)	12	(46,2)	15	(51,7)	17	(54,8)	21	(60,0)
Severe	Total	N = 12	(100)	N = 12	(100)	N = 13	(100)	N = 12	(100)	N = 17	(100)	N = 19	(100)
	pdSHL	6	(50,0)	<5	NA	<5	NA	<5	NA	<5	NA	<5	NA
	recSHL	6	(50,0)	6	(50,0)	<5	NA	<5	NA	<5	NA	0	(0,0)
	Total SHL	11	(91,7)	9	(75,0)	5	(38,5)	<5	NA	<5	NA	<5	NA
	recEHL	<5	NA	<5	NA	11	(84,6)	12	(100,0)	14	(82,4)	18	(94,7)
Non-Severe	Total	N = 18	(100)	N = 15	(100)	N = 13	(100)	N = 17	(100)	N = 13	(100)	N = 15	(100)
	pdSHL	7	(38,9)	7	(46,7)	5	(38,5)	<5	NA	<5	NA	<5	NA
	recSHL	6	(33,3)	<5	NA	5	(38,5)	6	(35,3)	<5	NA	5	(33,3)
	Total SHL	13	(72,2)	9	(60,0)	10	(76,9)	10	(58,8)	<5	NA	8	(53,3)
	recEHL	<5	NA	<5	NA	<5	NA	<5	NA	<5	NA	<5	NA

Supplemental Table 8 Number of Hemophilia B patients, with factor replacement prescriptions; by treatment group and product category, n patients with prescriptions from the product category (% of total patients) pdSHL – plasma-derived standard half-life factor; recSHL – recombinant standard half-life factor; recEHL – recombinant extended half-life factor; NA – Not Available