NHD
U.K.H.C.D.O NATIONAL HAEMOPHILIA DATABASE

Bleeding Disorder Statistics for Wales

April 2020 to March 2021

A report from the UK National Haemophilia Database

The following report is based on people who are registered with the National Haemophilia Database with a Welsh post code (unless otherwise stated), regardless of which Haemophilia Centre they were treated at. Some people who live in Wales are managed by English Centres. These are included and data provided on their numbers and the health authorities managing and supplying them. Data is also provided for people who live in England managed by Welsh Centres either regularly or as visitors to the principality.

Contents

Appendix 1: Glossary

AE	Adverse Event
AGM	Annual General Meeting
ASH	American Society of Hematology
BCSH	British Committee for Standards in Haematology
BMI	Body mass index
BMS	Biomedical Scientists
BSH	British Society for Haematology
CCC	Comprehensive Care Centre
CEO	Chief executive officer
CMWP	Co-morbidities Working Party
COVID-19	Corona Virus Disease
CPD	Continuing Professional Development
CQUIN	Commissioning for Quality and Innovation
CRG	Clinical Reference Group
DAG	Data Analysis Group
DMWP	Data Management Working Party
EAHAD	European Association for Haemophilia and Allied Disorders
EHL	Enhanced Half-life
EU	European Union
EUHASS	European Haemophilia Safety Surveillance
FEIBA	Factor eight inhibitor bypass agent
FIX	Factor nine
FVII	Factor seven
FVIII	Factor eight
GCP	Good clinical practice
GLH	Genomics Laboratory Hub
GLN	Genetic Laboratory Network
GOSH	Great Ormond Street Hospital
GWP	Genetics Working Party
HC	Haemophilia Centre
HCC	Hepatocellular carcinoma

HCIS	Haemophilia Clinical Information System
HCPA	Haemophilia Chartered Physiotherapists' Association
HCV	Hepatitis C virus
HEE	Health Education England
HJHS	Haemophilia Joint Health Score
HNA	Haemophilia Nursing Association
ICS	Integrated Clinical Academic
IPSG	International Prophylaxis Study Group
IQR	Interquartile range
ISTH	International Society on Thrombosis and Haemostasis
ITI	Immune tolerance induction
IU	International units
IU/dl	International units per decilitre
IU/kg	International units per kilogram
IWP	Inhibitor Working Party
kg	Kilogram
MAHA	Microangiopathic hemolytic anemia
MDSAS	Medical Data Solutions and Services
MDT	Multidisciplinary meeting
MTP	Minimally treated patients
NEQAS	National External Quality Assessment Service
NHD	National Haemophilia Database
NHF	National Hemophilia Foundation
NHS	National Health Service
NIBSC	National Institute for Biological Standards and Control
NIHR	National Institute for Health Research
PC	Personal computer
PDF	Portable Document Format
pd-FVIII	Plasma-derived factor eight
pd-FIX	Plasma-derived factor nine
PPIE	Patient and Public Involvement and Engagement
PUP	Previously untreated patient
PwHA	People with haemophilia A
PwHB	People with haemophilia B
PWP	Paediatric Working Party

PwSHA	People with severe haemophilia A
RCEM	Royal College of Emergency Medicine
RCPCH	Royal College of Paediatrics and Child Health
RfPB	NIHR Research for Patient Benefit
rEHL	Recombinant Enhanced Half-Life
rFIX	Recombinant factor IX
rFVIII	Recombinant factor VIII
rSHL	Recombinant Standard Half-Life
SAE	Serious Adverse Event
SHA	Severe Haemophilia A
SHL	Standard Half-life
SOP	Standard operating procedure
TF	Task Force
THS	The Haemophilia Society
UK	United Kingdom
UKHCDO	United Kingdom Haemophilia Centre Doctors' Organisation
UKNEQAS	United Kingdom National External Quality Assessment Service
VWD	Von Willebrand disease
VWF	Von Willebrand factor
WAPPS-Hemo	Web-Accessible Population Pharmacokinetic Service—Hemophilia
WFH	World Federation of Hemophilia
WP	Working party

New Registrations

Table 1 New registrations - Number of new registrations between April 2020 & March 2021, by diagnosis and gender

Diagnosis	Male	Female	Total
Acquired haemophilia A	4	4	8
Acquired von Willebrand disease	1	0	1
Dysfibrinogenemia	0	3	3
F.VII deficiency	2	1	3
F.XI deficiency	1	4	5
Haemophilia A	3	1	4
Haemophilia A carrier	0	3	3
Haemophilia B	5	0	5
Haemophilia B carrier	0	1	1
Heritable platelet disorder	2	2	4
Hypofibrinogenemia	3	1	4
Miscellaneous	1	0	1
Other platelet defects	1	6	7
Probable von Willebrand disease	1	0	1
Unclassified bleeding disorder	3	4	7
von Willebrand disease	6	5	11
Total	**33**	**35**	**68**

Carrier of Haemophilia A includes and Females with FVIII deficiency
Carrier of Haemophilia B includes and Females with FIX deficiency and Factor IX Leyden carriers

Table 1 shows the number of new registrations to the National Haemophilia Database of people with a Welsh postcode.

Table 2 New registrations of Haemophilia A & B between April 2020 & March 2021, by age and disease severity

Diagnosis	Age (years)	People by factor level (IU/dl)			
		< 1	1 - 5	> 5	Total
Haemophilia A	0-9	0	0	2	2
	10-19	0	0	0	0
	20-29	0	0	0	0
	30-39	0	0	0	0
	40-49	0	0	1	1
	50-59	0	1	0	1
	60-69	0	0	0	0
	70+	0	0	0	0
	Total	**0**	**1**	**3**	**4**
Haemophilia B	0-9	1	1	0	2
	10-19	0	1	2	3
	20-29	0	0	0	0
	30-39	0	0	0	0
	40-49	0	0	0	0
	50-59	0	0	0	0
	60-69	0	0	0	0
	70+	0	0	0	0
	Total	**1**	**2**	**2**	**5**

N.B Age calculated at mid-year, 30/09/2019

Table 2 shows the number of new registrations of people with Haemophilia A and B with a Welsh postcode. This is broken down by age and disease severity as per the ISTH severity classification.

In Register

Table 3 In Register – The total number of people in the register as of 31st March 2021 and the number treated between April 2020 & March 2021

Diagnosis	In register			Treated (n)	Treated %
	Males	Females	Total		
Acquired haemophilia A	26	13	39	5	12.82%
Acquired prothrombin deficiency	1	0	1	0	0.00%
Acquired von Willebrand disease	8	1	9	0	0.00%
Afibrinogenemia	1	0	1	1	100.00%
Bernard-Soulier syndrome	0	2	2	1	50.00%
Co-inherited diagnoses	3	10	13	0	0.00%
Dysfibrinogenemia	9	26	35	0	0.00%
F.V deficiency	1	3	4	0	0.00%
F.VII deficiency	20	22	42	1	2.38%
F.X deficiency	0	1	1	0	0.00%
F.XI deficiency	44	84	128	0	0.00%
F.XIII deficiency	0	1	1	1	100.00%
Glanzmann's thrombasthenia	1	2	3	0	0.00%
Haemophilia A	292	2	294	152	51.70%
Haemophilia A carrier	0	80	80	3	3.75%
Haemophilia A with liver transplant	1	0	1	0	0.00%
Haemophilia B	65	1	66	30	45.45%
Haemophilia B carrier	0	25	25	3	12.00%
Heritable platelet disorder	2	2	4	0	0.00%
Hypodysfibrinogenemia	1	1	2	0	0.00%
Hypofibrinogenemia	8	8	16	2	12.50%
Miscellaneous	4	4	8	1	12.50%
Other platelet defects	53	101	154	2	1.30%
Platelet-type pseudo von Willebrand disease	3	3	6	0	0.00%
Probable von Willebrand disease	4	4	8	0	0.00%
Prothrombin deficiency	1	1	2	0	0.00%
Unclassified bleeding disorder	11	63	74	1	1.35%
von Willebrand disease	174	295	469	39	8.32%
Totals	**733**	**755**	**1,488**	**242**	

Table 3 shows the total number of active registrations of people with a Welsh postcode and the number who were issued treatment during 2020/21.

Table 4 In Register – The total number of people in the register as of 31st March 2021, by diagnosis and Health Board

Diagnosis	Aneurin Bevan University Health Board	Betsi Cadwaladr University Health Board	Cardiff and Vale University Health Board	Cwm Taf Morgannwg University Health Board	Hywel Dda University Health Board	Powys Teaching Health Board	Swansea Bay University Health Board	Total
Acquired haemophilia A	3	5	9	10	5	2	5	39
Acquired prothrombin deficiency	0	0	1	0	0	0	0	1
Acquired von Willebrand disease	2	1	4	1	0	0	1	9
Afibrinogenemia	0	0	0	1	0	0	0	1
Bernard-Soulier syndrome	0	1	1	0	0	0	0	2
Co-inherited diagnoses	2	4	2	0	1	3	1	13
Dysfibrinogenemia	7	2	16	5	1	1	3	35
F.V deficiency	2	0	0	0	1	0	1	4
F.VII deficiency	7	13	6	4	8	1	3	42
F.X deficiency	0	0	1	0	0	0	0	1
F.XI deficiency	57	11	19	10	12	2	17	128
F.XIII deficiency	0	1	0	0	0	0	0	1
Glanzmann's thrombasthenia	0	0	1	0	2	0	0	3
Haemophilia A	58	55	56	41	28	8	48	294
Haemophilia A carrier	14	19	14	5	6	0	22	80
Haemophilia A with liver transplant	0	0	0	1	0	0	0	1
Haemophilia B	16	8	14	15	7	1	5	66
Haemophilia B carrier	5	1	6	7	2	2	2	25
Heritable platelet disorder	0	1	2	1	0	0	0	4
Hypodysfibrinogenemia	0	0	1	0	0	0	1	2
Hypofibrinogenemia	2	1	4	7	1	0	1	16
Miscellaneous	2	2	1	2	0	0	1	8
Other platelet defects	25	44	37	31	4	4	9	154
Platelet-type pseudo von Willebrand disease	0	0	0	1	2	3	0	6
Probable von Willebrand disease	3	2	2	0	0	1	0	8
Prothrombin deficiency	0	0	0	1	1	0	0	2
Unclassified bleeding disorder	22	3	19	13	4	1	12	74
von Willebrand disease	80	156	81	36	40	58	18	469
Total	**307**	**330**	**297**	**192**	**125**	**87**	**150**	**1,488**

Table 4 shows the number of people registered by health board. People are allocated to a health board based on their home postcode. The source database used for mapping postcodes to health boards is the ONS Postcode Directory (Nov 2020) and is available to download at https://ons.maps.arcgis.com/home/item.html?id=8da1cb5b6daa4d72b8bbef115cf26746.

Table 5 In register – The total number of people with haemophilia A & B in the register as of 31st March 2021, by severity and age group

Diagnosis	Age (years)	Number of people by factor level (IU/dl)			
		< 1	1 - 5	> 5	Total
Haemophilia A	<18 years	26	10	21	**57**
	≥18 years	62	35	140	**237**
Total		**88**	**45**	**161**	**294**
Haemophilia B	<18 years	3	8	8	**19**
	≥18 years	11	16	20	**47**
Total		**14**	**24**	**28**	**66**

N.B Age calculated at mid-year, 30/09/2021

Table 5 shows a more detailed breakdown of active registrations of people with a Welsh postcode with haemophilia A and B. This is broken down by age and disease severity as per the ISTH severity classification.

Table 6 In register – The number of people with other selected bleeding disorders in the register as of 31st March 2021 and the number treated between April 2020 & March 2021, by disease severity

Diagnosis	Number of people by factor level (IU/dl)							
	<5		≥5		N/K		Total	
	In reg	Treated	In reg	Treated	In reg	Treated	In reg	Treated
F.V deficiency	-	-	4	-	-	-	4	-
F.VII deficiency	2	1	40	-	-	-	42	1
F.X deficiency	-	-	1	-	-	-	1	-
F.XI deficiency	9	-	119	-	-	-	128	-
Total	**11**	**1**	**164**	**-**	**-**	**-**	**175**	**1**

Diagnosis	<2		5 - <10		10 - <15		Total	
	In reg	Treated	In reg	Treated	In reg	Treated	In reg	Treated
F.XIII deficiency	1	1	-	-	-	-	1	1
Total	**1**	**1**	**-**	**-**	**-**	**-**	**1**	**1**

Table 6 shows the number of people with other selected bleeding disorders and a Welsh postcode known to the NHD during 2020/21. It is acknowledged that these disorders have no recognised classification of disease severity. However, the table above gives an idea of the range of registered levels.

Table 7 In Register – The total number of people with von Willebrand Disease in the register as of 31st March 2021 and the number treated between April 2020 & March 2021, by disease severity, age group and gender

von Willebrand disease	VWD activity (IU/dl)										Total	Treated
	<10	10 - 29	≥30	N/K	Sub total	<10	10 - 29	≥30	N/K	Sub total		
	<18 years					≥18 years						
Males												
Type 1	6	9	8	0	**23**	19	32	12	0	**63**	**86**	**2**
Type 2A	3	0	0	0	**3**	10	3	1	0	**14**	**17**	**2**
Type 2B	1	0	0	0	**1**	0	2	1	0	**3**	**4**	**2**
Type 2M	1	0	0	0	**1**	3	3	0	0	**6**	**7**	**0**
Type 2N	0	0	0	0	**0**	0	0	0	0	**0**	**0**	**0**
Type 2 unspecified	1	0	0	0	**1**	2	1	1	0	**4**	**5**	**0**
Type 3	2	1	0	0	**3**	2	0	0	0	**2**	**5**	**4**
Type unreported	2	2	2	1	**7**	9	8	12	0	**29**	**36**	**2**
Low VWF	1	0	1	0	**2**	1	2	8	0	**11**	**13**	**0**
Other	0	0	0	0	**0**	0	0	1	0	**1**	**1**	**0**
										Sub total males	**174**	**12**
Females												
Type 1	7	10	2	0	**19**	20	47	37	0	**104**	**123**	**10**
Type 2A	3	1	0	0	**4**	11	6	6	0	**23**	**27**	**7**
Type 2B	0	1	0	0	**1**	0	0	5	1	**6**	**7**	**0**
Type 2M	0	1	0	0	**1**	6	2	5	0	**13**	**14**	**0**
Type 2N	0	0	1	0	**1**	0	0	6	0	**6**	**7**	**1**
Type 2 unspecified	1	1	1	0	**3**	2	3	0	0	**5**	**8**	**1**
Type 3	0	0	0	0	**0**	1	0	0	0	**1**	**1**	**1**
Type unreported	2	3	3	0	**8**	12	16	44	3	**75**	**83**	**6**
Low VWF	0	0	3	0	**3**	0	2	19	0	**21**	**24**	**1**
Other	0	0	0	0	**0**	0	0	1	0	**1**	**1**	**0**
										Sub total females	**295**	**27**
										Grand total - males and females	**469**	**39**

Table 7 shows people registered with von Willebrand disease broken down by age, activity level, subtype, gender and treatment. Whilst there is no generally agreed severity classification for VWD, it is reported here in subdivisions from "<10, 10-29 and ≥30" to give some indication of the distribution of severity.

Treatment

Table 8 People with a Welsh postcode, treated between April 2020 & March 2021 by diagnosis all severities, and region which issued the treatment

Diagnosis	Region issuing treatment	People (n)
Haemophilia A	Birmingham & Black Country	1
	Chesire, Warrington & Wirral	19
	Wales	132
	Wessex	1
Haemophilia A carrier	Wales	3
Acquired haemophilia A	Wales	5
Haemophilia B	Chesire, Warrington & Wirral	2
	Leicestershire & Lincolnshire	1
	Wales	27
Haemophilia B carrier	Wales	3
von Willebrand disease	Chesire, Warrington & Wirral	1
	London	1
	Wales	38
F.VII deficiency	Wales	1
F.XIII deficiency	Wales	1
Afibrinogenemia	Wales	1
Bernard-Soulier syndrome	Chesire, Warrington & Wirral	1
Hypofibrinogenemia	Chesire, Warrington & Wirral	1
	Wales	1
Other platelet defects	Wales	2
Miscellaneous	South Yorkshire & Bassetlaw	1
Unclassified bleeding disorder	Wales	1
	Grand total	**244**

N.B This table may contain duplicates where a person received treatment from more than one region

Table 8 reports people with a Welsh postcode by the region that issued the treatment. Some people received treatment outside of Wales. More detail on the treatment issued to people with severe haemophilia A and B can be found in tables 12 and 18 respectively.

Table 9 People with a non-Welsh postcode, registered & treated at a Welsh Haemophilia Centre between April 2020 & March 2021, by diagnosis, all severities

Diagnosis	Region of residence	Registered (n)	Treated (n)
Haemophilia A	East Midlands	2	0
	East of England	2	0
	London	2	0
	North West	1	0
	South Central	3	0
	South East Coast	1	0
	South West	5	0
	West Midlands	3	0
	Sub total	**19**	**0**
Haemophilia B	South Central	1	0
	South East Coast	1	0
	Sub total	**2**	**0**
von Willebrand disease	East Midlands	3	0
	East of England	1	0
	Greater Glasgow and Clyde	1	0
	London	1	0
	North West	1	0
	South West	3	0
	West Midlands	2	0
	Yorkshire and the Humber	2	0
	Sub total	**14**	**0**
Haemophilia A carrier	South West	1	0
	London	2	0
	Invalid postcode	2	0
	Sub total	**5**	**0**
Acquired von Willebrand disease	South West	1	0
	Sub total	**1**	**0**
F.VII deficiency	North East	1	0
	South West	1	0
F.XI deficiency	South Central	1	0
	South West	2	0
Hypofibrinogenemia	South West	1	0
Combined II+VII+IX+X deficiency	East Midlands	1	0
Glanzmann's thrombasthenia	London	1	0
Co-inherited diagnoses	West Midlands	2	0
Other platelet defects	East Midlands	1	0
	South West	1	0
Unclassified bleeding disorder	South West	4	0
	Grand total	**57**	**0**

Those reported in Table 9 were registered at or issued treatment from a Welsh Haemophilia Centre during 2020/21, however, they have a postcode recorded on the NHD which falls outside of Wales.

Haemophilia A and product use

Table 10 Factor VIII and Emicizumab issued, by diagnosis (all severities)

Diagnosis	FVIII (IU)				Emicizumab		Total
	People treated	Plasma-derived	Recombinant	Enhanced half-life	People treated	Emicizumab	
Acquired haemophilia A	1	-	9,500	-	0	-	9,500
Haemophilia A	140	392,640	15,805,500	5,193,536	24	65,208	21,456,884
Haemophilia A carrier	2	-	24,000	-	0	-	24,000
von Willebrand disease	30	733,500	-	-	0	-	733,500
Total	**173**	**1,126,140**	**15,839,000**	**5,193,536**	**24**	**65,208**	**22,223,884**

Includes products containing a combination of VWF and FVIII, which are reported in FVIII units

Table 10 shows the number of people with a Welsh postcode who were issued factor VIII concentrate during 2020/21. Also shown are the number of units issued broken down by diagnosis and product type. No investigational products were reported.

Table 11 Products issued to treat Haemophilia A (including inhibitors)

Manufacturer	Product	People (n)	Total units
BPL	Optivate	1	392,640
Novo Nordisk	Esperoct	12	2,080,500
	NovoEight	14	1,438,000
	NovoSeven	2	415
Pfizer	ReFacto AF	48	5,599,250
Roche	Hemlibra (mg)	24	65,208
SOBI/Biogen	Elocta	21	2,915,036
Takeda	ADYNOVI	2	198,000
	Advate	73	8,768,250
	FEIBA	3	67,000
Various manufacturers	Desmopressin	5	189

Units in IU unless otherwise stated

Table 11 shows the number of units of products issued to people with a Welsh postcode with Haemophilia A, all severities, including those with inhibitors, broken down by supplier.

Table 12 Products issued by Haemophilia Centre and Health Board for people with *Severe* Haemophilia A (incl. treatment for inhibitors)

Haemophilia centre issuing treatment	Health board based on person's postcode	Severe haemophilia A					
		Treated with FVIII (n)	Total FVIII units	Mean (FVIII) usage	Treated with Emicizumab (n)	Total Emicizumab units	Mean (Emicizumab) usage
Bangor	Betsi Cadwaladr University Health Board	9	3,713,140	412,571	0	0	0
Birmingham	Swansea Bay University Health Board	1	237,000	237,000	0	0	0
Cardiff	Aneurin Bevan University Health Board	14	3,232,500	230,893	3	6,150	2,050
	Cardiff and Vale University Health Board	10	1,698,000	169,800	3	14,700	4,900
	Cwm Taf Morgannwg University Health Board	17	4,178,000	245,765	1	30	30
	Hywel Dda University Health Board	3	497,000	165,667	2	5,250	2,625
	Powys Teaching Health Board	1	341,000	341,000	1	2,400	2,400
	Swansea Bay University Health Board	6	674,536	112,423	3	10,140	3,380
Liverpool	Betsi Cadwaladr University Health Board	7	2,144,000	306,286	1	750	750
Liverpool Childrens	Betsi Cadwaladr University Health Board	4	637,000	159,250	3	6,840	2,280
Manchester	Betsi Cadwaladr University Health Board	1	1,000	1,000	1	6,480	6,480
Swansea	Hywel Dda University Health Board	2	204,000	102,000	2	7,140	3,570
	Swansea Bay University Health Board	7	628,500	89,786	1	2,220	2,220
Totals		**82**	**18,185,676**	**197,957**	**21**	**62,100**	**2,360**

Table 12 reports the number of people with a Welsh postcode with severe haemophilia A treated and the number of units of products issued during 2020/21. This is broken down by the haemophilia centre which issued the treatment and by health board based on the person's postcode as recorded on the NHD.

Note: The total number of patients is the unique number of patients regardless of the number of centres a patients attends.

Table 13 Product usage by Health Board for people with *Severe Haemophilia A* only (incl. treatment for inhibitors)

Health board	General population	Severe haemophilia A							
		Treated with FVIII (n)	Total FVIII units (IU)	Mean usage	FVIII units per capita	Treated with Emicizumab (n)	Total Emicizumab units (IU)	Mean usage	Emicizumab units per capita
Aneurin Bevan University Health Board	598,194	14	3,232,500	230,893	5.40	3	6,150	2,050	0.01
Betsi Cadwaladr University Health Board	703,361	21	6,495,140	309,292	9.23	5	14,070	2,814	0.02
Cardiff and Vale University Health Board	504,497	10	1,698,000	169,800	3.37	3	14,700	4,900	0.03
Cwm Taf Morgannwg University Health Board	449,836	17	4,178,000	245,765	9.29	1	30	30	0.00
Hywel Dda University Health Board	389,719	5	701,000	140,200	1.80	4	12,390	3,098	0.03
Powys Teaching Health Board	133,030	1	341,000	341,000	2.56	1	2,400	2,400	0.02
Swansea Bay University Health Board	390,949	12	1,540,036	128,336	3.94	4	12,360	3,090	0.03
Totals	**3,169,586**	**80**	**18,185,676**	**223,612**	**5.74**	**21**	**62,100**	**2,626**	**0.02**

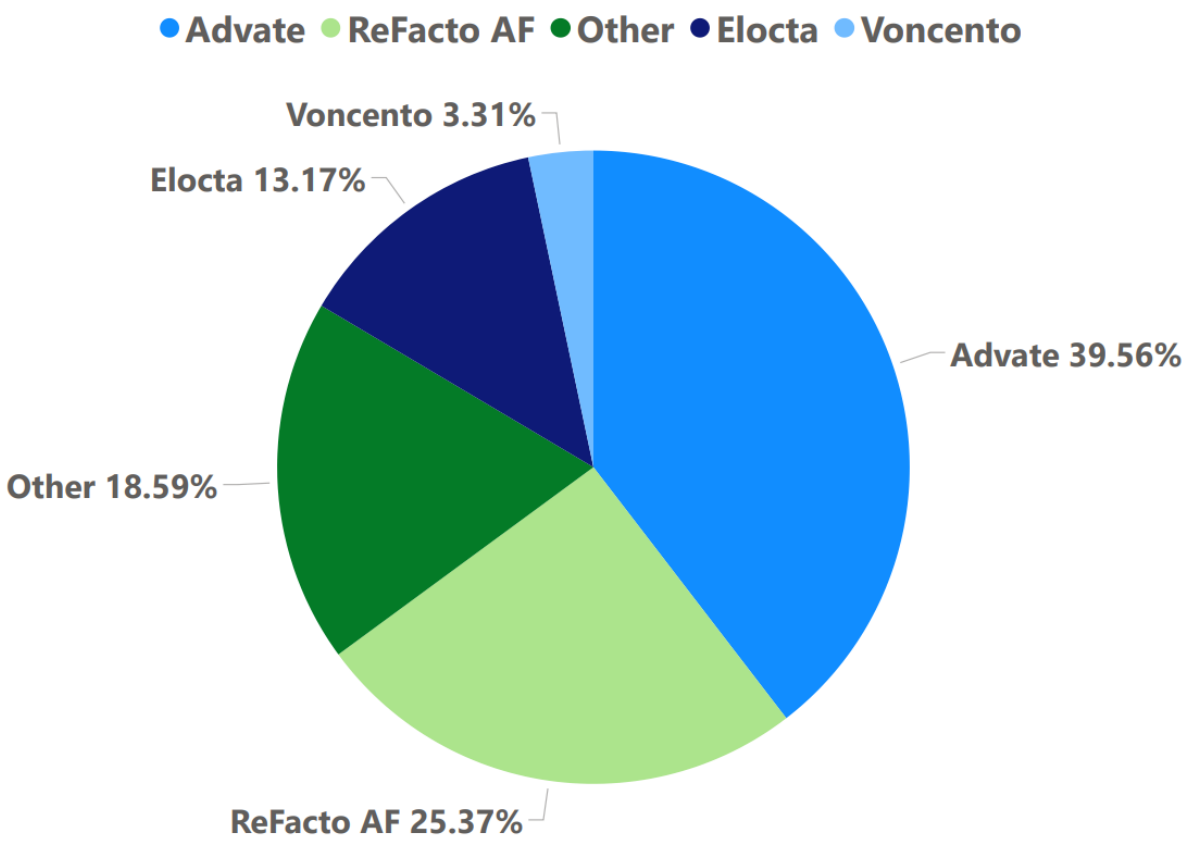
Mid-2020 population estimates, Office for National Statistics. Published by the Welsh Government, under the Open Government Licence v3.0. Updated June 2021

https://statswales.gov.wales/Catalogue/Population-and-Migration/Population/Estimates/Local-Health-Boards/populationestimates-by-lhb-age

Table 13 reports the number of people with severe haemophilia A treated and number of units of products issued broken down by Health Board and ranked by the mean number of units issued per person. Usage per capita of population is also reported.

Note: This table does not contain duplicates. People are allocated to a Health Board based on their home postcode.

Figure 1 Market share of FVIII products (IU) issued between April 2020 & March 2021



Includes products containing a combination of VWF and FVIII, which are reported in FVIII units (IU).

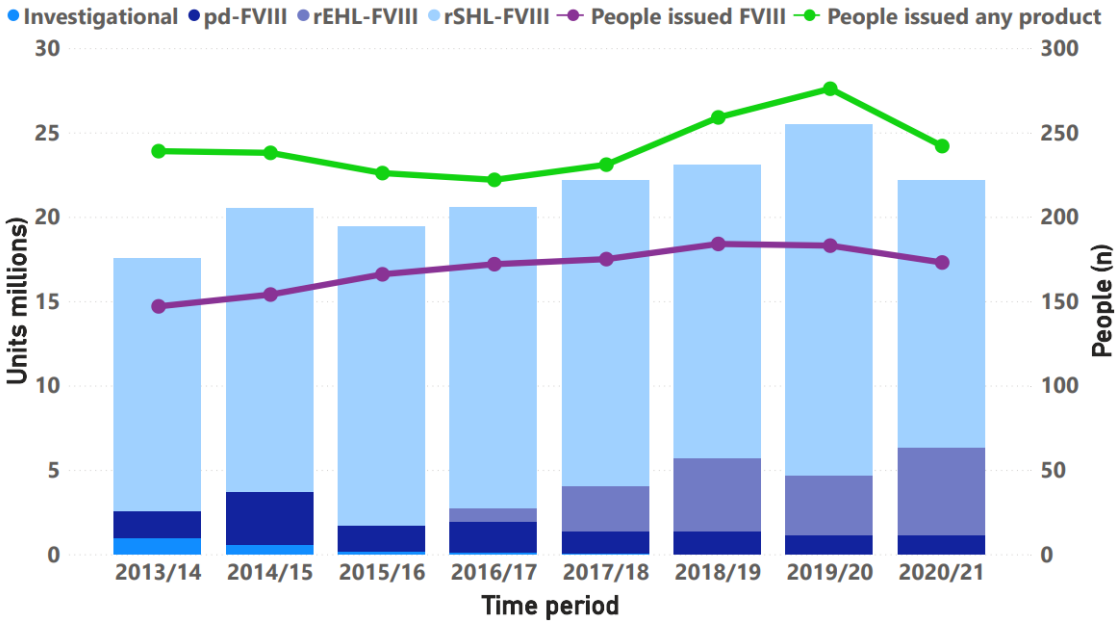
This pie chart does not contain the Hemlibra (mg) units issued.

Manufacturer	Product	People (n)	Units (IU)
Takeda	Advate	73	8,768,250
Pfizer	ReFacto AF	50	5,623,250
CSL Behring	Voncento	30	733,500
Roche	Hemlibra (mg)	24	65,208
SOBI/Biogen	Elocta	21	2,915,036
Various manufacturers	Other	30	4,118,640
	Total	**228**	**22,223,884**

Figure 1 shows the market breakdown of FVIII products issued for all diagnoses, including people with inhibitors. Table 1 shows the number of units and number of people issued with FVIII products and Hemlibra.

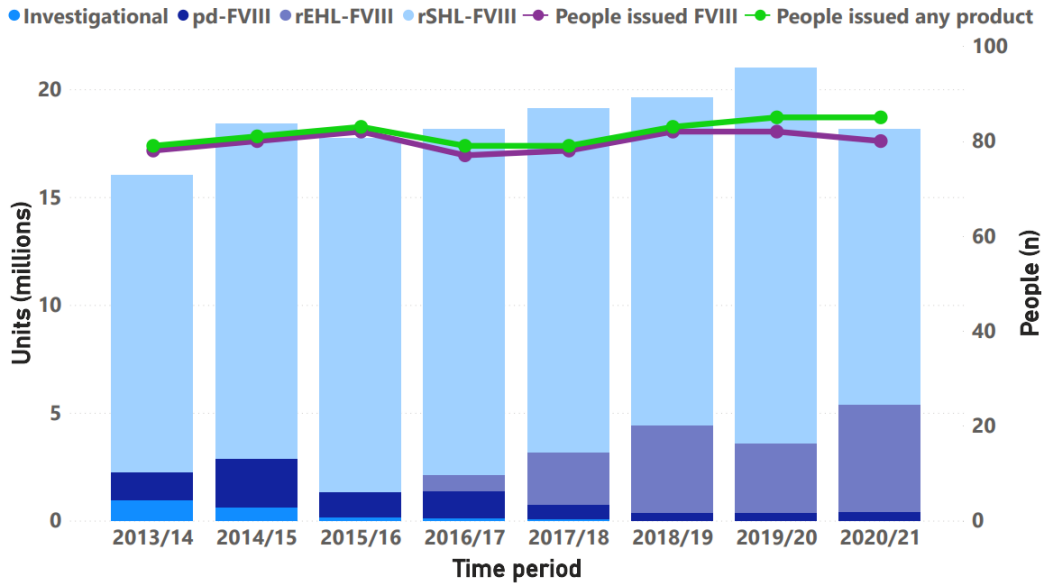
NOTE: The number of people in this table cannot be compared with Table 10 as this table includes people treated with more than one product type. The numbers in Table 10 do not contain duplicates.

Figure 2 Products issued by financial year between April 2013 & March 2021 – all diagnoses, all severities



Includes products containing a combination of VWF and FVIII, which are reported in FVIII units

Figure 3 Products issued by financial year between April 2013 & March 2021 – *Severe Haemophilia A only*



Includes products containing a combination of VWF and FVIII, which are reported in FVIII units

Figures 2 and 3 give an historical view of the number of factor VIII units issued between 2013/14 and 2020/21 for all diagnoses and for people with severe haemophilia A respectively. The number of people reported to have been treated with FVIII is shown by the purple line using a secondary axis, and the total number of patients treated with any product is shown by the green line.

Table 14 Data table for Figure 2 - Products issued by financial year between April 2013 & March 2021 - all diagnoses

Year	Plasma-derived		Recombinant		Investigational rFVIII		Enhanced half-life		Total		People issued FVIII		People issued Emicizumab		People issued any product	
	IU	% difference year on year	IU	% difference year on year	IU	% difference year on year	IU	% difference year on year	IU	% difference year on year	n	% difference year on year	n	% difference year on year	n	% difference year on year
2013/14	1,615,820	-	14,957,000	-	964,000	-	-	-	17,536,820	-	147	-	-	-	239	-
2014/15	3,091,000	+91.3	16,811,000	+12.4	604,170	-37.33	-	-	20,506,170	+16.9	154	+4.8	-	-	238	-0.42
2015/16	1,538,500	-50.23	17,740,000	+5.5	176,000	-70.87	-	-	19,454,500	-5.13	166	+7.8	-	-	226	-5.04
2016/17	1,774,975	+15.4	17,859,398	+0.7	134,875	-23.37	794,500	-	20,563,748	+5.7	172	+3.6	-	-	222	-1.77
2017/18	1,279,410	-27.92	18,133,500	+1.5	76,020	-43.64	2,668,000	+235.8	22,156,930	+7.7	175	+1.7	-	-	231	+4.1
2018/19	1,373,380	+7.3	17,359,750	-4.27	7,875	-89.64	4,351,500	+63.1	23,092,505	+4.2	184	+5.1	3	-	259	+12.1
2019/20	1,163,425	-15.29	20,799,250	+19.8	-	-	3,542,000	-18.60	25,504,675	+10.4	183	-0.54	14	+366.7	276	+6.6
2020/21	1,126,140	-3.20	15,839,000	-23.85	-	-	5,193,536	+46.6	22,158,676	-13.12	173	-5.46	24	+71.4	242	-12.32

Table 15 Data table for Figure 3 - Products issued by financial year between April 2013 & March 2021 - *Severe Haemophilia A*

Year	Plasma-derived		Recombinant		Investigational rFVIII		Enhanced half-life		Total		People issued FVIII		People issued Emicizumab		People issued any product	
	IU	% difference year on year	IU	% difference year on year	IU	% difference year on year	IU	% difference year on year	IU	% difference year on year	n	% difference year on year	n	% difference year on year	n	% difference year on year
2013/14	1,275,000	-	13,773,250	-	964,000	-	-	-	16,012,250	-	78	-	-	-	79	-
2014/15	2,291,500	+79.7	15,532,750	+12.8	604,170	-37.33	-	-	18,428,420	+15.1	80	+2.6	-	-	81	+2.5
2015/16	1,135,000	-50.47	16,410,500	+5.7	176,000	-70.87	-	-	17,721,500	-3.84	82	+2.5	-	-	83	+2.5
2016/17	1,236,475	+8.9	16,016,898	-2.40	134,875	-23.37	768,500	-	18,156,748	+2.5	77	-6.10	-	-	79	-4.82
2017/18	647,310	-47.65	15,968,000	-0.31	76,020	-43.64	2,455,000	+219.5	19,146,330	+5.5	78	+1.3	-	-	79	-
2018/19	361,880	-44.09	15,202,500	-4.79	7,875	-89.64	4,052,500	+65.1	19,624,755	+2.5	82	+5.1	3	-	83	+5.1
2019/20	372,925	+3.1	17,422,250	+14.6	-	-	3,217,000	-20.62	21,012,175	+7.1	82	-	14	+366.7	85	+2.4
2020/21	392,640	+5.3	12,790,000	-26.59	-	-	5,003,036	+55.5	18,185,676	-13.45	80	-2.44	21	+50	85	-

Tables 14 and 15 are the data tables for Figures 2 and 3.

Haemophilia B and Factor IX use

Table 16 Factor IX issued, by diagnosis

Diagnosis	People (n)	FIX (IU)			
		Plasma-derived	Recombinant		Total
			Standard half-life	Enhanced half-life	
Haemophilia B	30	-	1,526,750	663,250	2,190,000
Haemophilia B carrier	3	-	30,000	9,000	39,000
Total	**33**	**-**	**1,556,750**	**672,250**	**2,229,000**

Table 16 shows the number of people with a Welsh postcode who were issued factor IX concentrate during 2020/21. Also shown are the number of units issued broken down by diagnosis and product type.

Table 17 Products issued to treat Haemophilia B (including inhibitors)

Manufacturer	Product	People (n)	Total units
CSL Behring	IDELVION	4	322,500
NovoNordisk	Refixia	1	82,000
Pfizer	Benefix	22	1,438,750
SOBI/Biogen	ALPROLIX	3	258,750
Shire	RIXUBIS	2	88,000

Units in IU unless otherwise stated

Table 17 shows the number of units of products issued to people with a Welsh postcode with haemophilia B, all severities, including those with inhibitors, broken down by supplier.

Table 18 Factor IX issued to people with *Severe* Haemophilia B (incl. treatment for inhibitors), by Haemophilia Centre and Health Board

Haemophilia centre issuing treatment	Health board based on person's postcode	Severe haemophilia B		
		Treated (n)	Total FIX units	Mean usage
Cardiff	Aneurin Bevan University Health Board	3	385,750	128,583
	Cwm Taf Morgannwg University Health Board	5	566,250	113,250
	Swansea Bay University Health Board	1	82,000	82,000
Liverpool	Betsi Cadwaladr University Health Board	1	216,000	216,000
Swansea	Hywel Dda University Health Board	1	29,000	29,000
	Swansea Bay University Health Board	2	277,500	138,750
	Totals	**13**	**1,556,500**	**117,931**

Table 18 reports the number of people with severe haemophilia B treated and the number of units of factor IX issued during 2020/21. This is broken down by the haemophilia centre which issued the treatment and by health board based on the person's postcode as recorded on the NHD.

Note: One person was issued treatment from two different centres.

Table 19 Factor IX usage for people with *Severe Haemophilia B* only (incl. treatment for inhibitors), by Health Board

Health board	General population	Severe haemophilia B			
		Treated (n)	Total FIX units (IU)	Mean usage	FIX units per capita
Aneurin Bevan University Health Board	598,194	3	385,750	128,583	0.64
Betsi Cadwaladr University Health Board	703,361	1	216,000	216,000	0.31
Cwm Taf Morgannwg University Health Board	449,836	5	566,250	113,250	1.26
Hywel Dda University Health Board	389,719	1	29,000	29,000	0.07
Swansea Bay University Health Board	390,949	2	359,500	179,750	0.92
Totals	**2,532,059**	**12**	**1,556,500**	**133,317**	**3.20**

Ranked by mean usage

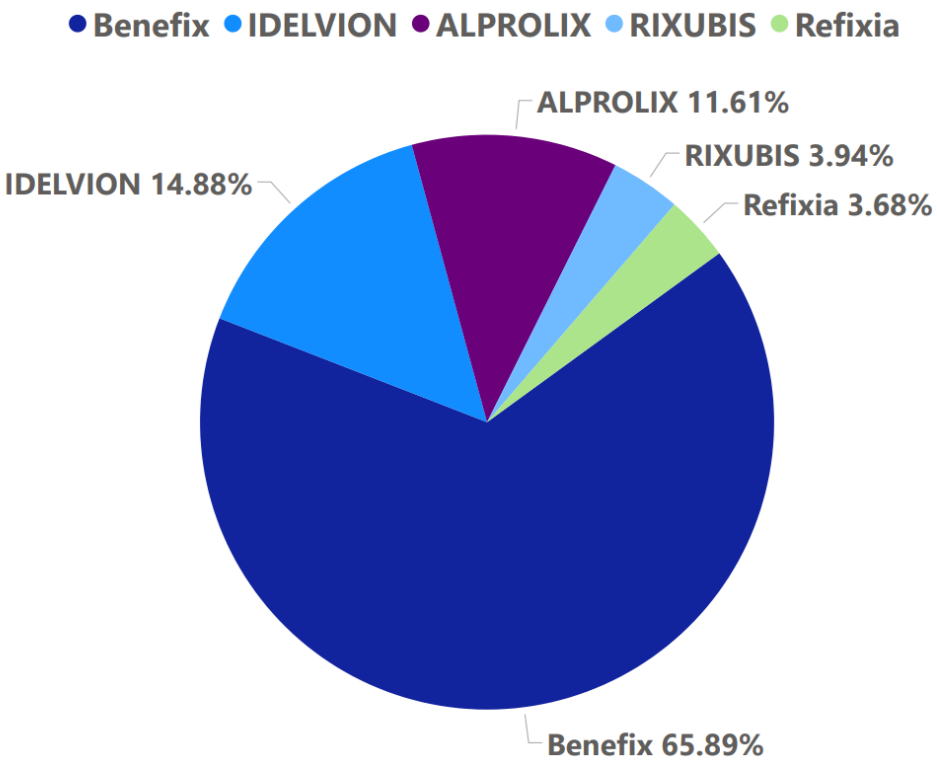
Mid-2020 population estimates, Office for National Statistics. Published by the Welsh Government, under the Open Government Licence v3.0. Updated June 2021

https://statswales.gov.wales/Catalogue/Population-and-Migration/Population/Estimates/Local-Health-Boards/populationestimates-by-lhb-age

Table 19 reports the number of people with severe haemophilia B treated and number of units of factor IX issued broken down by Health Board and ranked by the mean number of units issued per person. Usage per capita of population is also reported.

This table does not contain duplicates. People are allocated to a Health Board based on their home postcode.

Figure 4 Market share of factor IX concentrates (IU) issued to people with a Welsh postcode between April 2020 & March 2021



Manufacturer	Product	People (n)	Units (IU)
Pfizer	Benefix	24	1,468,750
CSL Behring	IDELVION	5	331,500
SOBI/Biogen	ALPROLIX	3	258,750
Takeda	RIXUBIS	2	88,000
NovoNordisk	Refixia	1	82,000
	Total	**35**	**2,229,000**

Figure 4 shows the market breakdown of factor IX concentrates issued for all diagnoses, including people with inhibitors. Also included is a table showing the number of units and number of people issued with these products.

NOTE: The number of people in this table cannot be compared with table 16 as this table includes people treated with more than one product type. The numbers in Table 16 do not contain duplicates.

Figure 5 Factor IX units by financial year between April 2013 & March 2021 - all diagnoses, all severities

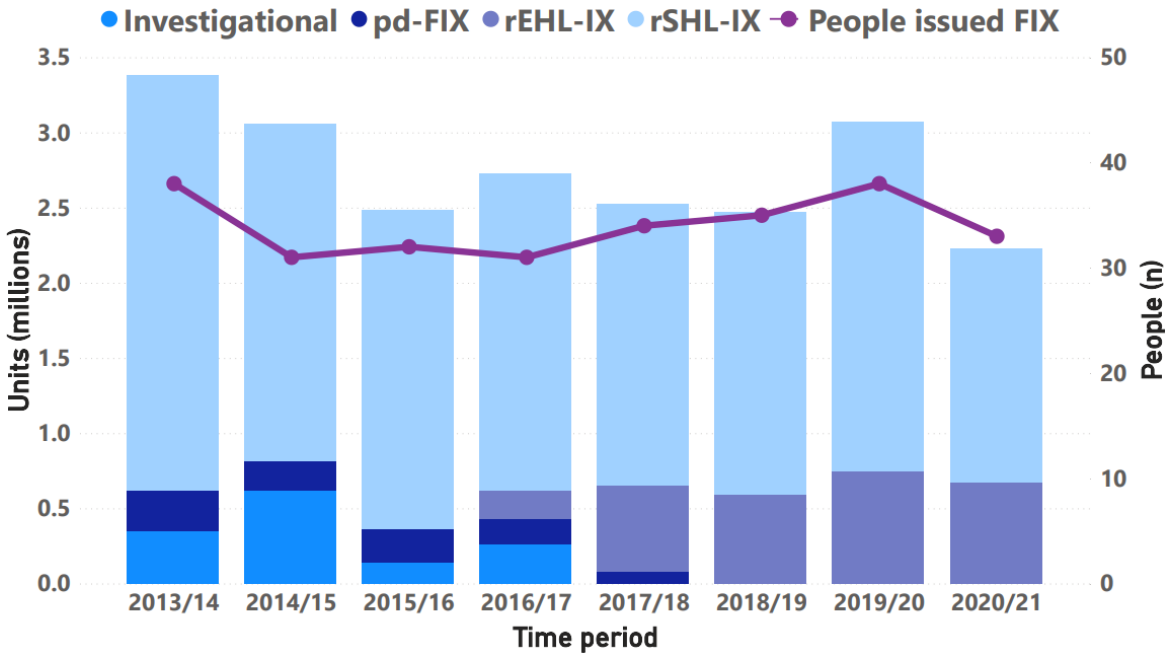


Figure 5 gives an historical view of the number of factor IX units issued between 2013/14 and 2020/21 for all diagnoses. The number of people reported to have been treated with FIX is shown by the purple line using a secondary axis.

Table 20 Data table for figure 5 - Factor IX units issued by financial year between April 2013 & March 2021 – all diagnoses

Year	Plasma-derived		Recombinant		Investigational rFVIII		Enhanced half-life		Total		People issued FIX	
	IU	% difference year on year	IU	% difference year on year	IU	% difference year on year	IU	% difference year on year	IU	% difference year on year	n	% difference year on year
2013/14	274,000	-	2,761,270	-	349,016	-	-	-	3,384,286	-	38	-
2014/15	198,000	-27.74	2,240,500	-18.86	617,447	+76.9	-	-	3,055,947	-9.70	31	-18.42
2015/16	228,000	+15.2	2,119,000	-5.42	136,553	-77.88	-	-	2,483,553	-18.73	32	+3.2
2016/17	170,000	-25.44	2,108,000	-0.52	263,692	+93.1	184,015	-	2,725,707	+9.8	31	-3.13
2017/18	78,000	-54.12	1,870,500	-11.27	-	-	578,500	+214.4	2,527,000	-7.29	34	+9.7
2018/19	-	-	1,876,000	+0.3	-	-	595,000	+2.9	2,471,000	-2.22	35	+2.9
2019/20	-	-	2,323,750	+23.9	-	-	748,750	+25.8	3,072,500	+24.3	38	+8.6
2020/21	-	-	1,556,750	-33.01	-	-	672,250	-10.22	2,229,000	-27.45	33	-13.16

Table 20 is the data table for Figure 5.

Von Willebrand Disease, selected other bleeding disorders and acquired defects

Tables 21 - 23 shows the number of people with Welsh postcodes and reported products issued to treat von Willebrand disease, selected other disorders and acquired bleeding disorders during 2020/21, broken down by supplier.

Table 21 Concentrates issued to treat von Willebrand Disease

Manufacturer	Product	People (n)	Total units
CSL Behring	Voncento	30	733,500
Various manufacturers	Desmopressin	9	335

Units in IU unless otherwise stated
Products containing VWF as well as FVIII are reported in FVIII units

Table 22 Concentrates issued to treat selected other bleeding disorders

Manufacturer	Product	People treated (n)	F.VII	F.XIII
CSL Behring	Fibrogammin P	1	-	18,750
Novo Nordisk	NovoSeven (mg)	1	8	-

Units in IU unless otherwise stated

Table 23 Concentrates issued to treat Acquired Defects

Manufacturer	Product	People treated (n)	Acquired haemophilia A
Takeda	OBIZUR	1	9,500
	FEIBA	4	89,000

Units in IU unless otherwise stated
Products containing VWF as well as FVIII are reported in FVIII units

Table 24 Inhibitors by disease severity

Diagnosis	Severity (IU/dl) / Subtype	In register *	Inhibitors		
			Ongoing n (%)	New n (%)	Historical n (%)
Haemophilia A	< 1	102	10 (9.8)	0 (0.0)	19 (18.6)
	1 - 5	52	1 (1.9)	0 (0.0)	2 (3.8)
	> 5	174	2 (1.1)	0 (0.0)	5 (2.9)
	Total	**328**	**13 (4.0)**	**0 (0.0)**	**26 (7.9)**
Haemophilia B	< 1	15	0 (0.0)	0 (0.0)	0 (0.0)
	1 - 5	26	0 (0.0)	0 (0.0)	0 (0.0)
	> 5	30	0 (0.0)	0 (0.0)	0 (0.0)
	Total	**71**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
von Willebrand disease	Type 3	9	0 (0.0)	0 (0.0)	1 (11.1)
	Others	476	0 (0.0)	0 (0.0)	0 (0.0)
	Total	**485**	**0 (0.0)**	**0 (0.0)**	**1 (0.2)**

** Including people not regularly treated*

Table 24 shows the incidence of new inhibitors during 2020/21, the prevalence of those still considered active and those considered inactive inhibitors for haemophilia A, B and von Willebrand disease, broken down by disease severity.

Those labelled “new” were reported for the first time in the year 2020/21. Those labelled “ongoing” are those reported in previous years which have not been eradicated. Those reported as “historical” are those reported to have been previously eradicated or disappeared and not ongoing.

Table 25 Products issued to people with congenital bleeding disorders reported to have a positive inhibitor during 2020/21

Manufacturer	Product	People (n)	Units
Haemophilia A			
Baxter	Advate	2	955,750
	FEIBA	3	67,000
Novo Nordisk	NovoSeven (mg)	2	415
Pfizer	ReFacto AF	1	30,000
Roche	Hemlibra (mg)	3	4,860
SOBI/Biogen	Elocta	6	956,036

Units in IU unless otherwise stated

Table 25 shows the number of people with a Welsh postcode and an inhibitor newly reported or ongoing during 2020/21 plus reported products issued, broken down by diagnosis and supplier. As people may be issued with more than one product in the year, there is some double counting in this table.

Table 26 Adverse Events

Adverse event	Number of events
Allergy event	0
Infection event	0
Inhibitor event	0
ICH event	3
Malignancy event	3
Neurological event	0
Other event	2
Poor efficacy event	0
Thrombotic event	1
COVID-19 event	3
Total	**12**

See table 24 for breakdown of inhibitors by disease severity in Haemophilia A, B and von Willebrand disease

Table 27 shows the type and number of adverse events reported in people with a Welsh postcode during 2020/21.

Table 27 Causes of Death

Diagnosis	Cause of death	Severity by factor level (IU/dl)		
		1 - 5	> 5	Total
Haemophilia A	COAD	0	1	**1**
	COVID-19	0	1	**1**
	Carcinoma	1	0	**1**
	Ischaemic heart disease	0	1	**1**
	Unknown	0	1	**1**
Haemophilia A carrier	ARDS	0	2	**2**
	Unknown	0	1	**1**
Haemophilia B carrier	COVID-19	0	1	**1**
Acquired haemophilia A	ARDS			**1**
	Carcinoma			**1**
	Infection (bacterial)			**1**
	Ischaemic heart disease			**1**
	Renal failure			**1**
	COVID-19			**1**
	Unknown			**1**
von Willebrand disease	Venous thromboembolism			**1**
	Unknown			**1**
Acquired von Willebrand disease	Cerebral haemorrhage			**2**
Miscellaneous	Unknown			**2**
Unclassified bleeding disorder	Unknown			**5**
Total				**27**

Table 27 shows the causes of death reported in people with a Welsh postcode during 2020/21, broken down by diagnosis and disease severity.