NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Commissioning Support Programme

Scope to inform clinical evidence review of: Emicizumab for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in patients with haemophilia A without factor VIII inhibitors

NICE ID014 / NHS England Policy URN 1819

Final Scope

July 2018

Remit	To support the development of an NHS England specialised commissioning clinical policy on emicizumab within its marketing authorisation for routine prophylaxis of bleeding episodes in patients with haemophilia A without factor VIII inhibitors
Company	Roche Products Limited
Regulatory status and licensed indication	Emicizumab does not currently have a marketing authorisation in the UK for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in patients with haemophilia A **without** inhibitors. It has been studied in clinical trials in people with haemophilia A without inhibitors compared to no prophylaxis (episodic/on-demand factor VIII treatment only) and to a historical control arm of prophylaxis with factor VIII. Emicizumab does currently have a marketing authorisation in the UK for routine prophylaxis of bleeding episodes in patients of all ages with haemophilia A with factor VIII inhibitors.
Dosing information	For people with inhibitors the SPC states that the recommended dose for emicizumab is 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. Alternative maintenance doses were used in the clinical trials involving people with haemophilia A without inhibitors. In HAVEN 3 some participants received emicizumab 3 mg/kg every 2 weeks, and in HAVEN 4 participants received emicizumab 6 mg/kg every 4 weeks.
Population	Adults and children with congenital haemophilia A without factor VIII inhibitors
Intervention	Emicizumab (Hemlibra) solution for subcutaneous injection
Comparator(s)	• factor VIII therapy either prophylaxis (primarily) or on-demand treatment (less common) • extended half-life factor VIII therapy prophylaxis

Outcomes	Efficacy outcomes related to prophylaxis of bleeding, including: • Total number of bleeds • Annualised bleed rates • Joint bleeding events • Target-joint bleeding events and number of joints affected • Bleeding events treated with Factor VIII • Spontaneous/critical bleeding events (for example, intracranial haemorrhaging or intramuscular bleeding) • Pain • Development of neutralising anti-emicizumab antibodies • Development of FVIII inhibitors • Haem-A-QoL physical health score • EQ-5D • Number of days away from school or work • Number of days hospitalised • Patient preferences/preferences scores • Compliance with treatment/administration of treatment Safety outcomes: • Incidence and severity of adverse events • Discontinuations due to adverse events • Overall adverse events • Drug-drug interactions The following outcomes are included as standard and will be considered where evidence allows: survival; progression free survival; health related quality of life (including mobility; self-care; usual activities; anxiety/depression); replacement of more toxic treatment; dependency on care giver/supporting independence; safety (including adverse effects); and delivery of intervention.
Background – a brief summary of the disease, epidemiology, proposed benefit of treatment and current treatment in the NHS in England (*no more than 400 words*).	Haemophilia is a rare condition that affects the blood's ability to clot. Congenital haemophilia A is a deficiency of coagulation factor VIII, which causes increased bleeding and usually affects males, with a prevalence of between 1 in 5,000 and 1 in 10,000 in males. Recurrent bleeds lead to progressive joint damage and other complications. Diagnosis is normally made in early childhood for patients with moderate and severe disease. People diagnosed with severe haemophilia A and some with moderate disease require treatment with recombinant factor VIII in order to prevent bleeds. The UK National Haemophilia Database Bleeding Disorder Statistics for 2016-2017 reports that between April 2016 and March 2017 there were 5,601 people in the UK with mild (n= 3038), moderate (n= 800) or severe (n=1763) forms of

	haemophilia A without inhibitors (not including low-level carriers; factor VIII level ≥40 IU/dL).