**Guideline for the use of emicizumab for routine prophylaxis of bleeding episodes in patients with haemophilia A with factor VIII inhibitors.**

<table>
<thead>
<tr>
<th>Full Title of Guideline:</th>
<th>Guideline for the use of emicizumab for routine prophylaxis of bleeding episodes in patients aged 1 year and over with haemophilia A with factor VIII inhibitors. Includes guidance for treatment of bleeding episodes whilst being treated with emicizumab</th>
</tr>
</thead>
</table>
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Clinical Haematology |
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Dr Joannes Hermans (Consultant Haematologist)  
Dr Gill Swallow (Consultant Haematologist) |
| Scope (Target audience, state if Trust wide): | Haematologists and Clinical Nurse Specialists in Nottingham Haemophilia Comprehensive Care Centre |
| Review date (when this version goes out of date): | October 2019 |
| Explicit definition of patient group to which it applies (e.g. inclusion and exclusion criteria, diagnosis): | Patients aged 1 year and over with haemophilia A with factor VIII inhibitors who:  
- have failed ITI (immune tolerance induction), or  
- are bleeding on by-passing agents or high dose FVIII or  
- are bleeding excessively whilst still on ITI |
| Changes from previous version (not applicable if this is a new guideline, enter below if extensive): | New recommendations to monitor for loss of efficacy due to antibody development. |
| Summary of evidence base this guideline has been created from: | Kruse-Jarres R, Callaghan MU, Croteau SE, Jimenez-Yuste V, Khoo L, Liesner R, Matsushita T, Recht M, Young G, Chang T, Dhalluin C, Mu Y, Xu J, Devenport J, Ko RH Solari P* and Oldenburg J. Surgical experience in two multicenter, open-label phase 3 studies of Emicizumab in persons with hemophilia A with inhibitors (HAVEN 1 and HAVEN 2). ASH 2017 abstr 89  
P Collins, R Liesner, M Makris, K Talks, P Chowdary, E Chalmers, G Hall, C Percy, C Hay, and D Hart  


Hemlibra/ Emicizumab prescription and dosing: guidance from UKHCDO and NHSE

This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date or outside of the Trust.
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Guideline for the use of emicizumab for routine prophylaxis of bleeding episodes in patients with haemophilia A with factor VIII inhibitors

Introduction and background

Emicizumab is a bispecific antibody that binds to factor (F)IX/IXa and FX/FXa and activates FX to FXa in the absence of FVIII. It has been shown to reduce bleeding episodes in people with haemophilia A complicated by a FVIII inhibitor (Oldenburg 2017). Patients with severe haemophilia A and inhibitors suffer frequent bleeding episodes which may be life or limb threatening and result in significant morbidity. Prophylaxis with bypassing agents (activated prothrombin complex concentrate- aPCC, (Factor Eight Inhibitor Bypassing Activity,( FEIBA), or FVIIa - Novoseven) may reduce the incidence of bleeding, but the efficacy of bypassing agents remains suboptimal and many patients suffer significant bleeding episodes despite prophylaxis. Emicizumab prophylaxis has been found to be associated with a significantly lower rate of bleeding events than no prophylaxis or previous prophylactic treatment with bypassing agents among patients with hemophilia A with inhibitors, and it improved health-related quality of life.

Co-administration of Emicizumab and activated prothrombin complex concentrate (aPCC, FEIBA) has been associated with thrombotic microangiopathy (TMA), venous thrombosis and skin necrosis. These adverse events have been observed when aPCC was used for more than one day and at cumulative doses higher than 100micrograms/kg/day (Oldenberg 2017). The number of reported patients treated with Emicizumab and aPCC for more than one day at doses lower than 100 micrograms/kg/day is small (n=5), therefore, the risk of adverse events at lower doses of aPCC cannot be assumed to be zero, especially if aPCC is used for more than 24 hours. To date there have been no TMA or thrombotic adverse events associated with the co-administration of Emicizumab and recombinant FVIIa (rFVIIa, Novoseven) or FVIII concentrates but the number of patients treated for bleeds on Emicizumab remains relatively small.

This purpose of this document is to provide guidance for the management of patients at NUH with emicizumab.
Patient selection

Inclusion criteria

Severe haemophilia A with FVIII inhibitor confirmed on more than one occasion by Bethesda assay which interferes with prophylaxis or treatment of bleeds at standard FVIII doses. One of the following must also apply:

- Failed inhibitor eradication following immune tolerance induction therapy (ITI)
- Sub-optimal control of bleeding episodes despite on demand or prophylactic bypassing therapy or high dose FVIII
- Experiencing breakthrough bleeding episodes during ITI. Safety data for this indication is not yet available, so discussion with regional/national MDT is strongly recommended before commencing treatment.

Exclusion criteria

- Hypersensitivity to the active substance or to any of the excipients
- Patients who are at high risk for thrombotic microangiopathy (e.g., have a previous medical or family history of thrombotic microangiopathy)

Initiation of treatment

Patients who are prescribed commercial Emicizumab must be registered on the NHSE High Cost Drug Management System. A BlueTeq™ form must be submitted to register each patient https://www.blueteq-secure.co.uk/trust/. A BlueTeq™ form is required for people who have previously received Emicizumab as part of a clinical trial but NOT those on the Early Access Medicines Scheme (EAMS) because the Blueteq™ approval process has already be completed.

The following section will address the medical management of patients being initiated on emicizumab.

The decision to commence treatment with emicizumab must be made by a haematologist experienced in the management of haemophilia and bleeding disorders. The use of emicizumab must be discussed at the Nottingham
Haemophilia Comprehensive Care Centre MDT and use in a particular patient approved. It is strongly recommended that difficult cases are discussed at the East Midlands Regional Haemophilia MDT and in some cases advice may be required from other expert haemophilia treaters (members of the UK Haemophilia Centre Doctors’ Organisation Inhibitor Working Party).

Patients will have 24 hour access to advice from the Nottingham Haemophilia Comprehensive Care Centre. In normal working hours, all queries from patients on emicizumab must be discussed with Dr Charlotte Grimley (Centre Director Nottingham Haemophilia Comprehensive Care Centre), Dr Joannes Hermans, (Consultant Haematologist) or Dr Gill Swallow, (Consultant Haematologist). Out of hours, all queries from patients on treatment with emicizumab must be discussed with the consultant on call for non-malignant haematology. If the consultant on call does not have the required experience in managing complex patients with haemophilia and inhibitors, arrangements for exceptional advice and cover will be put in place.

**Medical assessments prior to emicizumab treatment**

- Review of haemophilia medical history
- Review of any other relevant medical history
- Review of any personal or family history to suggest an increased risk of thrombotic microangiopathy
- 12 lead ECG
- Discussion about bleed treatments during treatment with emicizumab and formulation of personalised treatment plan (see below page 2)

**Patient information and informed consent**

- All patients/carers must receive written patient information in advance of their initial consultation to discuss emicizumab treatment. Information can be obtained from the haemophilia team or downloaded from https://www.medicines.org.uk/emc/rmm/1195/Document
- Patients must be given adequate time to review all the information available and be given an opportunity to have any questions answered.
- Written consent should be signed by the patient (or parent/carer where applicable) prior to the initiation of treatment. If a specific consent form is not available, the relevant NUH consent form should be used.
Modification of home treatment for bleeding episodes

Because of the risk of thrombotic microangiopathy (TMA), venous thrombosis and skin necrosis, concurrent treatment with aPCC (FEIBA) and emicizumab is contra-indicated unless no other alternative is available or other treatment for bleeding episodes is ineffective.

Prior to initiation of emicizumab:

- Home delivery of FEIBA must be suspended
- The patient must return all unused vials of FEIBA to the centre and this must be recorded using standard stock control procedures.
- Cross checking of usage with Haemtrack and Healthcare at Home records for patient deliveries should be performed to ensure that all unused stock has been returned and the patient will be asked to confirm this in writing.
- Suspension of deliveries and return of product should be recorded on the patient’s individual treatment plan (see Appendix 2), and a copy retained in the notes.
- The patient will be provided with an individualised treatment plan for bleeding episodes during emicizumab treatment (see section ‘Treatment of bleeding episodes’ below page 9.
- Emicizumab has a long half-life and the treatment recommendations described in this guidance should be observed for 6 months after stopping the drug.

Laboratory testing prior to the initiation of emicizumab

Emicizumab interferes with the one stage FVIII assay and chromogenic FVIII assays using human coagulation factors. Once Emicizumab has been started a chromogenic assay using plasma containing bovine coagulation factors must be used to monitor FVIII replacement. The Bethesda assay utilising a bovine-based FVIII chromogenic assay must be used.

- On the day of starting emicizumab, prior to treatment, the following baseline blood tests should be performed:
  o Full blood count
  o Renal function
  o Liver function
  o LDH
Dimer
- Reticulocytes
- anti-human and anti-porcine Bethesda assays

Administration of emicizumab

Bypassing agents (FEIBA and Novoseven) must be stopped 24 hours prior to starting emicizumab treatment.

Dosing

The recommended dose is emicizumab 3 mg/kg once weekly for the first 4 weeks (loading dose), followed by 1.5 mg/kg once weekly (maintenance dose), administered as a subcutaneous injection.

The patient dose (in mg) and volume (in mL) should be calculated as follows:
- Loading dose (3 mg/kg) once weekly for the first 4 weeks:
  Patient bodyweight (kg) x dose (3 mg/kg) = total amount (mg) of emicizumab to be administered
- Followed by a maintenance dose (1.5 mg/kg) once weekly from week 5 onwards:
  Patient bodyweight (kg) x dose (1.5 mg/kg) = total amount (mg) of emicizumab to be administered

Commercial stock is supplied in 4 vial sizes
- 30 mg in 1.0 ml
- 60 mg in 0.4 ml
- 105 mg in 0.7 ml
- 150 mg in 1.0 ml

The licensed dosing for the product is 3mg/kg per week subcutaneously once a week for 4 weeks and then 1.5mg/kg weekly thereafter. It is very likely that there will be an extension of the label to include less frequent but higher dosing in the near future. In order to avoid wastage of the product, the UKHCDO recommendation is that in some cases Emicizumab should be prescribed every 2 weeks (3mg/kg/two week) rather than 1.5 mg/kg weekly. For larger subcutaneous volumes there is a suggestion that the dose of drug may need to be split and given as 2 subcutaneous injections. Further advice on dose banding can be found in Appendix 1 and http://www.ukhcdo.org/wp-content/uploads/2018/07/UKHCDO-Hemlibra_Emicizumab-dosing-guidance-2018-final.pdf
Method of administration

Emicizumab is administered by sub-cutaneous injection.

The first 3 doses of emicizumab will be given in hospital.

At least the first 2 doses of emicizumab will be given on the Haematology Day Case (at Nottingham City Hospital for adults, at Queens Medical Centre for children). Full resuscitation facilities must be available.

Patients will be observed for a minimum of 60 minutes post dose for at least the first 2 doses.

If the patient has a history of hypersensitivity reactions, further precautions may be taken such as prior placement of IV cannula.

The first dose will be given on the day case unit (adults or paediatrics as above) by a Haemophilia Clinical Nurse Specialist. After that the CNS will train the patient/carer to self-administer. Subsequent doses can be given by the patient or carer but must be under supervision by the CNS. The second dose must also be given on the day case unit, but after that, if no reactions have occurred, subject to agreement by a haemophilia specialist, further administration may occur at the Haemophilia Centre at QMC.

Patients will be trained to self-administer emicizumab by a Haemophilia CNS. Patients (or parents/carers) will be allowed to self-administer at home once the CNS is satisfied that they have achieved the required level of competency. A minimum of 3 doses must have been given at the hospital. (The patient or parent/carer is already highly likely to have competency in self administration of intravenous medication such as bypassing therapy, and so training for administration of subcutaneous emicizumab should be straightforward).

A follow up phone call will be made to the patient (or parent/carer) by the haemophilia CNS within 24 hours of the first 5 doses.

The patient will need to attend the haemophilia centre for the 5th dose (dose reduction) to be instructed on how to give the reduced dose which will continue thereafter.
Laboratory monitoring during treatment

A patient on a clinical trial with Emicizumab developed an antibody that inhibited Emicizumab function (anti-drug antibody, ADA). This happened soon after Emicizumab had been started and resulted in a loss of efficacy and increased bleeding. The patient was withdrawn from the study and returned to standard care. Since this event was reported, it has been recommended that all patients on Emicizumab are closely followed and if bleeding events occur, inhibitory antibodies are considered as a cause.

Emicizumab interferes with the aPTT and factor VIII assays (one stage and chromogenic) performed with human reagents. If Emicizumab is functional the aPTT will be normal and the factor VIII (human reagents) measurable. Once a patient has been started on Emicizumab they should have an aPTT and a factor VIII assay (human reagents) performed at week 2 and 4 during loading. After the loading month, check monthly for another 2 months and then minimum of 6 monthly thereafter or if any break through bleeds occur and before surgery.

Treatment of bleeding episodes in patients receiving emicizumab

Each patient (or parent/carer) will be provided with written information including a personalised treatment plan (see Appendix 2)

As loss of emicizumab function due to antibody development has been reported (see above), it is important to test for possible loss of function in a patient with a suspected bleed.

If a patient experiences a suspected bleeding episode while taking emicizumab, coagulation tests should be performed prior to treating with bypassing agents. The aPTT can be used as a quick screening test to confirm whether Emicizumab is functional (the aPTT will be normal). Samples should be saved for F8 chromogenic assays (assay using human reagents will give a measurable level).

Bleeds should not be treated with aPCC unless no other alternative is available.

First line treatment of bleeds that require treatment should be rFVIIa. To reduce the risk of thrombosis, the initial dose of rFVIIa should not exceed 90 micrograms/kg. Both Emicizumab and rFVIIa cause thrombin generation and rFVIIa given at doses of 45 micrograms/kg 4 hourly may be efficacious for
some bleeds. However, if lower doses of rFVIIa do not result in an adequate haemostatic response rFVIIa should be increased to 90 micrograms/kg 2 hourly before rFVIIa is assumed to have failed. The total treatment period may be shortened in some cases because Emicizumab is likely to give partial protection against bleed recurrence.

In patients receiving Emicizumab, for less severe mucosal bleeds tranexamic acid alone may be sufficient. Tranexamic acid should not be used in conjunction with aPCC but can be used with rFVIIa.

- The patient should have a supply of oral tranexamic acid at home at all times.

Treatment with additional haemostatic therapy should only be started if a bleed has definitely occurred. In patients receiving Emicizumab minor bleeds may resolve without additional haemostatic therapy.

- If the patient experiences a minor bleeding episode during normal working hours, he (or the parent/carer) should contact the Haemophilia centre by telephone immediately and discuss symptoms with a haemophilia CNS.
- The haemophilia CNS should discuss management with a senior haematologist (see above page 6) before giving advice about minor bleeding episodes to the patient.

In some case assessment of the symptoms and signs may be needed before deciding whether to initiate additional haemostatic therapy. Definite or severe bleeds should continue to be treated as soon as possible.

- All significant bleeds (or symptoms suggesting a significant bleed) should be assessed by the patient attending the centre prior to treatment, unless the assessing clinician feels, after discussion with the patient or parent/carer on the telephone, that there would be clinical risk if treatment is delayed until the patient reaches hospital.
- The patient’s treatment plan will document emergency home treatment that can be given prior to assessment at hospital.
- In the rare instance that the patient is unable to contact a haemophilia health care professional, the patient’s treatment plan will include a plan for emergency home treatment.
- Clinicians and patients/parents/carers should agree the exact dose and frequency of rFVIIa that can be used at home.
Treatment of bleeds failing to respond to FVIIa

If a bleed does not respond to full dose rFVIIa (NovoSeven) and the anti-human FVIII inhibitor titre is low, human FVIII can be considered to treat bleeds, although it is recognised that this may lead to an amnestic response and an increased inhibitor titre. A chromogenic assay using plasma containing bovine coagulation factors should be used to ensure that adequate FVIII levels have been achieved.

Recombinant porcine factor VIII (rpFVIII, Obizur) is not licensed for treatment of congenital haemophilia A. However, if the porcine inhibitor is low, treatment of bleeding episodes with rpFVIII can be considered if a bleed has not responded to rFVIIa and aPCC cannot be used at doses less than <100 units/kg/day or the patient develops clinical or laboratory signs of TMA or thrombosis whilst receiving aPCC.

If a severe bleed has not responded to rFVIIa and other treatment options are not available then use of FEIBA should be considered. All treatment with FEIBA should be initiated and controlled by a senior clinician (see above page 6)

The first dose of FEIBA should not exceed 50 units/kg, even for a severe bleed. A dose of 25 units/kg may be efficacious for some bleeds. A second dose of 25-50 units/kg can be considered on day one, if necessary.

If further treatment with FEIBA is required the cumulative dose should not usually exceed 100 units/kg/day. If the bleed does not respond to FEIBA at doses less than 100 units/kg/day, and no other treatment options are available, then higher doses of FEIBA can be considered if the treating clinician decides that the risk of not treating the bleed clearly outweighs the risk of adverse events.

In patients treated with Emicizumab and FEIBA, clinicians should have a high level of suspicion for TMA and venous and arterial thrombotic events.

o If treatment with FEIBA is required for more than one dose, the patient should be admitted to hospital

o Assess twice a day for laboratory evidence of TMA with the following blood tests:
  - FBC to look for a decrease in haemoglobin and/or platelets,
  - blood film for red cell fragments
  - reticulocytes
  - D-dimer
  - renal function
  - Bilirubin
- LDH
- haptoglobin.

If laboratory monitoring suggests the development of TMA, aPCC should be stopped.

The reported episode of skin necrosis was observed in an area of skin that had been treated with local ice therapy. Whether this was causally related or co-incidental is not known, however, clinicians should be cautious about the use of ice therapy in patients receiving concomitant Emicizumab and FEIBA.

**Management of surgery in patients taking emicizumab**

Data describing surgery in patients receiving Emicizumab are very limited and responses are unpredictable. An abstract describes 29 surgeries in 22 patients receiving Emicizumab. Of these 29 surgeries, 15 were dental extractions or central venous access devices (CVAD) procedures, 12 were other minor procedures and 2 were major procedures. No bypassing agent cover was given in 19 cases whilst bypassing agents were used in 10 cases (Kruse-Jarres R 2017).

Of the 19 surgeries managed without bypassing agents there were 5 (26%) post-operatives bleeds of which 3 followed dental extractions. One of these 5 post-operative bleeds required rFVIIa treatment, this was an arthroscopic orthopaedic procedure including synovectomy and debridement.

Of the 10 cases who received a bypassing agent at the time of surgery (9 rFVIIa and one aPCC, doses or frequencies not reported) there were two post-operative bleeds and both required rFVIIa treatment (Kruse-Jarres R 2017).

A further case report described a hip replacement performed following 100 micrograms/kg rFVIIa before the procedure and 80 micrograms/kg 3 hourly following the procedure. Despite this treatment a thigh haematoma developed on the first post-operative day which required FVIII replacement by continuous infusion. Of note, thrombin generation parameters were in the normal range whilst the patient was on Emicizumab prophylaxis and in the peri-operative period (Santagostino 2017).

There are no data to support the use of thrombin generation or thromboelastography to monitor haemostasis during surgery with Emicizumab.

- Consideration should be given to delaying non-urgent surgery until further data are available, especially for major surgery.
• All potential surgical procedures however minor must be discussed as far in advance as possible with a senior haemophilia doctor.
• All procedures must be carried out in a Comprehensive Care Centre where at all possible.
• A written treatment protocol should be available to all clinicians involved with the surgery, and a copy provided for the patient/carer.
• aPTT and F8 assay (human reagents) should be performed prior to surgery to ensure that emicizumab is functional.
• For minor surgery such as CVAD procedures and dental extractions consideration may be given to undertaking the procedure using tranexamic acid without additional haemostatic cover. There should be close clinical review for bleeding and rFVIIa used to manage surgical related bleeding if necessary.
• Alternatively, a single dose of rFVIIa, between 45-90 micrograms/kg can be used with further treatment as required.
• Based on very limited data, major orthopaedic procedures are likely to require additional haemostatic replacement therapy although this does not guarantee adequate haemostasis.

**Treatment monitoring, record keeping and adverse event reporting**

For safety reasons, it is essential that emicizumab treatment and the use of bypassing therapies is monitored very closely.

Patients (or parents/carers) will be required to record all usage of emicizumab, as well as use of bypassing agents using the Haemtrack system. Patients (or parents/carers) will have signed a contract with the centre already committing to the use of Haemtrack to support home delivery of previous bypassing therapy.

Records must be entered weekly where possible. Failure to receive timely records (within 4 weeks of use of product) will result in a discussion by centre staff with the patient (or parent/carer) and support will be offered. A written confirmation of the discussion will be sent to the patient. If no records are received within 2 weeks of the verbal discussion, a further discussion will be held with the patient (or parent/carer) and the option of withdrawing treatment will be discussed with the patient if clinically appropriate.
All adverse events must be discussed within 24 hours with Dr Charlotte Grimley (or Dr Joannes Hermans/Dr Gill Swallow in her absence).
Appendix 1

Emicizumab maintenance dose dependent of weight

All patients should be loaded with 3mg/kg/week for 4 weeks.

<table>
<thead>
<tr>
<th>Lower (kg)</th>
<th>Upper (kg)</th>
<th>Dose to be given and frequency</th>
<th>Vials required</th>
<th>Volume/dose to be given</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>11</td>
<td>3mg/kg every 2 weeks</td>
<td>30 mg/1ml</td>
<td>Give 30mg from 1ml vial (3mg/kg)</td>
</tr>
<tr>
<td>11</td>
<td>22</td>
<td>1.5mg/kg week</td>
<td>30 mg/1ml</td>
<td>Give 1.5mg/kg/week from a 30mg / 1ml vial. Discard any unused volume</td>
</tr>
<tr>
<td>22</td>
<td>33</td>
<td>3mg/kg every 2 weeks</td>
<td>30 mg/1ml + 60mg/0.4ml</td>
<td>Give the 60mg/ 0.4ml vial and the rest of the dose from a 30mg/1ml vial to give total of 3mg/kg. Discard any unused volume</td>
</tr>
<tr>
<td>33</td>
<td>38</td>
<td>3mg/kg every 2 weeks</td>
<td>105mg/0.7ml</td>
<td>Give 3mg/kg from a 0.7ml vial. Discard any unused volume</td>
</tr>
<tr>
<td>38</td>
<td>44</td>
<td>1.5mg/kg week</td>
<td>60mg/0.4ml</td>
<td>Give 1.5mg/kg/week from a 0.4 ml vial. Discard any unused volume</td>
</tr>
<tr>
<td>44</td>
<td>49</td>
<td>3mg/kg every 2 weeks</td>
<td>30 mg/1ml + 105mg/0.7ml</td>
<td>Give the 105mg/0.7ml vial and the rest from the 30mg/1ml vial to give total of 3mg/kg. Discard any unused volume</td>
</tr>
<tr>
<td>49</td>
<td>53</td>
<td>3mg/kg every 2 weeks</td>
<td>150mg/1ml</td>
<td>Give 3mg/kg from a 1ml vial. Discard any unused volume</td>
</tr>
<tr>
<td>53</td>
<td>66</td>
<td>1.5mg/kg week</td>
<td>30 mg/1ml + 60mg/0.4ml</td>
<td>Give the 60mg/0.4ml vial and the rest of the dose from a 30mg/1ml vial to give total of 1.5mg/kg. Discard any unused volume</td>
</tr>
<tr>
<td>66</td>
<td>76</td>
<td>1.5mg/kg week</td>
<td>105mg/0.7ml</td>
<td>Give 1.5mg/kg from a 0.7ml vial. Discard any unused volume</td>
</tr>
<tr>
<td>77</td>
<td>86</td>
<td>1.5mg/kg week</td>
<td>60mg/0.4ml x 2</td>
<td>Give one 60mg/0.4ml vial and the rest from the other 60mg/0.4ml vial to give total of 1.5mg/kg. Discard any unused volume</td>
</tr>
<tr>
<td>86</td>
<td>96</td>
<td>1.5mg/kg week</td>
<td>30 mg/1ml + 105mg/0.7ml</td>
<td>Give the 105mg/0.7ml vial and the rest from a 30mg/1ml vial to give total of 1.5mg/kg. Discard any unused volume</td>
</tr>
<tr>
<td>96</td>
<td>100*</td>
<td>1.5mg/kg week</td>
<td>150mg/1ml</td>
<td>Give 1.5mg/kg from a 2ml vial. Discard any unused volume</td>
</tr>
</tbody>
</table>

* patients who weigh >100 kg should be dosed with 150 mg/week.
## Appendix 2

### Personalised treatment plan for emicizumab (example)

<table>
<thead>
<tr>
<th>Patient name</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital number</td>
<td></td>
</tr>
<tr>
<td>NHS Number</td>
<td></td>
</tr>
<tr>
<td>DOB</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>BASELINE inhibitor titre</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>75kg</td>
</tr>
<tr>
<td><strong>Baseline blood results</strong></td>
<td></td>
</tr>
<tr>
<td>FBC</td>
<td></td>
</tr>
<tr>
<td>U&amp;E</td>
<td></td>
</tr>
<tr>
<td>Bilirubin</td>
<td></td>
</tr>
<tr>
<td>LDH</td>
<td></td>
</tr>
<tr>
<td>Haptoglobin</td>
<td></td>
</tr>
<tr>
<td>Reticulocytes</td>
<td></td>
</tr>
<tr>
<td>D dimer</td>
<td></td>
</tr>
<tr>
<td><strong>Emicizumab dose</strong></td>
<td></td>
</tr>
<tr>
<td>Week 1-4: 225mg (1.5ml of 150mg/ml solution)</td>
<td>Week 5 onwards: 112.5mg (0.75ml of 150mg/ml solution)</td>
</tr>
<tr>
<td><strong>Bleed treatment plan</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Minor bleed</strong> eg nose bleed or minor cut</td>
<td></td>
</tr>
<tr>
<td>During normal working hours, call haemophilia centre and speak to centre staff. Out of hours, call hospital switchboard and ask to speak to the haematology doctor on call.</td>
<td></td>
</tr>
<tr>
<td>Minor bleeding episodes may respond to local treatment, for example pressure.</td>
<td></td>
</tr>
<tr>
<td>Centre staff may advise tranexamic acid 1g by mouth three times a day for 1-5 days.</td>
<td></td>
</tr>
<tr>
<td>Do not give NovoSeven treatment for a minor bleed without speaking to nurse or doctor at the haemophilia centre</td>
<td></td>
</tr>
<tr>
<td>We may ask you to come to hospital to have some blood taken to ensure that the emicizumab is still working as we expect.</td>
<td></td>
</tr>
<tr>
<td><strong>Major bleed</strong> eg suspected joint or muscle bleed</td>
<td></td>
</tr>
<tr>
<td>During normal working hours, call haemophilia centre and speak to centre staff.</td>
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<td>We will usually ask you to come into the centre to see a doctor to decide if your bleed needs treatment. We will tell you where to come to be seen.</td>
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<td>Out of hours, please call the hospital switchboard and ask to speak to the haematology doctor on call. We will usually ask you to come to the centre to see a doctor. Out of hours, this is likely to be in A&amp;E, but might be SRU at the City Hospital.</td>
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<td>If your bleed is an emergency, the doctor may tell you to take a dose of Novoseven before you come to hospital. Your dose of Novoseven is shown below.</td>
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</table>
Do not take a dose of Novoseven without speaking to a centre staff or a doctor unless you have been unable to contact someone after trying for at least half an hour and your bleed is getting worse. When you come to hospital we will take some blood samples to ensure that the emicizumab is still working as expected. This will be done as soon as we see you.

**Very serious bleed:** for example serious head injury (please see the head injury guidance we will give you)
In this situation you or your carer will need to administer the dose of Novoseven that you keep at home.
Your dose is given below (serious bleed dose).
You or your carer should contact the haemophilia centre immediately after the bleed and you must attend hospital as soon as possible to be seen by a doctor.
When you come to hospital we will take some blood samples to ensure that the emicizumab is still working as expected. This will be done as soon as we see you.

| **Dose of Novoseven for a joint or muscle bleed** | 45 micrograms/kg  
Your dose is 3mg (1 x 1mg vial plus 1 x 2mg vial) |
| **Dose of Novoseven for a serious bleed** | 90 micrograms/kg  
Your dose is 6mg (1 x 1mg vial plus 1 x 5 mg vial) |

No more than one dose of Novoseven should be given at home unless directed by a haemophilia centre doctor.
If your bleed is not improving with the treatment you have been advised to take, you must contact the centre again and speak to a member of the haemophilia centre staff or the doctor on call.
References


P Collins, R Liesner, M Makris, K Talks, P Chowdary, E Chalmers, G Hall, C Percy, C Hay, and D Hart


EAMS Information for HCP [Emicizumab] January 2018
Roche information