Integrated Impact Assessment Report for Clinical Commissioning Policies			
Policy Reference Number	ID014		
Policy Title	Emicizumab as prophylaxis in people with congenital haemophilia A without factor VIII inhibitors (all ages) Proposal **for routine commission** (ref A3.1)		
Lead Commissioner	William Horsley	**Clinical Lead**	P Chowdary
Finance Lead	Craig Charlton	**Analytical Lead**	

Integrated Impact Assessment – Index		
Section A – Activity	**Section B - Service**	**Section C – Finance**
A1 Current Patient Population & Demography / Growth	B1 Service Organisation	C1 Tariff
A2 Future Patient Population & Demography	B2 Geography & Access	C2 Average Cost per Patient
A3 Activity	B3 Implementation	C3 Overall Cost Impact of this Policy to NHS England
A4 Existing Patient Pathway	B4 Collaborative Commissioning	C4 Overall cost impact of this policy to the NHS as a whole
A5 Comparator (next best alternative treatment) Patient Pathway		C5 Funding
A6 New Patient Pathway		C6 Financial Risks Associated with Implementing this Policy
A7 Treatment Setting		C7 Value for Money
A8 Coding		C8 Cost Profile
A9 Monitoring		

About this Impact Assessment: instructions for completion and explanatory notes
• Each section is divided into themes. • Each theme sets out a number of questions. • All questions are answered by selecting a drop down option or including free text. • Free text boxes are provided to enable succinct relevant commentary to be added which explains the rationale for response or assumption. Please limit responses to 3 sentences of explanatory text. • Data in this document is either drawn from one of the relevant policy documents or a source for the information is provided. • Where assumptions are included where data is not available, this is specified.

<table>
<tr><th colspan="2">Section A - Activity Impact</th></tr>
<tr><td colspan="2">A1 Current Patient Population & Demography / Growth</td></tr>
<tr><td>A1.1 Prevalence of the disease/condition.</td><td>The UK National Haemophilia Database Bleeding Disorder Statistics for April 2016 to March 2017 reports that there are 6,478 people in the UK with mild, moderate or severe forms of haemophilia A (not including low-level carriers; factor VIII level ≥40 IU/dL). For England only, 5,205 people do not have inhibitors to factor VIII. Of these people 1,419 have severe haemophilia. The eligible patient population for emicizumab in England is considered to be equivalent to the patients with severe haemophilia A without current inhibitors. See section A1.2
Source: Policy Proposition section 6</td></tr>
<tr><td>A1.2 Number of patients currently eligible for the treatment according to the proposed policy commissioning criteria.</td><td>1,419
Source: UK National Haemophilia Database 2017/18

<table><tr><th>Regimen</th><th>Severe</th></tr><tr><td>Prophylaxis</td><td>1,382</td></tr><tr><td>On-demand</td><td>37</td></tr><tr><td>Total</td><td>1,419</td></tr></table>Most but not quite all severe patients are treated with a prophylaxis regimen. The availability of emicizumab could have an impact on prophylaxis rates by encouraging or enabling more patients to adopt a prophylaxis regimen although clinical advice is that this may have, at best, only a small impact on treatment numbers if at all.</td></tr>
<tr><td>A1.3 Age group for which the treatment is proposed according to the policy commissioning criteria.</td><td><u>All ages</u>
Please specify
Emicizumab will be routinely commissioned as prophylaxis for adults and children with severe congenital haemophilia A (defined as factor VIII level</td></tr>
</table>

<table>
<tr><td></td><td><1 IU/dL, or <1% of normal) without current inhibitors to prevent bleeding episodes.</td></tr>
<tr><td>A1.4 Age distribution of the patient population eligible according to the proposed policy commissioning criteria</td><td>Not applicable</td></tr>
<tr><td>A1.5 How is the population currently distributed geographically?</td><td><u>Unevenly</u>
If unevenly, estimate regional distribution by %:
<table><tr><td>North</td><td>23%</td></tr><tr><td>Midlands & East</td><td>17%</td></tr><tr><td>London</td><td>40%</td></tr><tr><td>South</td><td>20%</td></tr></table>Source
Please specify
UK National Haemophilia Database 2017</td></tr>
<tr><td colspan="2">A2 Future Patient Population & Demography</td></tr>
<tr><td>A2.1 Projected changes in the disease/condition epidemiology, such as incidence or prevalence (prior to applying the new policy) in 2, 5, and 10 years?</td><td><u>Constant</u>
No known factors other than demographic growth in patient population identified.
A large proportion of the growth in UK haemophilia patient numbers over the last decade has been attributed to net inward migration from the EU. (ref UKHCDO) We have modelled the same rate of growth for the next ten years, although one could reasonably expect that this will slow or diminish.
Source: Clinical Evidence Review, Policy Working Group</td></tr>
</table>

<table>
<tr><td>A2.2 Are there likely to be changes in demography of the patient population and would this impact on activity/outcomes?</td><td><u>No</u>
Source: Policy Proposition section 6/other</td></tr>
<tr><td>A2.3 Expected net increase or decrease in the number of patients who will be eligible for the service, according to the proposed service specification commissioning criteria, per year in years 2-5 and 10?

Are these numbers in line with ONS growth assumptions for the age specific population? If not please justify the growth assumptions made.</td><td>Cumulative growth<table><tr><td>YR2 +/-</td><td>+19</td></tr><tr><td>YR3 +/-</td><td>+28</td></tr><tr><td>YR4 +/-</td><td>+37</td></tr><tr><td>YR5 +/-</td><td>+45</td></tr><tr><td>YR10 +/-</td><td>+83</td></tr></table>Source: Service specification proposition section 3.1

<u>No</u>
We have used historical trends from the National Haemophilia Database</td></tr>
<tr><td colspan="2">A3 Activity</td></tr>
<tr><td>A3.1 What is the purpose of new policy?</td><td><u>Confirm routine commissioning position of an additional new treatment</u>
The purpose of the new policy is to routinely commission emicizumab as prophylaxis in people with congenital haemophilia A without factor VIII inhibitors to prevent bleeding episodes where the patient has severe haemophilia A (defined as factor VIII level <1 IU/dL, or <1% of normal) in line with the United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO) guideline which state that prophylaxis should be commenced once a person has had 1 joint bleed; or 1 significant soft tissue bleed</td></tr>
</table>

A3.2 What is the annual activity associated with the existing pathway for the eligible population?	**1,419** *Source:* United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO) Please specify These are people with severe haemophilia A without inhibitors registered with the National Haemophilia Database for the full twelve months period starting April 2017 -31 March 2018 and issued with FVIII at least once within that period either prophylaxis or on-demand.
A3.3 What is the estimated annual activity associated with the proposed policy proposition pathway for the eligible population?	**1,419** *Source* UK National Haemophilia Database 2017. *Policy Proposition section 6:*
A3.4 What is the estimated annual activity associated with the next best alternative comparator pathway for the eligible population? If the only alternative is the existing pathway, please state 'not applicable' and move to A4.	Not applicable
A4 Existing Patient Pathway	
A4.1 **Existing pathway:** Describe the relevant currently routinely commissioned: • Treatment or intervention • Patient pathway • Eligibility and/or uptake estimates.	Current treatment options for haemophilia A without inhibitors are prophylactic or episodic (on-demand) treatment with recombinant factor VIII (either standard or enhanced half-life), the choice of which is guided primarily by disease severity and bleeding history. Treatment is to replace the missing FVIII via regular IV infusions 2-4 times weekly, or less commonly with on-demand infusion as needed. However, the relatively short half-life of recombinant FVIII results in peaks and troughs of protection, with the potential for breakthrough bleeds highest during trough periods. Since 2016, enhanced half-life factor VIII has been commissioned in England although multiple IV administrations per week

	(usually 2 or 3) remain typical. There are still a few patients who choose to use plasma-derived FVIII (prophylaxis or on-demand). *Source:* Policy proposition
A4.2. What are the current treatment access and stopping criteria?	*Source:* Defined by BCSH Guidelines: https://onlinelibrary.wiley.com/doi/full/10.1111/j.1365-2141.2010.08139.x
A4.3 What percentage of the total eligible population is expected to: a) Be clinically assessed for treatment b) Be considered to meet an exclusion criteria following assessment c) Choose to initiate treatment d) Comply with treatment e) Complete treatment?	If not known, please specify a) 100% b) 0% c) 100% d) 100% e) 100% *Source:* Policy Working Group
A5 Comparator (next best alternative treatment) Patient Pathway (NB: comparator/next best alternative does not refer to current pathway but to an alternative option)	
A5.1 **Next best comparator**: Is there another 'next best' alternative treatment which is a relevant comparator? *If yes, describe relevant* • *Treatment or intervention* • *Patient pathway* • *Actual or estimated eligibility and uptake*	**Yes** Recombinant standard half-life and enhanced half-life factor VIII (8). A few patients still use plasma-derived FVIII.
A5.2 What percentage of the total eligible population is estimated to:	N/A

a) Be clinically assessed for treatment b) Be considered to meet an exclusion criteria following assessment c) Choose to initiate treatment d) Comply with treatment e) Complete treatment?	
A6 New Patient Pathway	
A6.1 What percentage of the total eligible population is expected to: a) Be clinically assessed for treatment b) Be considered to meet an exclusion criteria following assessment c) Choose to initiate treatment d) Comply with treatment e) Complete treatment?	If not known, please specify a) 100% b) 0% c) 100% d) 100% e) 100% *Source:* Policy Working Group
A6.2 Specify the nature and duration of the proposed new treatment or intervention.	**Life long** Emicizumab is intended for long-term prophylactic treatment. ***Source: Roche submission***
A7 Treatment Setting	
A7.1 How is this treatment delivered to the patient?	*Select all that apply:* Emergency/Urgent care attendance ☐ Acute Trust: inpatient ☐ Acute Trust: day patient ☐

<table>
<tr>
<td></td>
<td>
<table>
<tr><td>Acute Trust: outpatient</td><td>☒</td></tr>
<tr><td>Mental Health provider: inpatient</td><td>☐</td></tr>
<tr><td>Mental Health provider: outpatient</td><td>☐</td></tr>
<tr><td>Community setting</td><td>☐</td></tr>
<tr><td>Homecare</td><td>☒</td></tr>
<tr><td>Other</td><td>☐</td></tr>
</table>
Please specify:
Treatment with emicizumab should be initiated and monitored under the supervision of a physician experienced in the treatment of haemophilia and/or bleeding disorders at a haemophilia comprehensive care centre. Once established, treatment may be continued under direction of a HCompCC at a Haemophilia Care Centre.
</td>
</tr>
<tr>
<td>A7.2 What is the current number of contracted providers for the eligible population by region?</td>
<td>
Haemophilia COMPREHENSIVE Care Centres
<table>
<tr><td>NORTH</td><td>7</td></tr>
<tr><td>MIDLANDS & EAST</td><td>5</td></tr>
<tr><td>LONDON</td><td>4</td></tr>
<tr><td>SOUTH</td><td>5</td></tr>
</table>
</td>
</tr>
<tr>
<td>A7.3 Does the proposition require a change of delivery setting or capacity requirements?</td>
<td>
<u>Yes</u>

Treatment would be restricted, initially at least, to comprehensive care centres only – treatment and Blueteq registration will only be permitted at HCompCC’s although patients may have their routine treatment once established from their local haemophilia provider.
Source: Policy Working Group.
</td>
</tr>
</table>

A8 Coding

A8.1 Specify the datasets used to record the new patient pathway activity.

*expected to be populated for all commissioned activity

Select all that apply:

Aggregate Contract Monitoring *	☐
Patient level contract monitoring	☐
Patient level drugs dataset	☐
Patient level devices dataset	☐
Devices supply chain reconciliation dataset	☐
Secondary Usage Service (SUS+)	☐
Mental Health Services DataSet (MHSDS)	☐
National Return**	☐
Clinical Database**	☒
Other**	☐

**If National Return, Clinical database or other selected, please specify: The UK National Haemophilia Database

A8.2 Specify how the activity related to the new patient pathway will be identified.

Select all that apply:

OPCS v4.8	☐
ICD10	☒
Treatment function code	☐
Main Speciality code	☐
HRG	☐
SNOMED	☐

	Clinical coding / terming methodology used by clinical profession ☐
A8.3 **Identification Rules for Drugs:** How are drug costs captured?	**Already specified in current NHS England Drugs List document**
A8.4 **Identification Rules for Devices:** How are device costs captured?	**Not applicable**
A8.5 **Identification Rules for Activity:** How are activity costs captured?	**Already correctly captured by an existing specialised service line (NCBPS code within the PSS Tool** If activity costs are already captured please specify whether this service needs a separate code. **No**
A9 Monitoring	
A9.1 **Contracts** Specify any new or revised data flow or data collection requirements, needed for inclusion in the NHS Standard Contract Information Schedule.	**None**
A9.2 **Excluded Drugs and Devices (not covered by the Zero Cost Model)** For treatments which are tariff excluded drugs or devices not covered by the Zero Cost Model, specify the pharmacy or device monitoring required, for example reporting or use of prior approval systems.	*Select all that apply:* Drugs or Device MDS ☒ Blueteq ☒ Other prior approval ☐

	Please specify: Blueteq is already established for Emicizumab for a different patient group.
A9.3 **Business intelligence** Is there potential for duplicate reporting?	**No**
A9.4 **Contract monitoring** Is this part of routine contract monitoring?	**Yes** If yes, please specify contract monitoring requirement: Standard processes for high-cost drugs
A9.5 **Dashboard reporting** Specify whether a dashboard exists for the proposed intervention?	**Yes** Haemophilia dashboard. Metric already exists concerning extent of prophylactic regimen use. There is no metric planned for this specific drug or indication.
A9.6 **NICE reporting** Are there any directly applicable NICE or equivalent quality standards which need to be monitored in association with the new policy?	**No**

<table>
<tr><th colspan="2">Section B - Service Impact</th></tr>
<tr><td colspan="2">B1 Service Organisation</td></tr>
<tr><td>B1.1 Describe how the service is currently organised? (i.e. tertiary centres, networked provision etc.)</td><td>Access is through nominated Haemophilia Comprehensive Care Centres only, confirmed by UKHCDO National network, plus local networks.
Source: Policy Working Group</td></tr>
<tr><td>B1.2 Will the proposition change the way the commissioned service is organised?</td><td><u>Yes</u> Currently, some severe prophylaxis patients are managed entirely at some HCC’s which would need to change if the patient wished to be treated with emicizumab. This is expected to impact only a small proportion of patients but is balanced by improved clinical oversight.</td></tr>
<tr><td>B1.3 Will the proposition require a new approach to the organisation of care?</td><td><u>No change to delivery of care</u></td></tr>
<tr><td colspan="2">B2 Geography & Access</td></tr>
<tr><td>B2.1 Where do current referrals come from?</td><td>Select all that apply:
GP ☐
Secondary care ☐
Tertiary care ☐
Other ☒
Please specify:
People will be referred from within comprehensive care centres or haemophilia centres as they will already be receiving treatment</td></tr>
<tr><td>B2.2 What impact will the new policy have on the sources of referral?</td><td><u>No impact</u></td></tr>
</table>

B2.3 Is the new policy likely to improve equity of access?	**No impact** *Source: Equalities Impact Assessment*
B2.4 Is the new policy likely to improve equality of access and/or outcomes?	**No impact** *Source: Equalities Impact Assessment*
B3 Implementation	
B3.1 Will commissioning or provider action be required before implementation of the proposition can occur?	**No action required**
B3.2 **Time to implementation:** Is a lead-in time required prior to implementation?	**No - go to B3.4**
B3.3 **Time to implementation:** If lead-in time is required prior to implementation, will an interim plan for implementation be required?	**No - go to B3.4**
B3.4 Is a change in provider physical infrastructure required?	**No**
B3.5 Is a change in provider staffing required?	**No**
B3.6 Are there new clinical dependency and/or adjacency requirements that would need to be in place?	**No**
B3.7 Are there changes in the support services that need to be in place?	**No**

<table>
<tr><td>B3.8 Is there a change in provider and/or inter-provider governance required? (e.g. ODN arrangements / prime contractor)</td><td><u>No</u></td></tr>
<tr><td>B3.9 Is there likely to be either an increase or decrease in the number of commissioned providers? If yes, specify the current and estimated number of providers required in each region</td><td><u>No change</u>
However there will be a restriction in access to a sub-group of providers (21 out of 39) with a commitment to review this position within the first 24 months of the policy. There is wide clinical support for this restriction due to the novelty of the treatment for this patient group.</td></tr>
<tr><td>B3.10 Specify how revised provision will be secured by NHS England as the responsible commissioner.</td><td>Select all that apply:
<table><tr><td>Publication and notification of new policy</td><td>☒</td></tr><tr><td>Market intervention required</td><td>☐</td></tr><tr><td>Competitive selection process to secure increase or decrease provider configuration</td><td>☐</td></tr><tr><td>Price-based selection process to maximise cost effectiveness</td><td>☐</td></tr><tr><td>Any qualified provider</td><td>☐</td></tr><tr><td>National Commercial Agreements e.g. drugs, devices</td><td>☐</td></tr><tr><td>Procurement</td><td>☐</td></tr><tr><td>Other</td><td>☒</td></tr></table>Please specify:
Through restricted availability of Blueteq prior approval funding request forms.</td></tr>
<tr><td colspan="2">B4 Place-based Commissioning</td></tr>
</table>

B4.1 Is this service currently subject to, or planned for, place-based commissioning arrangements? (e.g. future CCG lead, devolved commissioning arrangements, STPs)	**No**

Section C - Finance Impact

C1 Tariff/Pricing

C1.1 How is the service contracted and/or charged?
Only specify for the relevant section of the patient pathway

Select all that apply:

Drugs	Not separately charged – part of local or national tariffs	☐
	Excluded from tariff – pass through	☒
	Excluded from tariff - other	☐
Devices	Not separately charged – part of local or national tariffs	☐
	Excluded from tariff (excluding ZCM) – pass through	☐
	Excluded from tariff (excluding ZCM) – other	☐
	Via Zero Cost Model	☐
Activity	Paid entirely by National Tariffs	☐
	Paid entirely by Local Tariffs	☐
	Partially paid by National Tariffs	☐
	Partially paid by Local Tariffs	☐
	Part/fully paid under a Block arrangement	☐
	Part/fully paid under Pass-Through arrangements	☐
	Part/fully paid under Other arrangements	☐

C1.2 **Drug Costs** Where not included in national or local tariffs, list each drug or combination, dosage, quantity, **list** price including VAT if applicable and any other key information e.g. Chemotherapy Regime. NB discounted prices or local prices must not be included as these are subject to commercial confidentiality and must not be disclosed.	Emicizumab has not yet been granted marketing authorisation in the UK for people with haemophilia A without inhibitors. However, it was approved by the EMA on 23 February 2018: Hemlibra is indicated for routine prophylaxis of bleeding episodes in patients with haemophilia A with factor VIII inhibitors. Hemlibra can be used in all age groups. List prices are as follows: 30 mg / 1 mL SC = £2,415.30 60 mg / 0.4 mL SC = £4,830.60 105 mg / 0.7 mL SC = £8,453.55 150 mg / 1 mL SC = £12,076.50 For budget impact purposes, the list price has been used. This can be amended in the model (cells D13 in the supporting worksheet, - unit costs worksheet) and will carry through the model. The annual treatment cost per patient for factor VIII prophylaxis and on-demand regiments are based on list prices. See resource impact template, supporting info – unit costs sheet for more details.
C1.3 **Device Costs** Where not included in national or local tariff, list each element of the excluded device, quantity, **list or expected** price including VAT if applicable and any other key information. NB: Discounted prices or local prices must not be included as these are subject to commercial confidentiality and must not be disclosed.	Not applicable
C1.4 **Activity Costs covered by National Tariffs** List all the HRG codes, HRG descriptions, national tariffs (excluding MFF), volume and other key costs (e.g. specialist top up %)	Outpatient activity can be identified by activity under the treatment function code of 303 (Clinical Haematology) or 420 (Paediatrics). There is also a national tariff (2018/19) top up for specialist services for haemophilia and other related blood disorders (NCBPS03Z) of 30.6% and

	for specialist haematology services for children (NCBPS23H) of 20.2%. See NHS Commissioning Board Manual for Prescribed Specialised Services 2018/19.
C1.5 **Activity Costs covered by Local Tariff** List all the HRGs (if applicable), HRG or local description, estimated average tariff, volume and any other key costs. Also indicate whether the Local Tariff(s) is/are newly proposed or established and if newly proposed how is has been derived, validated and tested.	Not applicable
C1.6 **Other Activity Costs not covered by National or Local Tariff** Include descriptions and estimates of all key costs.	Not applicable
C1.7 Are there any prior approval mechanisms required either during implementation or permanently?	**No** Emicizumab is likely to be used to ensure only patients who meet the commissioning criteria as set out in the final policy are treated.
C2 Average Cost per Patient	
C2.1 What is the estimated cost per patient to NHS England, in years 1-5, including follow-up where required?	This is the cost per severe Haem A patient per annum which reflects an increasing proportion of patients being treated with emicizumab. The increase over time is due to the higher cost of Emicizumab compared with the current standard of care (rFVIII); as emicizumab replaces the lower cost rFVIII so the overall average cost per patient increases, even though the cost per emicizumab patient, and the cost per rFVIII patient, are not by themselves increasing. YR1: 140,610

Are there any changes expected in year 6-10 which would impact the model?	<table><tr><td>YR2</td><td>186,184</td></tr><tr><td>YR3</td><td>188,093</td></tr><tr><td>YR4</td><td>189,461</td></tr><tr><td>YR5</td><td>190,500</td></tr></table> No: The cost per patient is expected to be steady from year 5 – year 10 reflecting emicizumab treatment saturation at the end of year 5. All products used to treat haemophilia are subject to confidential UK wide tenders and as such contract prices paid by the NHS are usually lower than list price. As a result the true annual cost per patient and the net budget impact may be considerably different to that currently demonstrated.
C3 Overall Cost Impact of this Policy to NHS England	
C3.1 Specify the budget impact of the proposal on NHS England in relation to the relevant pathway.	**Cost pressure**: Year 1 £60.2m Year 2 £100.4m Year 3 £122.5m Year 4 £144.8m Year 5 £167.4m All products used to treat haemophilia are subject to confidential UK wide tenders and as such contract prices paid by the NHS are usually lower than list price. As a result the true annual cost per patient and the net budget impact may be considerably different to that currently demonstrated.

C3.2 If the budget impact on NHS England cannot be identified set out the reasons why this cannot be measured.	Not applicable
C3.3 If the activity is subject to a change of commissioning responsibility, from CCG to NHS England, has a methodology for the transfer of funds been identified, and calculated?	Not applicable
C4 Overall cost impact of this policy to the NHS as a whole	
C4.1 Specify the budget impact of the proposal on other parts of the NHS.	Budget impact for CCGs: **No impact on CCGs** Budget impact for providers: **No impact on providers**
C4.2 Taking into account responses to C3.1 and C4.1, specify the budget impact to the NHS as a whole.	**Cost pressure**
C4.3 Where the budget impact is unknown set out the reasons why this cannot be measured	N/A
C4.4 Are there likely to be any costs or savings for non-NHS commissioners and/or public sector funders?	**No**
C5 Funding	
C5.1 Where a cost pressure is indicated, state known source of funds for investment, where identified, e.g. decommissioning less clinically or cost-effective services.	CPAG prioritisation reserve

C6 Financial Risks Associated with Implementing this Policy	
C6.1 What are the material financial risks to implementing this policy?	No material financial risk
C6.2 How can these risks be mitigated?	Not applicable
C6.3 What scenarios (differential assumptions) have been explicitly tested to generate best case, worst case and most likely total cost scenarios?	Not applicable
C6.4 What scenario has been approved and why?	Not applicable
C7 Value for Money	
C7.1 What published evidence is available that the treatment is cost effective as evidenced in the evidence review?	The clinical evidence review for this technology found no studies relating to cost effectiveness
C7.2 Has other data been identified through the service specification development relevant to the assessment of value for money?	*Select all that apply:* Available pricing data suggests the treatment is equivalent cost compared to current/comparator treatment ☐ Available pricing data suggests the treatment is lower cost compared to current/comparator treatment ☐ Available clinical practice data suggests the new treatment has the potential to improve value for money ☐ Other data has been identified ☐ No data has been identified ☐

	The data supports a high level of certainty about the impact on value	☒
	The data does not support a high level of certainty about the impact on value	☐
C8 Cost Profile		
C8.1 Are there non-recurrent capital or revenue costs associated with this policy?	**No**	
C8.2 If yes, confirm the source of funds to meet these costs.	N/A	