

MSAC Application 1834

**Efanesoctocog alfa for routine
prophylaxis in patients with
haemophilia A**

PICO Set

Population

Describe the population in which the proposed health technology is intended to be used:

This application seeks to include efanesoctocog alfa on the National Product Price List (NPPL) for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adults, adolescents, and children with haemophilia A (HMA) without factor VIII (FVIII) inhibitors¹ (Table 1). Funding is also requested for the perioperative management of bleeding (surgical prophylaxis) of all HMA patients without inhibitors (Table 1).

Table 1 Proposed populations for treatment with efanesoctocog alfa

Prophylaxis	Perioperative management
Moderate or severe haemophilia A without inhibitors	All haemophilia A patients without inhibitors

HMA is an X-linked recessive genetic condition that results in a deficiency in FVIII and is characterised by protracted and excessive bleeding (Srivastava *et al.*, 2020). This disorder typically affects males. Females are normally classified as carriers with 20-30% having bleeding symptoms, typically mild HMA (ABDR, 2024-25, p19-20). The primary characteristics of HMA are prolonged spontaneous and/or traumatic haemorrhages, most commonly within the musculoskeletal system and into large synovial joints such as ankles, knees, and hip joints (Srivastava *et al.*, 2020). Internal bleeds may lead to serious complications and even become life threatening without adequate treatment. Joint or muscle bleeds can cause acute pain. Recurrent and sub-optimally controlled joint bleeds can cause chronic haemophilic arthropathy, a severe and common complication where repeated bleeding into joints causes progressive damage to the joint and significant joint pain (Srivastava *et al.*, 2020). The long-term complications of haemophilia can have substantial detrimental impacts on quality of life (O'Hara *et al.*, 2018).

The severity of haemophilia informs the treatment required (Table 2). Mild HMA may require no treatment or treatment only under special circumstances, such as surgery (Rodriguez-Merchan, 2026) (ABDR, 2023-24, p7). More severe HMA may require regular interventions. The guidelines by the World Federation of Hemophilia (WFH), which have been adopted by the Australian Haemophilia Centre Director's Organisation (AHCDO), recommend that '*Prophylaxis is the standard of care for people with severe hemophilia, and for some people with moderate hemophilia*' and that on-demand treatment '*...should not be considered a long term option for the management of hemophilia as it does not alter its natural history of spontaneous bleeding and related complications*' (Srivastava *et al.*, 2020, p13). An analysis of the ABDR 2023-24 showed that 92% of severe patients and 63% of moderate HMA patients were prescribed prophylaxis (ABDR data request, 2025).

Table 2 Relationship of bleeding severity to clotting factor

Severity	Clotting factor level	Bleeding episodes
Severe	<0.01 IU/mL (<1% of normal)	Spontaneous bleeding into joints or muscles, predominantly in the absence of identifiable haemostatic challenge
Moderate	0.01-0.05 IU/mL (1-5% of normal)	Occasional spontaneous bleeding; prolonged bleeding with minor trauma or surgery
Mild	0.05-0.40 IU/mL (5-<40% of normal)	Severe bleeding with major trauma or surgery; spontaneous bleeding is rare

Source: Srivastava *et al.* (2020), Table 2-1, p22

Breakthrough bleeding may be the result of injuries or trauma or there may be spontaneous bleeds that occur without an apparent cause. Additional FVIII replacement therapy is required to stop the bleeding. Some types of bleeds can be life-threatening and require immediate treatment and medical attention (Table 3).

¹ Without FVIII inhibitors is referred to as without inhibitors from this point on

Table 3 Sites of bleeding in haemophilia

Serious	• Joints (haemarthrosis) • Muscles, especially deep compartments (iliopsoas, calf, forearm) • Mucous membranes of the mouth, nose, and genitourinary tract
Life-threatening	• Intracranial • Neck/throat • Gastrointestinal

Source: Srivastava *et al.* (2020), Table 2-3, p23

Another reason for breakthrough bleeding is if a patient has developed inhibitors to FVIII replacement. Patients are most likely to develop inhibitors within their first 75 exposure days to FVIII replacement therapy (Gouw *et al.*, 2013). Immune tolerance induction therapy is recommended to eradicate anti-FVIII antibodies; this is not successful in 10-40% of patients (Oomen *et al.*, 2023, Srivastava *et al.*, 2020). Patients who fail immune tolerance induction are recommended to switch to a non-FVIII replacement therapy.

Surgery poses a high bleeding risk to patients with HMA of all severities. Perioperative management aims to prevent abnormal bleeding resulting from surgery. The clinical needs are (i) maintenance of normal to near-normal FVIII factor levels for extended periods, (ii) consistent haemostatic protection throughout the perioperative period, (iii) reduced risk of breakthrough bleeding during recovery, (iv) better surgical outcomes with fewer complications, and (v) convenient dosing with fewer infusions than current FVIII replacement products.

Efanesoctocog alfa is for the treatment of HMA patients without inhibitors. Most HMA patients requiring routine prophylaxis do not have FVIII inhibitors. The most recent analysis of the Australian Bleeding Disorders Registry (ABDR) showed that there were 146 patients with inhibitors, which corresponds to 5.1% (146/2,874) of HMA patients (ABDR 2024-25, p11, 14). Efanesoctocog alfa provides high bleed protection for all HMA patients and meets an unmet need for those (i) who are highly active, and/or (ii) have a high bleed phenotype. Both cohorts are at increased risk of breakthrough traumatic or spontaneous bleeds. Furthermore, efanesoctocog alfa addresses the unmet need for a more effective treatment option for perioperative management in patients with HMA of all severities.

Specify any characteristics of patients with, or suspected of having, the medical condition, who are proposed to be eligible for the proposed health technology, describing how a patient would be investigated, managed and referred within the Australian health care system in the lead up to being considered eligible for the technology:

Characteristics of eligible patients

Adult, adolescent, and paediatric patients with moderate or severe HMA without inhibitors requiring routine prophylaxis to prevent or reduce the frequency of bleeding episodes. The pivotal trials of efanesoctocog alfa enrolled severe HMA patients aged ≥ 12 years (XTEND-1) and < 12 years (XTEND-Kids) (von Drygalski *et al.*, 2023, Malec *et al.*, 2024). The proposed population for NPPL includes patients with moderate HMA, which aligns with the treatment guidelines (Srivastava *et al.*, 2020, p13). Both trials required patients to have received at least 150 exposure days of recombinant and/or plasma-derived FVIII in patients aged ≥ 6 years or ≥ 50 exposure days in patients aged < 6 years (von Drygalski *et al.*, 2023, p311; Malec *et al.*, 2024, p236). Patients were excluded if they had a or a history of a positive inhibitor test.

Patients proposed for perioperative management are adults, adolescent, and paediatric HMA patients for whom surgery is required and includes both trauma and elective surgeries. The requested population includes all HMA patients and is aligned with treatment guidelines, where perioperative management is recommended for HMA patients of any severity for whom surgery is required (ABDR, 2024-25, p7). The clinical evidence for perioperative management is derived

from patients in the XTEND-1 and XTEND-Kids trials who underwent surgery (Klamroth *et al.*, 2025a).

The ABDR is a clinical registry for patients in Australia with bleeding disorders. The most recent analysis showed that there were 2,874 patients with HMA, of whom approximately 788 patients had severe HMA, approximately 294 had moderate HMA and 1,571 had mild HMA. Only 146 were reported to have inhibitors (ABDR, 2024-25, p11, Table 4).

Table 4 Detailed breakdown of haemophilia A patients from the ABDR 2024-25

Haemophilia A (Hereditary)	NSW	VIC	QLD	SA	WA	TAS	NT	ACT	National
Number of patients	770	699	611	275	363	85	16	55	2,874
Severe	220	181	192	59	97	19	<5	15	<788
Moderate	99	53	51	41	27	7	<5	11	<294
Mild	421	333	325	165	233	53	13	28	1,571
Not applicable/Unknown	30	132	43	10	6	6	–	<5	<232
Age range									
0–19	223	163	182	70	86	21	<5	17	<767
20–39	226	198	185	75	114	25	6	13	842
40–59	171	205	151	65	89	21	6	17	725
60–79	118	118	82	50	63	14	<5	5	<455
80 and over	32	15	11	15	11	<5	–	<5	<94
Average Weight (kg)	68	59	70	75	73	61	63	70	67

Source: ABDR (2024-25), Table 6, p14

Investigations

According to the WFH guidelines (Srivastava *et al.*, 2020), haemophilia should be suspected in individuals with a history of any of these symptoms:

- Easy bruising
- ‘Spontaneous’ bleeding (i.e., bleeding for no apparent/known reason), particularly into joints, muscles, and soft tissues
- Excessive bleeding following trauma or surgery.

Accurate diagnosis of haemophilia is essential to inform appropriate management. A definitive haemophilia diagnosis is based on a factor assay to demonstrate deficiency of FVIII (for HMA) or factor IX (for haemophilia B) (Srivastava *et al.*, 2020). The most frequently used assays are based on activated partial thromboplastin time, using a one-or two-stage process (Peyvandi *et al.*, 2020). These assays can also be used to determine to monitor FVIII levels.

Systematic surveillance for FVIII inhibitors is recommended to guide treatment decisions. The Australian guidance for inhibitor monitoring is presented in Table 5. Laboratory assays, particularly the Bethesda assay, are essential for detecting these inhibitors and assessing their levels (Favaloro *et al.*, 2024). An inhibitor titre of ≥ 0.6 Bethesda units/mL is considered be considered clinically significant. Only HMA patients without inhibitors should be treated with efanesoctocog alfa.

Table 5 Australian guidance on inhibitor monitoring

Point	Recommendation
6.2.10	In all cases, inhibitors render treatment with replacement factor concentrates difficult. Patients on clotting factor therapy should therefore be screened for development of inhibitors
6.2.11	Confirmation of the presence of an inhibitor and quantification of the titre is performed in the laboratory, preferably using the Nijmegen-modified Bethesda assay
6.2.12	For children, inhibitors should be screened once every 5 exposure days until 20 exposure days, then every 10 exposure days between 21 and 50 exposure days and at least two times a year until 150 exposure days
6.2.13	For adults with more than 150 exposure days, apart from a 6–12 monthly review, any failure to respond to adequate factor concentrate replacement therapy in a previously responsive patient is an indication to assess for an inhibitor
6.2.14	Inhibitors should also be assessed in all patients who have been intensively treated for more than 5 days, within 4 weeks of the last infusion

Point	Recommendation
6.2.15	Inhibitors should also be assessed before surgery or if recovery assays are not as expected, and when clinical response to treatment of bleeding is suboptimal in the postoperative period

Source: Favaloro et al. (2024); AHCDO (2016)

Management

Treatment of haemophilia is co-ordinated by Haemophilia Treatment Centres (HTC) in Australia, which are located in major public hospitals. HTC comprise a multidisciplinary team including clinicians, nurses, physiotherapists, and social workers, counsellors or psychologists with expertise in the treatment of patients with haemophilia (Haemophilia Foundation Australia, 2026). They operate using a 'comprehensive care' approach to cover the range of care needs. Patients and carers can record bleeds and treatment administered at home through the MyABDR app (National Blood Authority, 2024).

Provide a rationale for the specifics of the eligible population:

The eligible populations proposed for treatment with efanesoctocog alfa are (i) prophylaxis and breakthrough treatment of adult, adolescent, and paediatric patients with moderate or severe HMA without inhibitors, and (ii) perioperative management of all HMA patients without inhibitors (Table 1).

Efanesoctocog alfa is proposed to be used for managing breakthrough bleeds in patients already receiving prophylaxis with efanesoctocog alfa. It is not proposed as an on-demand option for patients receiving prophylaxis with another treatment, nor for patients not on prophylaxis. This approach reflects the advantage of managing breakthrough bleeds with the same prophylaxis regimen.

The proposed populations are within the TGA-approved indication:

'ALTUVIIIIO is a long-acting recombinant anti-haemophilic factor (coagulation FVIII) indicated in adults, adolescents and children with haemophilia A (congenital FVIII deficiency) for:

- *Routine prophylaxis to prevent or reduce the frequency of bleeding episodes*
- *Treatment and control of bleeding episodes*
- *Perioperative management of bleeding (surgical prophylaxis).*

ALTUVIIIIO does not contain von Willebrand factor, and therefore is not indicated in patients with von Willebrand's disease.'

The populations are aligned with the evidence from the pivotal trials in adults and adolescents aged ≥ 12 years (XTEND-1) and paediatric patients aged < 12 years (XTEND-Kids). All the patients in XTEND-1 and XTEND-Kids were previously treated with (prophylaxis or on demand) (von Drygalski et al., 2023, Malec et al., 2024). Prophylaxis included treatment with a FVIII product or emicizumab, and on-demand with a FVIII product.²

² Current regimen included one of the following:

- Prophylactic treatment regimen with a FVIII product or prophylactic emicizumab therapy for at least 6 months during the previous 12 months. Appropriate washout time needs to be considered.
- On-demand regimen with a FVIII product with a history of at least 12 bleeding episodes in the previous 12 months or at least 6 bleeding episodes in the previous 6 months prior to study enrolment.

Intervention

Name of the proposed health technology:

Efanesoctocog alfa (ALTUVIIIIO®).

Describe the key components and clinical steps involved in delivering the proposed health technology:

Efanesoctocog alfa is presented as a powder in a single-use vial (ALTUVIIIIO PI). It must be reconstituted with a prefilled syringe containing sterilised water prior to intravenous administration. The entire dose of efanesoctocog alfa is intravenously administered over 1- to 10 minutes, based on the patient's comfort level.

The recommended dosing for routine prophylaxis for adults, adolescents and children is 50 IU/kg of efanesoctocog alfa administered once weekly (QW) (ALTUVIIIIO PI). The recommended dosing for breakthrough bleeds occurring in patients receiving efanesoctocog alfa prophylaxis is provided in Table 6. The recommended dosing is consistent with that used in the XTEND-1 and XTEND-Kids trials (von Drygalski *et al.*, 2023, p311; Malec *et al.*, 2024, p236). In the event that an efanesoctocog alfa prophylaxis patient experiences a breakthrough bleed, treatment will be covered by their own home inventory.

Table 6 Dosing for treatment and control of bleeding episodes

Type of bleeding	Recommended dose	Additional information
Minor and moderate For example: Uncomplicated joint bleeds, minor muscular bleeds, mucosal or subcutaneous bleeds	Single dose of 50 IU/kg	For minor and moderate bleeding episodes occurring within 2 to 3 days after a prophylactic dose, a lower dose of 30 IU dose may be used
Major For example: Intracranial, retroperitoneal, iliopsoas and neck bleeds, muscle bleeds with compartment syndrome and bleeds associated with a significant decrease in the haemoglobin level	Single dose of 50 IU/kg	Additional doses of 30 or 50 IU/kg every 2 to 3 days may be considered

Source: ALTUVIIIIO PI, p3

The dosing of efanesoctocog alfa for perioperative management is provided in Table 7. The recommended dose is consistent with that used in XTEND-1 and XTEND-Kids (Klamroth *et al.*, 2025b, p391).

Table 7 Dosing for perioperative management

Type of surgery	Recommended dose	Additional information
Minor surgery	Single dose of 50 IU/kg	An additional dose of 30 or 50 IU/kg after 2 to 3 days may be considered.
Major surgery For example: Intracranial, intraabdominal, joint replacement surgery or complicated dental procedures	Single dose of 50 IU/kg	Additional doses of 30 or 50 IU/kg every 2 to 3 days may be administered as clinically needed for postoperative management.

Source: ALTUVIIIIO PI, p3

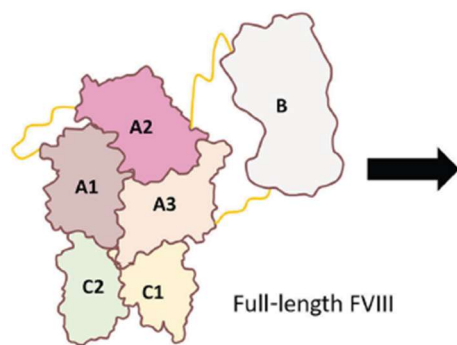
Identify how the proposed technology achieves the intended patient outcomes:

The proposed health technology is efanesoctocog alfa, a first-in-class high sustained FVIII replacement product that provides high bleed protection. It is a B domain deleted single chain fusion FVIII connected to the Fc region of human immunoglobulin G1, D'D3 fragment of von Willebrand factor (VWF), and unstructured hydrophilic recombinant polypeptides (XTEN) (Figure 1).

It is designed to decouple recombinant FVIII from endogenous VWF and overcome the VWF imposed half-life ceiling, allowing for once weekly injection while maintaining FVIII activity levels >40% (near normal) for most of the week. Clinically, this translates to sustained clotting

factor levels throughout the week, which reduces the risk of spontaneous and breakthrough bleeding episodes. For patients, this means fewer injections per week compared to standard FVIII products, moving from multiple weekly doses to a single weekly injection, while maintaining superior bleed protection. This improved dosing convenience enhances treatment adherence and quality of life, allowing patients greater freedom and flexibility in managing their haemophilia.

A. Factor VIII



B. Efanesoctocog alfa

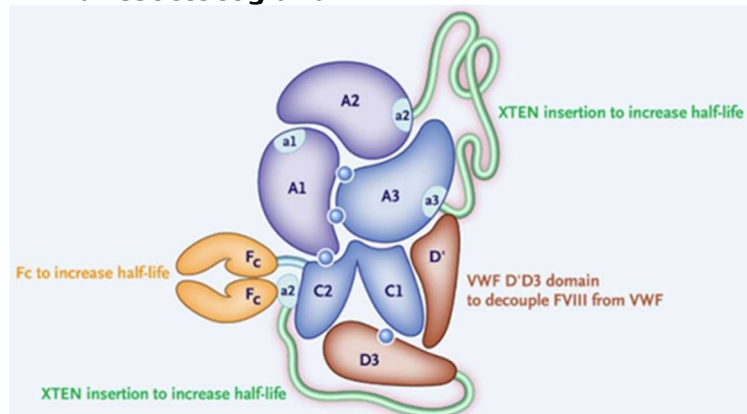


Figure 1 Structure of factor VIII (A) compared with efanesoctocog alfa (B)

Abbreviations: a1, a2, a3: acidic region 1, 2, 3, Fc: fragment crystallizable, FcRn: neonatal Fc receptor, FVIII: factor VIII, VWF: von Willebrand factor

Source: Adapted from Dargaud et al. (2024), Figure 1, p2438 and von Drygalski et al. (2023), Figure S1B, suppl., p11

Owing to its novel design, efanesoctocog alfa can function independently of endogenous VWF and elicits 2 to 4 times longer half-life compared with extended half-life (EHL) and standard half-life (SHL) FVIII products (Figure 2). The longer half-life contributes to a high-sustained level of FVIII activity for most of the week and has led to an excellent haemostatic effect with once weekly administration (Yada and Nogami, 2025). This provides patients with both efficacy and convenience.

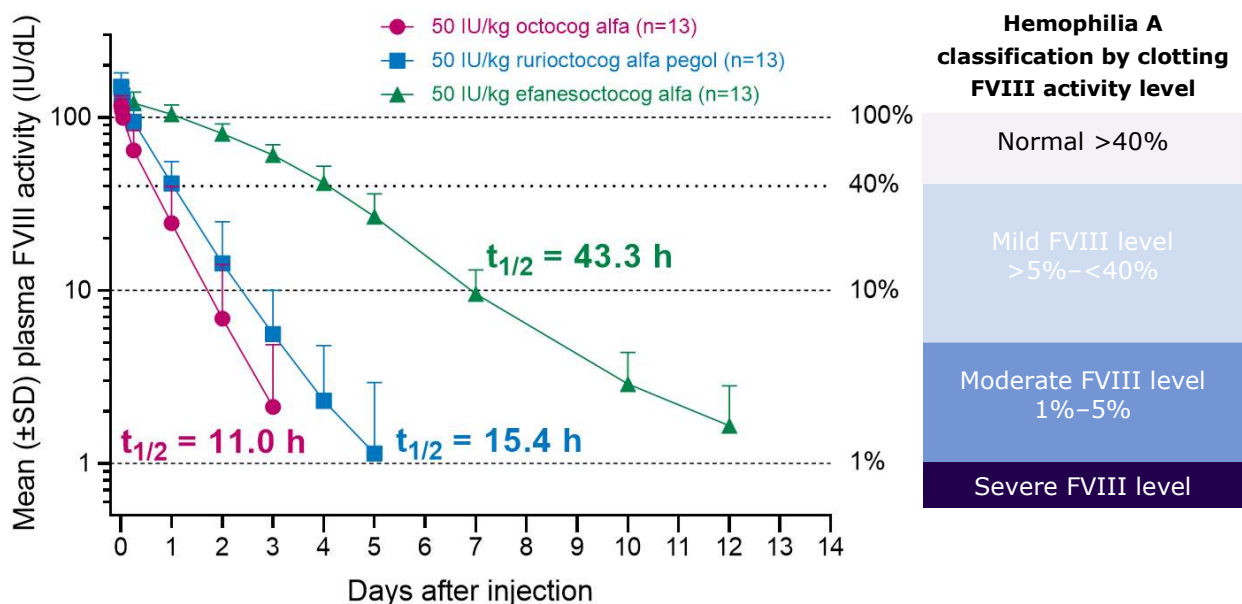


Figure 2 Plasma baseline-corrected factor VIII activity-time profile

*Units of IU/dL are equivalent to percent FVIII activity

†Mean baseline-corrected FVIII activity for efanesoctocog alfa was below the lower limit of quantitation by 14 days after the dose. The lower limit of quantitation for octocog alfa was 0.5 IU/dL, that for rurioctocog alfa was 0.6 IU/dL, and that for efanesoctocog alfa was 1 IU/dL. $t_{1/2}$, half-life

Source: Lissitchkov et al. (2023), Figure 2, p4

Does the proposed health technology include a registered trademark component with characteristics that distinguishes it from other similar health components?

Yes. Efanesoctocog alfa is a recombinant protein which contains additional sequences to increase the half-life of efanesoctocog alfa (Figure 1).

Explain whether it is essential to have this trademark component or whether there would be other components that would be suitable:

An infusion kit is provided to administer efanesoctocog alfa and no other components are required.

Are there any proposed limitations on the provision of the proposed health technology delivered to the patient (For example: accessibility, dosage, quantity, duration or frequency):

Yes, there are minor limitations on the provision of the proposed health technology due to accessibility for regional or remote patients. Efanesoctocog alfa requires intravenous administration, which may occur in an in- or outpatient setting in hospital. Alternatively, efanesoctocog alfa can be administered at home by the patient or patient's caregiver once they have been properly trained in monitoring hypersensitivity reactions and the patient or patient's caregiver are comfortable administering efanesoctocog alfa outside of a healthcare setting (ALTUVIIIIO PI).

Provide details and explain:

Not applicable

If applicable, advise which health professionals will be needed to provide the proposed health technology:

Treatment with efanesoctocog alfa should be initiated under the supervision of a qualified healthcare professional experienced in the treatment of HMA (ALTUVIIIIO PI). Efanesoctocog alfa for perioperative management is also likely to be administered by healthcare professionals. The patient should be monitored for hypersensitivity reactions during the infusion and to establish the rate of infusion most appropriate for the patient. Healthcare professionals trained in efanesoctocog alfa administration will likely include:

- Haematologists
- Haemophilia nurses
- Surgical healthcare professionals
- Allied healthcare professionals (e.g., physiotherapists) in HTC.

Efanesoctocog alfa can be self-administered by the patient or by a caregiver after they are trained.

If applicable, advise whether delivery of the proposed health technology can be delegated to another health professional:

Not applicable (see above).

If applicable, advise if there are any limitations on which health professionals might provide a referral for the proposed health technology:

Not applicable.

Is there specific training or qualifications required to provide or deliver the proposed service, and/or any accreditation requirements to support delivery of the health technology?

No.

Provide details and explain:

Not applicable.

Indicate the proposed setting(s) in which the proposed health technology will be delivered:

- ☐ Consulting rooms
- ☒ Day surgery centre
- ☒ Emergency Department
- ☒ Inpatient private hospital
- ☒ Inpatient public hospital
- ☐ Laboratory
- ☒ Outpatient clinic
- ☒ Patient's home
- ☐ Point of care testing
- ☐ Residential aged care facility
- ☐ Other (please specify)

Efanesoctocog alfa prophylaxis may be administered in an outpatient clinic or in a patient's home, if the patient or caregiver is trained in the administration. Efanesoctocog alfa may also be administered in the same settings for the treatment of breakthrough bleeds if minor or moderate in severity. Major bleeds may require treatment in an emergency department or as an inpatient in a public or private hospital. HTC are mainly located in public hospitals, patients may be treated at private hospitals if advice is sought from a specialist clinician (Clarke *et al.*, 2021, NSW Health, 2023). Efanesoctocog alfa may be administered for perioperative management in day surgery centres, emergency departments, public or private hospitals.

Is the proposed health technology intended to be entirely rendered inside Australia?

Yes.

Provide additional details on the proposed health technology to be rendered outside of Australia:

Not applicable.

Comparator

Nominate the appropriate comparator(s) for the proposed medical service (i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system). This includes identifying health care resources that are needed to be delivered at the same time as the comparator service:

Prophylaxis

Patients with moderate or severe HMA without inhibitors are currently managed with emicizumab prophylaxis (with FVIII replacement for breakthrough bleeds) or FVIII replacement therapy for both prophylaxis and breakthrough bleeding. Two comparators have, therefore, been nominated (

Table 8).

EHL FVIII is nominated as the primary FVIII comparator as it is the most used FVIII replacement therapy in Australia and is associated with improved outcomes compared with SHL FVIII (Brennan *et al.*, 2020, George *et al.*, 2023).

The comparator varies by population, which reflects three distinct populations defined by emicizumab eligibility and current treatment choice (

Table 8). Across the populations, efanesoctocog alfa 50 IU/kg QW for prophylaxis with it also available to treat breakthrough bleeding.

Table 8 Comparators to efanesoctocog alfa as prophylaxis and to treat breakthrough bleeds

Moderate or severe HMA without inhibitors	Comparator		Intervention	
	Prophylaxis	Breakthrough bleeding	Prophylaxis	Breakthrough bleeding
Population 1. Emicizumab eligible AND receiving emicizumab	Emicizumab	EHL FVIII	Efanesoctocog alfa 50 IU/kg QW	Efanesoctocog alfa*
Population 2. Emicizumab eligible BUT receiving FVIII prophylaxis	EHL FVIII	EHL FVIII	Efanesoctocog alfa 50 IU/kg QW	Efanesoctocog alfa*
Population 3. Emicizumab ineligible AND receiving FVIII prophylaxis	EHL FVIII	EHL FVIII	Efanesoctocog alfa 50 IU/kg QW	Efanesoctocog alfa*

Abbreviations: EHL = extended half-life; FVIII = factor VIII; QW = once weekly

Note: a small minority of patients are still being treated with standard-half life

*Per efanesoctocog alfa dosing recommendations (refer Table 6)

Emicizumab prophylaxis

Emicizumab is indicated for routine prophylaxis in adult, adolescent and paediatric patients with HMA with or without inhibitors (HEMLIBRA PI, p1-2). The recommended dosing consists of a loading dose of 3 mg/kg administered as a subcutaneous injection once weekly for the first 4 weeks, followed by a maintenance dose from Week 5, administered subcutaneously either:

- 1.5 mg/kg QW, or
- 3 mg/kg every 2 weeks (Q2W), or
- 6 mg/kg every 4 weeks (Q4W).

The maintenance dose of emicizumab is selected based on the preferences of the physician and patient/caregiver to support adherence (HEMLIBRA PI, p2).

An analysis of emicizumab dosing frequency in Australia, based on ABDR data, is presented in Table 9. The most common in paediatric patients (aged <18 years) was 3 mg/kg Q2W (70%) followed by 1.5 mg/kg QW (21%), and only 8% patients received emicizumab 6 mg/kg Q4W. Most adults (aged ≥18 years) received emicizumab 3 mg/kg Q2W (43%) or 1.5 mg/kg QW (39%), followed by 6 mg/kg Q4W (18%).

Analyses of emicizumab clinical trials, HAVEN 1-4, in HMA patients with and without inhibitors have shown that there was no apparent trend in the distribution of bleeds within the dosing interval, regardless of the dosing regimen chosen (Pipe *et al.*, 2023). All dosing regimens are expected to deliver consistent bleeding control.

Table 9 Emicizumab dosing frequency in Australian patients with HMA treated with emicizumab* on the Australian Bleeding Disorders Registry (6 April 2022)

Dosing regimen	Paediatric population (n=236)	Adult population (n=223)	Total population (N=459)
Weekly	50 (21)	87 (39)	137 (30)
Every 2 weeks	166 (70)	95 (43)	261 (57)
Every 4 weeks	20 (8)	41 (18)	61 (13)

*a minimum of 6 months post-emicizumab commencement data

Source: Ramanan *et al.* (2024), Table 2, p3

Emicizumab is not designed or approved to treat acute bleeding episodes (Srivastava *et al.* (2020), p28). This means that, for patients receiving emicizumab prophylaxis, FVIII replacement therapy is required to treat the acute event. EHL FVIII is likely to be the most used FVIII replacement for treating breakthrough bleeds in this setting, given its longer half-life and improved bleeding outcomes compared with SHL FVIII (Brennan *et al.*, 2020, George *et al.*, 2023).

EHL FVIII prophylaxis

EHL FVIII for prophylaxis and breakthrough bleeding is also nominated as a comparator. Among patients receiving FVIII replacement prophylaxis, most receive EHL FVIII rather than SHL FVII (Table 10). There are two EHL FVIII treatment options listed on the NPPL: rurioctocog alfa (ADYNOVATE) and efmoroctocog alfa (ELOCTATE). Prophylaxis with EHL VIII accounts for 75.6% (385/509) of all prophylaxis with FVIII replacement prophylaxis in HMA patients in the most recent analysis of the ABDR. The remaining patients received prophylaxis with SHL VIII: octocog alfa (Advate) or moroctocog alfa (Xyntha), or plasma-derived FVIII (Biostate) (Table 10).

Table 10 Proportion of patients on FVIII prophylaxis

FVIII (IUs) Haemophilia A	Patients (n) ³	Prophylaxis (total IU)	Prophylaxis Average (IU/kg)
EHL FVIII			
ADYNOVATE	120	10,303,250	150
ELOCTATE	265	19,992,840	172
SHL FVIII			
Advate	59	8,117,250	301
Xyntha Dual Chamber	58	9,509,500	313
Biostate	7	450,750	134

Note the source table also includes <5 patients treated with prophylaxis with FEIBA -NF which is only used in patients with inhibitors, which is not part the proposed population for treatment with efanesoctocog alfa

Abbreviations: EHL = extended half-life; FVIII = factor VIII; SHL = standard half-life

Source: ABDR (2024-25), Table 9, p17

The recommended prophylaxis dosing regimens for the two EHL FVIII therapies are presented in Table 11. The recommended prophylaxis dose is 40-50 IU/kg every 4 to 5 days for rurioctocog alfa, and 50 IU/kg every 3 to 5 days for efmoroctocog alfa (i.e., on average twice weekly). More frequent dosing or higher doses may be necessary in some patients to provide adequate bleed protection.

Table 11 Prophylaxis dosing regimens for EHL FVIII therapies

FVIII replacement therapies	Dose	Additional comments
Rurioctocog alfa pegol (ADYNOVATE)	40-50 IU/kg every 4 to 5 days	Dose and/or frequency should be adjusted to provide the necessary coverage to prevent bleeding. In some cases, doses up to 60 IU per kg can be used
Efmoroctocog alfa (ELOCTATE)	50 IU/kg every 3 to 5 days	The dose may be adjusted based on patient response in the range of 25-65 IU/kg. More frequent or higher doses up to 80 IU/kg may be required in children <12 years of age

Source: ADYNOVATE PI, p3; ELOCTATE PI, p4

³ These numbers must be viewed with caution as they do not reflect the data we have on file for ELOCTATE

The recommended dose regimens for breakthrough bleeding are presented in Table 12.

Table 12 Dose regimen for breakthrough bleeds with EHL FVIII therapies

FVIII replacement therapies	Factor VIII level required (IU/dL or % of normal)	Frequency of doses (hours)/duration of therapy (days)
<i>Rurioctocog alfa pegol (ADYNOVATE)</i>		
Early haemorrhage, muscle bleeding or oral bleeding	20-40	Repeat injections every 12 to 24 hours for at least 1-day, until the bleeding episode, as indicated by pain, is resolved or healing is achieved
More extensive haemarthrosis, muscle bleeding or haematoma	30-60	Repeat injections every 12 to 24 hours for 3–4 days or more until pain and acute disability are resolved
Life threatening haemorrhages	60-100	Repeat injections every 8 to 24 hours until threat is resolved
<i>Efmoroctocog alfa (ELOCTATE)</i>		
Minor and moderate haemorrhage	40-60	20-30 IU/kg. Repeat every 24-48 hours (12-24 hours for patients <12 years of age) until bleeding is resolved
Major haemorrhage	80-100	40-50 IU/kg. Repeat every 12-24 hours (8-24 hours for patients <12 years of age) until bleeding is resolved

Note: The calculation of the required dosage of factor VIII is based upon the empirical finding that on average 1 IU of factor VIII per kg body weight raises the plasma factor VIII activity by approximately 2 IU/dL. The required dosage is determined using the following formula:

Required units (IU) = body weight (kg) x desired factor VIII rise (%) x 0.5 IU/kg

Source: ADYNOVATE PI, p3; ELOCTATE PI, p4

Perioperative management

EHL FVIII is nominated as the comparator to efanesoctocog alfa in patients with HMA, of any severity, without inhibitors requiring perioperative management (Table 13). Patients receive EHL FVIII for perioperative management irrespective of prior treatment. Although SHL FVIII replacement can also be used for perioperative management, EHL FVIII is considered the gold standard due to the advantage of less frequent dosing (Fox *et al.*, 2023). Patient requiring perioperative management may be receiving prophylaxis with emicizumab or EHL FVIII (e.g., moderate to severe HMA) or receiving on-demand treatment (e.g., mild HMA). Patients are not on receiving prophylaxis would receive on-demand treatment with EHL FVIII to treat any bleeds.

Table 13 Comparators to efanesoctocog alfa when used for perioperative management

Perioperative management	Prior treatment		Comparator
	Prophylaxis	On demand	Perioperative management
All HMA patients without inhibitors			
Population 1. On prophylaxis, undergoing major surgery	Emicizumab or EHL FVII replacement*	-	EHL FVIII
Population 2. On-demand, undergoing major surgery	-	EHL FVIII*	EHL FVIII
Population 3. On prophylaxis, undergoing minor surgery	Emicizumab or EHL FVIII replacement*	-	EHL FVIII
Population 4. On-demand, undergoing minor surgery	-	EHL FVIII*	EHL FVIII

**Most patients who receive prophylaxis or on-demand treatment with FVIII receive on the NPPL are treated with EHL FVIII with a minority being treated with SHL FVIII*

The doses and frequency of dosing for perioperative treatment are presented in Table 14.

Table 14 Perioperative treatment with EHL FVIII therapies

	Factor VIII level required (IU/dL or % of normal)	Frequency of doses (hours)/duration of therapy (days)
<i>Rurioctocog alfa pegol (ADYNOVATE)</i>		
Minor surgery	30-60	Every 24 hours (12 to 24 hours for patients <6 years), at least 1-day, until healing is achieved
Major surgery	80-100 (pre- and post-operative)	Repeat injections every 8 to 24 hours (6 to 24 hours for patients <6 years) until adequate wound healing then continue therapy for at least another 7 days to maintain a factor VIII activity of 30% to 60% (IU/dl)
<i>Efmoroctocog alfa (ELOCTATE)</i>		
Minor surgery	50-80	25-40 IU/kg. A single infusion may be sufficient. Repeat every 24 hours (12-24 hours for patients <12 years of age) as needed to control bleeding
Major	80-120	An initial preoperative dose of 40-60 IU/kg followed by a repeat dose of 40-50 IU/kg after 8-24 hours (6-24 hours for patients <12 years of age) and then every 24 hours to maintain FVIII activity within the target range

Note: The calculation of the required dosage of factor VIII is based upon the empirical finding that on average 1 IU of factor VIII per kg body weight raises the plasma factor VIII activity by approximately 2 IU/dL. The required dosage is determined using the following formula:

Required units (IU) = body weight (kg) x desired factor VIII rise (%) x 0.5 IU/kg

Source: ADYNOVATE PI, Table 1, p3, ELOCTATE PI, Table 2, p4 PI, p3

Provide a name for your comparator:

Prophylaxis

The nominated comparators in patients with moderate or severe HMA without inhibitors requiring prophylaxis are:

- Emicizumab prophylaxis plus EHL FVIII replacement therapy for breakthrough bleeds
- EHL FVIII replacement therapy for prophylaxis and additional doses to treat breakthrough bleeds.

Perioperative treatment

The nominated comparator in patients with HMA, of any severity, without inhibitors requiring perioperative management is:

- EHL FVIII replacement therapy.

Provide an identifying number for your comparator (if applicable):

Not applicable. Emicizumab and FVIII replacement products are listed on the NPPL managed by the NBA.

Provide a rationale for why this is a comparator:

Emicizumab prophylaxis

Emicizumab is the nominated comparator as it is the most utilised routine prophylaxis treatment for the populations proposed. An analysis of the ABDR up to December 2021 showed 61.6% of patients with moderate or severe HMA on prophylaxis were treated with emicizumab, followed by EHL FVIII (21.3%) and SHL FVIII (17.1%) (Parikh *et al.*, 2022). This analysis reflects a very high uptake of emicizumab, which only became available 2 November 2020 (Parikh *et al.*, 2022). Current estimates suggest that more than 80% of prophylaxis patients now receive emicizumab, as the use of FVIII replacement therapies has continued to decline substantially since 2021 in parallel with increasing emicizumab use (Figure 3).

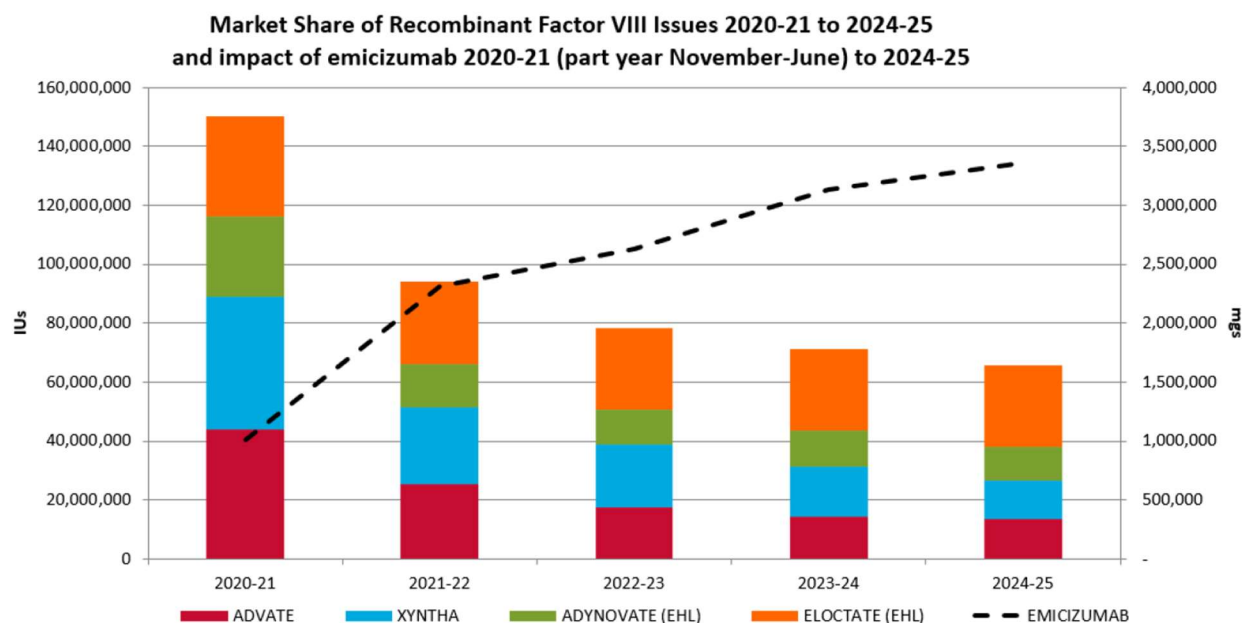


Figure 3 Market share of recombinant factor VIII and impact of emicizumab from 2020-21 to 2024-25

Abbreviations: EHL = extended half-life

Source: ABDR (2024-25), p10

International treatment guidelines recommend that '*Prophylaxis is the standard of care for people with severe hemophilia, and for some people with moderate hemophilia*' such as those with '*a severe bleeding phenotype and/or a high risk of spontaneous life-threatening bleeding*' (Srivastava *et al.*, 2020, AHDCO, 2024). These treatment guidelines, together with the availability of emicizumab from 2 November 2020, have resulted in an increased use of prophylaxis. The proportion of patients with severe HMA treated with prophylaxis has increased from 87.1%, in an analysis up to December 2021 ((Parikh *et al.*, 2022) to 92% in the most recently analysis (ABDR data request, 2025). Similarly, the proportion of patients with moderate HMA treated with prophylaxis has increased from 35.7% (December 2021) to 63% in the most recent analysis (ABDR data request, 2025). This reflects a transition from on-demand treatment to prophylaxis for those patients for whom prophylaxis is appropriate. Patients with moderate HMA for whom prophylaxis is not standard of care will continue to be treated with FVIII replacement on-demand. Therefore, the availability of efanesoctocog alfa as prophylaxis will not impact the use of FVIII on-demand treatment. Therefore, FVIII on-demand treatment is not a comparator for efanesoctocog alfa as prophylaxis.

The population proposed for efanesoctocog alfa (HMA patients without inhibitors) overlaps with that for emicizumab. While emicizumab may also be used in patients with inhibitors, as it has no structural relationship or sequence homology to FVIII and does not induce or enhance the development of direct inhibitors to FVIII (HEMLIBRA PI), most use is in patients with severe or moderate HMA without inhibitors.

Table 15 presents the characteristics of HMA patients treated with emicizumab on the ABDR as of 6 April 2022, with at least 6 months of post-emicizumab data. Of the 459 patients meeting these criteria, most had severe disease (86%) and were without inhibitors (87%). Disease severity and inhibitors status were similar across the paediatric and adult populations (

Table 15). As only four mild HMA patients received emicizumab, use of efanesoctocog alfa outside its proposed population is unlikely.

Table 15 Characteristics of HMA patients treated with emicizumab* from the Australian Bleeding Disorders Registry (6 April 2022)

	Paediatric population (n=236)	Adult population (n=223)	Total population (N=459)
Age (y), median (IQR)	9 (5-14)	36 (26-50)	17 (9-35)
Diagnosis severity, n (%)			
Severe	205 (87)	192 (86)	397 (86)
Moderate	31 (13)	27 (12)	58 (13)
Mild	0 (0)	4 (2)	4 (1)
Inhibitor response, n, (%)			
No current inhibitor	210 (89)	190 (85)	400 (87)
High responding	22 (9)	24 (11)	46 (10)
Low responding	4 (2)	9 (4)	13 (3)

*a minimum of 6 months post-emicizumab commencement data

Source: Ramanan *et al.* (2024), Table 2, p3

EHL FVIII is nominated as a component of the comparator for the treatment of breakthrough bleeds in patients receiving prophylaxis with emicizumab. Emicizumab is only indicated for prophylaxis and is not intended to treat acute bleeding episodes (Srivastava *et al.*, 2020), p28). Patients treated with emicizumab prophylaxis, therefore, require a different treatment for breakthrough bleeds. EHL FVIII requires less frequent dosing than SHL FVIII to resolve a bleed (Brennan *et al.*, 2020; George *et al.*, 2023).

EHL FVIII prophylaxis

EHL FVIII for is also nominated as a comparator in patients with moderate or severe HMA without inhibitors requiring prophylaxis. As previously described, EHL FVIII is more commonly used for prophylaxis than SHL FVIII, as shown in the most recent analysis of the ABDR (Table 10). Australian clinicians have advised that the same FVIII replacement therapy used for prophylaxis is also used to treat breakthrough bleeds, as it is not practical for patients to store a separate FVIII product at home solely for the treatment of breakthrough bleeds.

EHL FVIII perioperative management

EHL FVIII is nominated as the comparator to efanesoctocog alfa in patients with HMA, of any severity, without inhibitors requiring perioperative management. EHL FVIII is currently the gold standard for perioperative management as it requires less frequent dosing than SHL FVIII, simplifying pre- and post-operative management, and provides better bleed protection coverage, as demonstrated by the higher sustained FVIII levels achieved with EHL FVIII ruriotocog alfa pegol compared with SHL FVIII octocog alfa (refer Figure 2) (Fox *et al.*, 2023).

Although emicizumab is not indicated for perioperative management (HEMLIBRA PI), some patients undergo minor surgeries without additional FVIII (Kruse-Jarres *et al.*, 2022). This is analogous to patients receiving efanesoctocog alfa prophylaxis, where minor surgery can be managed without an additional dose if timed appropriately so that the usual once weekly prophylaxis dose substitutes for a single perioperative dose of 50 IU/kg (Table 7).

Pattern of substitution – Will the proposed health technology wholly replace the proposed comparator, partially replace the proposed comparator, displace the proposed comparator or be used in combination with the proposed comparator?

- ☐ None (used with the comparator)
- ☐ Displaced (comparator will likely be used following the proposed technology in some patients)
- ☒ Partial (in some cases, the proposed technology will replace the use of the comparator, but not all)
- ☐ Full (subjects who receive the proposed intervention will not receive the comparator)

Outline and explain the extent to which the current comparator is expected to be substituted:

Prophylaxis

The current HMA population treated with prophylaxis can be categorised as the following populations:

- Population 1: Emicizumab eligible AND receiving emicizumab prophylaxis
- Population 2: Emicizumab eligible BUT receiving FVIII replacement
- Population 3: Emicizumab ineligible AND receiving FVIII replacement.

Population 1

Patients who are dissatisfied with emicizumab are likely to switch to efanesoctocog alfa (Rauch *et al.*, 2026). Treatment with emicizumab does not achieve high sustained FVIII equivalence (typically 10-15%) and is not sufficient to eliminate all bleeds, requiring FVIII replacement to treat breakthrough bleeds (Hermans and Pierce, 2023). This is especially problematic for patients who (i) are highly active (e.g., play sport, have a physical occupation) and are at increased risk of breakthrough traumatic or spontaneous bleeds, and (ii) have a high bleed phenotype. In contrast, efanesoctocog alfa provides FVIII activity levels >40% (near normal) for most of the week (Figure 4). For patients and carers, this higher and more sustained level of bleed protection can be transformative, providing the confidence to engage more fully in everyday life. This includes children participating in sport and school activities, and adults undertaking physically demanding jobs (e.g., labouring), without the same fear of breakthrough bleeds. Reduced bleed frequency also supports improved work and school participation and helps preserve long-term joint health, an important driver of health-related quality of life for people with HMA.

Older patients on emicizumab with multiple cardiovascular risk factors may also switch, given the boxed warning for thrombotic microangiopathy and thromboembolism, a concern that does not apply to efanesoctocog alfa (HEMLIBRA PI, ALTUVIIIO PI). Being well tolerated, efanesoctocog alfa offers an alternative for patients who do not tolerate emicizumab (e.g., those with injection site reactions) (Rauch *et al.*, 2026).

Patients who prefer the convenience of once weekly prophylaxis, and the ability to use the same treatment for prophylaxis and breakthrough bleeding, may also wish to switch from emicizumab plus EHL FVIII to efanesoctocog alfa. This allows patients and/or caregivers to maintain their intravenous injection skills, which is harder to achieve with emicizumab, as it is administered subcutaneously. Patients and caregivers who do not have the skills to administer FVIII replacement therapy at home need to attend a hospital for treatment of breakthrough bleeds. This may be inconvenient, delay the time to FVIII administration, result in worse outcomes, and incur additional healthcare costs compared with earlier treatment at home. This is particularly important for patients living in remote or regional areas with limited access to hospital-based care, who may prefer FVIII replacement therapy as it allows them to maintain their intravenous infusion skills and have immediate access to factor for self-administration in an emergency.

Patients who prefer subcutaneous administration, have poor venous access, or are satisfied with the bleed protection offered by emicizumab are unlikely to switch to efanesoctocog alfa. As efanesoctocog alfa is not indicated for the use in patients with FVIII inhibitors, emicizumab will continue to be used as prophylaxis in patients with FVIII inhibitors.

Populations 2 & 3

The reasons for switching in patients currently receiving FVIII replacement for prophylaxis and breakthrough bleeding are likely to be similar irrespective of eligibility for emicizumab. Australian clinicians have provided feedback that the emicizumab-ineligible population (i.e., Population 3) is likely less than 1%, given that contraindications include allergy to

emicizumab or its excipients, and a boxed warning exists for thrombotic microangiopathy and thromboembolism (HEMLIBRA PI).

Most patients are expected to switch from EHL FVIII because of the superior bleed protection offered by efanesoctocog alfa prophylaxis (Rauch *et al.*, 2026). EHL FVIII products and efanesoctocog alfa are FVIII replacement treatment sharing the same route of administration (i.e., intravenous injection). However, efanesoctocog alfa is a first-in-class, high-sustained FVIII replacement that provides high bleed protection with a convenient once weekly intravenous injection, compared with twice-weekly injections required with EHL FVIII prophylaxis (Table 11), and FVIII activity levels drop more rapidly (Figure 2). For patients and carers, the reduction from twice-weekly to once-weekly injections represents a meaningful reduction in treatment burden, supporting improved quality of life and greater freedom to engage in daily activities.

The minority of patients still being treated with SHL FVIII replacement may be less likely to switch to efanesoctocog alfa because they have not switched to EHL FVIII or emicizumab despite these being available for many years (Figure 3, Table 11). Feedback from Australian clinicians is that patients who remain on SHL FVIII replacement understand their how their product works and are satisfied.

Perioperative management

The current population of HMA patients requiring perioperative management can be categorised as follows:

- Population 1: On prophylaxis, undergoing major surgery
- Population 2: On demand treatment, undergoing major surgery
- Population 3: On prophylaxis, undergoing minor surgery
- Population 4: On demand, undergoing minor surgery.

In all these populations, EHL FVIII is currently the gold standard for perioperative management, as it has the advantage of less frequent dosing than SHL FVIII (Fox *et al.*, 2023). Efanesoctocog alfa is expected to replace EHL FVIII as the preferred treatment for perioperative management due to its distinct advantages: less frequent dosing than EHL FVIII and, critically, the ability to achieve and sustain factor activity levels in the non-haemophilia range (>40%) throughout the perioperative period (Figure 3). Maintaining near-normal factor activity levels perioperatively reduces the risk of surgical and post-operative bleeding complications, which is not consistently achievable with EHL FVIII. This is expected to apply to both minor and major surgery, irrespective of current treatment regimen (i.e., prophylaxis or on-demand).

Outcomes

List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator):

- ☒ Health benefits
- ☒ Health harms
- ☐ Resources

Prophylaxis

The outcomes of XTEND-1 (von Drygalski *et al.*, 2023) and XTEND-Kids (Malec *et al.*, 2024), relevant to the assessment of prophylaxis are:

Health benefits:

- Annualised bleeding rate
 - Any bleed (treated or untreated)
 - Treated bleeds
 - Treated joint bleeds
 - Treated spontaneous bleeds

- Joint health (Haemophilia Joint Health Score).

Health harms:

- Adverse events
- FVIII inhibitor development.

Perioperative management

The outcomes of the analysis of patients undergoing major and minor surgery in XTEND-1 and XTEND-Kids relevant to the assessment of perioperative management are (Klamroth *et al.*, 2025b):

Health benefits:

- Surgeon/investigator's assessment of haemostatic response.

Health harms:

- Estimated blood loss during surgery and in the post-operative period
- Safety in the surgical/rehabilitation period.

Resource use:

- Number of doses, total consumption of FVIII
- Number and type of blood transfusions.

Outcome description – please include information about whether a change in patient management, or prognosis, occurs as a result of the test information:

Not applicable

Claims

In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)?

- ☒ Superior (for efficacy)
☒ Non-inferior (for safety)
☐ Inferior

Please state what the overall claim is, and provide a rationale:

Prophylaxis

Efanesoctocog alfa versus emicizumab

Overall claim: Efanesoctocog alfa is superior versus emicizumab as prophylaxis in adult and adolescent HMA patients aged ≥ 12 years without inhibitors based on a matching-adjusted indirect comparison (MAIC) informed by XTEND-1 and the pivotal emicizumab trial, HAVEN 3 (Álvarez Román *et al.*, 2025).

Rationale: An indirect comparison of annualised bleeding rates (ABR) showed that once weekly prophylaxis with efanesoctocog alfa was associated with statistically significantly fewer bleeds compared with once weekly prophylaxis with emicizumab in patients previously on prophylaxis (HAVEN 3 Arm C) (Álvarez Román *et al.*, 2025). The MAIC demonstrated that efanesoctocog alfa significantly reduced any bleed (IRR [95% CI] 0.32 [0.19, 0.56]), any treated bleed (0.50 [0.29, 0.86]) and treated joint bleeding (0.48 [0.24, 0.95]); all favoured efanesoctocog alfa versus emicizumab. Treatment with efanesoctocog alfa also demonstrated statistically significant functional improvements in major synovial joints compared with emicizumab, which is likely to translate to enhanced quality of life.

Table 16. Matching-adjusted indirect comparison (MAIC) of efanesoctocog alfa vs. emicizumab for prophylaxis in adult and adolescent patients with HMA aged ≥ 12 years without inhibitors (XTEND-1 vs. HAVEN 3)

Bleeding outcome	Incidence rate ratio (IRR)	95% CI	Interpretation
Any bleed	0.32	0.19, 0.56	Efanesoctocog alfa reduced any bleeds by 68% vs. emicizumab
Any treated bleed	0.50	0.29, 0.86	Efanesoctocog alfa reduced treated bleeds by 50% vs. emicizumab
Treated joint bleeding	0.48	0.24, 0.95	Efanesoctocog alfa reduced treated joint bleeds by 52% vs. emicizumab

Source: Álvarez Román *et al.*, 2025

XTEND-Kids provided evidence that efanesoctocog alfa was an effective treatment in paediatric patients aged <12 years without inhibitors (Malec *et al.*, 2024). Efanesoctocog alfa prophylaxis was associated with a median ABR of 0 for all types of bleeding (any treated, treated spontaneous, treated joint, and treated traumatic) and a mean ABR close to 0 when administered weekly per protocol. These results are consistent with those observed in adult and adolescent patients in XTEND-1.

There is no comparable direct evidence for emicizumab in paediatric patients without inhibitors. HAVEN 2 enrolled paediatric HMA patients aged <12 years with inhibitors (Oldenburg *et al.*, 2017), and HAVEN 7 enrolled paediatric patients aged ≤ 12 months without inhibitors who were previously untreated or minimally treated patients (1-5 exposure days with FVIII) (Pipe *et al.*, 2024), a population not comparable to that enrolled in XTEND-Kids, which required at least 150 exposure days in those aged ≥ 6 years or 50 exposure days in those aged <6 years (Malec *et al.*, 2024).

In its previous consideration of emicizumab in patients without inhibitors, MSAC noted that “...no evidence comparing emicizumab and FVIII in terms of effectiveness was presented for the smaller subpopulations of paediatric patients...” and “...advised the evidence in adults could be extrapolated to the paediatric population...” (MSAC PSD for 1579, p3). Applying the same approach and given that efanesoctocog alfa demonstrates superior efficacy compared with emicizumab for any bleed in adult and adolescent patients (aged ≥ 12 years), it follows that by extrapolation that efanesoctocog alfa would be at least as efficacious as emicizumab in paediatric patients (aged <12 years) without inhibitors.

Efanesoctocog alfa versus EHL FVIII

Overall claim: Efanesoctocog alfa is superior versus EHL FVIII as prophylaxis in adults and adolescents with HMA without inhibitors based on meta-analyses of MAICs (Klamroth *et al.*, 2025a).

Rationale: XTEND-1 provided the clinical evidence for efanesoctocog alfa. Clinical trials of the following EHL FVIII therapies were included in the analysis: rurioctocog alfa pegol and efmoroctocog alfa, turoctocog alfa pegol, and damoetocog alfa pegol. Only rurioctocog alfa pegol and efmoroctocog alfa are on the NPPL, but all are TGA-approved for prophylaxis. Notably, when MSAC recommended EHL FVIII treatments, this was based on pooled evidence across different EHL FVIII therapies (MSAC PSD for 1511). In meta-analyses, efanesoctocog alfa was associated with significantly lower ABRs versus EHL FVIII therapies for any bleeds (mean difference [95% CI] -2.24 [-3.24; -1.25]), spontaneous (-1.52 [-2.33; -0.72]), and joint bleeds (-1.60 [-2.32; -0.88]).

The claim of superior efficacy for efanesoctocog alfa versus EHL FVIII is also expected to apply to paediatric patients, based on XTEND-Kids. A systematic review has identified a number of paediatric clinical trials of EHL FVIII (Feng *et al.*, 2025). This review does not report pooled annualised bleeding rate data for EHL FVIII in paediatric patients and includes a heterogeneous population of previously treated and untreated patients. As such, it does not provide suitable evidence for a valid indirect comparison with XTEND-Kids. The efficacy claim for efanesoctocog alfa versus EHL FVIII in paediatric patients without inhibitors will instead be supported by

extrapolation from the adult and adolescent evidence (XTEND-1 vs. EHL FVIII meta-analyses), consistent with the precedent accepted by MSAC for emicizumab (MSAC PSD for 1579).

Perioperative management

Overall claim: Efanesoctocog alfa is superior versus EHL FVIII for perioperative management.

Rationale: The clinical evidence for efanesoctocog alfa for perioperative management is derived from analyses of patients undergoing major and minor surgery in XTEND-1 and XTEND-Kids (Klamroth *et al.*, 2025b). Staber *et al.* (2026) estimated the total FVIII consumption during the perioperative period for patients with efanesoctocog alfa and EHL FVIII therapies in patients with severe HMA aged ≥ 12 years (Table 17). The median total FVIII consumption for perioperative management with efanesoctocog alfa was 163 IU/kg for an average adult male in the US (91 kg),⁴ which was substantially lower than that for perioperative management with efmoroctocog alfa (493 IU/kg) or rurioctocog alfa pegol (629 IU/kg) (Table 17). No blood transfusions were required for any surgery where patients received efanesoctocog alfa, compared with three of the surgeries in which patients received efmoroctocog alfa and four of the surgeries where rurioctocog alfa pegol.

Table 17 FVIII consumption estimated for a 91 kg adult male undergoing major surgery during the postoperative period

FVIII Therapy (clinical data source)	Clinical data description	Postoperative outcomes	Median (range) FVIII consumption (IU/kg) during entire perioperative period
Efanesoctocog alfa (NCT04161495)	11 patients (aged ≥ 12 years) with severe HMA who underwent 12 major surgeries ¹	100% rated excellent; no postoperative bleeding episodes; no blood transfusions required	163 (45–361) ²
Efmoroctocog alfa (NCT01181128 and NCT01454739)	21 patients (aged ≥ 12 years) with severe HMA who underwent 23 major surgeries ³	100% rated excellent/good; 1 postoperative bleeding episode; blood transfusions required in 3 surgeries	493 (121–733) ²
Rurioctocog alfa pegol (NCT01913405)	21 previously treated male patients (aged ≥ 12 –75 years) with severe HMA who underwent 21 major surgeries ⁴	100% rated excellent; 5 postoperative bleeding episodes (2 requiring additional treatment); blood transfusions needed for 4 surgeries	629 (464–1457) ⁵

Note 91 kg

1 Major surgeries included cubital tunnel release and ulnar nerve transposition, knee and hip replacements, tooth extraction, osteosynthesis material removal, laparoscopic hernia repair, neurolysis of ulnar nerve, and removal of implanted devices from bone

2 Perioperative period was 14 days

3 Major surgeries included ankle fusion, appendectomy, arthroscopy, endoscopic third ventriculostomy, laparoscopic inguinal hernia repair, spinal surgery, unilateral elbow arthroplasty, unilateral hip arthroplasty, unilateral knee arthroscopy, bilateral knee arthroplasty, unilateral knee arthroplasty, and amputation

4 Major surgeries included orthopaedic surgeries (knee replacement, arthroscopic synovectomy, alloplastic knee surgery, hip replacement and revision, elbow cyst extirpation, needle removed from elbow, and Achilles tendon reconstruction) and non-orthopaedic surgeries (multiple tooth extractions, CVAD placement, and gastric band insertion).

5 Perioperative period was 7 days

Source: Staber *et al.* (2026), Table 1, p3

Why would the requestor seek to use the proposed investigative technology rather than the comparator(s)?

A requestor is likely to seek to use efanesoctocog alfa for its superior bleed protection compared with emicizumab and EHL FVIII therapies (Rauch *et al.*, 2026). The long half-life of efanesoctocog alfa results in sustained FVIII activity levels in the non-haemophilia range ($>40\%$) for most of the week, enabling a higher proportion of patients to achieve zero bleeds

⁴ In Australia, the average weight of HMA patients receiving treatment is: 85 kg for adults aged ≥ 18 years, 64 kg for adolescents aged 12 and <18 years, and 23 kg for paediatrics aged 0 to <12 years (ABDR data request, 2025)

with convenient once-weekly administration (Figure 4). This level of bleed protection is particularly important for physically active patients and those who want to participate more fully in school and work, where the risk of traumatic bleeds is higher. For patients currently on emicizumab who continue to experience breakthrough bleeds, switching to efanesoctocog alfa offers the opportunity to preserve long-term joint health by reducing the cumulative burden of joint bleeding. A more detailed discussion is provided in the section on 'Pattern of substitution'.

Identify how the proposed technology achieves the intended patient outcomes:

Efanesoctocog alfa is a high-sustained FVIII replacement product. Once weekly prophylaxis provides FVIII activity in the normal to near normal range (>40 IU/dL) for 4 days in adults and adolescents, and 3 days in paediatric patients aged <12 years (Figure 4). FVIII activity levels then gradually decline, with a mean of 15 IU/dL remaining at Day 7 in adults and adolescents. In paediatric patients, mean FVIII activity remained above 15 IU/dL for 5.6 days and above 10 IU/dL for 6.7 days.

By maintaining FVIII activity levels within, or close to, the non-haemophilia range for most of the week, efanesoctocog alfa provides consistent and sustained bleed protection between doses. This sustained protection underpins the clinical outcomes observed in XTEND-1 and XTEND-Kids, including the high proportion of patients achieving zero bleeds, and supports patients' ability to engage confidently in physically demanding activities, sport, work, and school, while preserving long-term joint health.

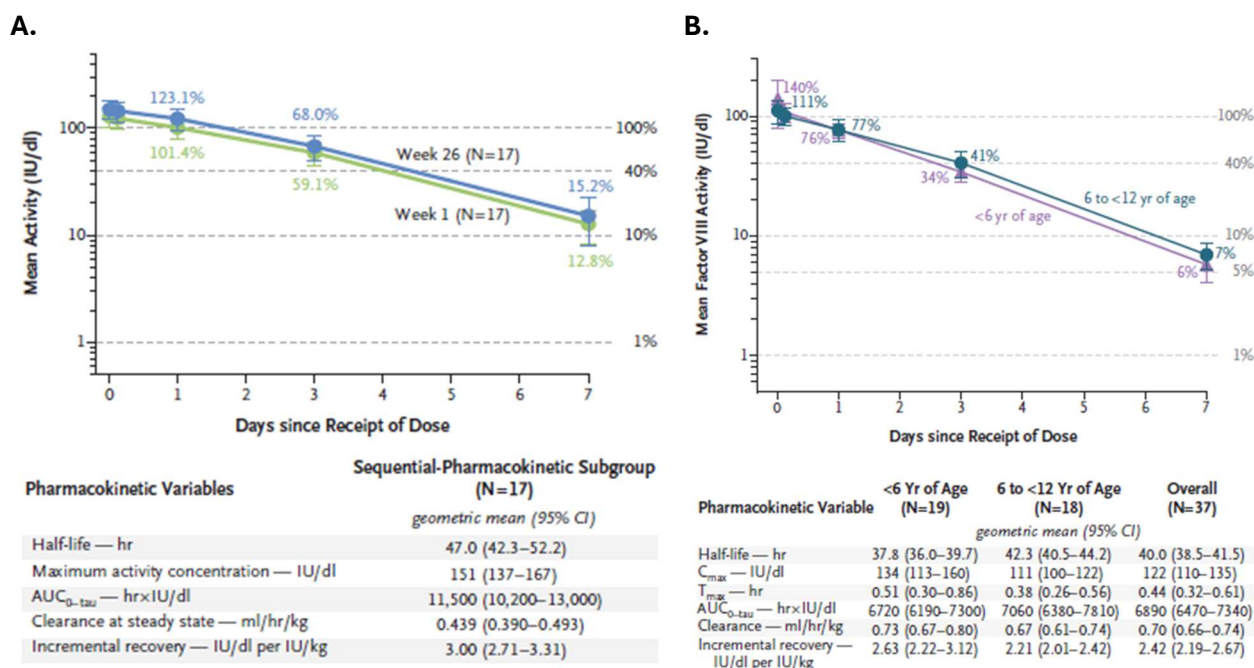


Figure 4 Pharmacokinetics of efanesoctocog alfa in adults and adolescents aged ≥ 12 years in XTEND-1 (A) and paediatric patients aged <12 years in XTEND-Kids (B)

Source: von Drygalski et al. (2023), Figure 2, p316; Malec et al. (2024), Figure 2, p243

For some people, compared with the comparator(s), does the test information result in:

A change in clinical management? Not applicable

A change in health outcome? Not applicable

Other benefits? Not applicable

Provide a rationale, and information on other benefits if relevant:

Not applicable

In terms of the immediate costs of the proposed technology (and immediate cost consequences, such as procedural costs, testing costs etc.), is the proposed technology claimed to be more costly, the same cost or less costly than the comparator?

- ☐ More costly
- ☒ Same cost (as emicizumab prophylaxis)
- ☒ Less costly (than EHL FVIII for perioperative)

Provide a brief rationale for the claim:

The data for efanesoctocog alfa as prophylaxis supports a clinical claim of superior efficacy and non-inferior safety claim versus emicizumab and EHL FVIII. Cost equivalence is sought for efanesoctocog alfa prophylaxis and breakthrough bleeds versus:

- Emicizumab prophylaxis plus FVIII replacement for breakthrough bleeds
- EHL FVIII prophylaxis and breakthrough bleeds.

This is consistent with approach taken for emicizumab (MSAC PSD for 1579, p12).

For perioperative management, the evidence supports a clinical claim of superiority for efanesoctocog alfa versus EHL FVIII. The total cost of efanesoctocog alfa is expected to be lower than EHL FVIII, as fewer IU/kg are required to achieve haemostasis (Table 17), resulting in reduced total FVIII consumption and cost per surgical episode (Staber *et al.*, 2026). Together with reduced postoperative bleeding episodes, blood transfusions required, and length of hospital stay, efanesoctocog alfa represents less costly option.

Algorithms

PREPARATION FOR USING THE HEALTH TECHNOLOGY

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, before patients would be eligible for the proposed health technology:

HMA is usually diagnosed at a young age, often in infancy or early childhood, and patients are managed throughout their lives by specialist HTC. Patients proposed to be eligible for treatment with efanesoctocog alfa are already expected to have had their disease diagnosed, including confirmation of disease severity. The treating haematologist at an HTC would be responsible for assessing a patient's suitability for treatment with efanesoctocog alfa, including:

- Confirmation of HMA diagnosis and severity classification
- Assessment of inhibitor status (Bethesda assay)
- Review of prior FVIII treatment history and exposure days.

At present, there are limited data for efanesoctocog alfa in previously untreated patients (PUPs). XTEND-1 and XTEND-Kids enrolled patients with aged ≥ 6 years with ≥ 150 exposure days to FVIII, and patients aged < 6 years with ≥ 50 exposure days (von Drygalski *et al.*, 2023, Malec *et al.*, 2024). As such, PUPs are not included in the proposed eligible population currently. An ongoing study, the efanesoctocog alfa module of ATHN Transcends (NCT04398628), is investigating the efficacy and safety of efanesoctocog alfa in PUPs and may inform future use. ATHN Transcends is a longitudinal, observational cohort study of patients with a congenital or acquired blood disorders.

Is there any expectation that the clinical management algorithm before the health technology is used will change due to the introduction of the proposed health technology?

No.

Describe and explain any differences in the clinical management algorithm prior to the use of the proposed health technology vs. the comparator health technology:

Not applicable.

USE OF THE HEALTH TECHNOLOGY

Explain what other healthcare resources are used in conjunction with delivering the proposed health technology:

Efanesoctocog alfa is administered by intravenous injection and may be administered at a hospital by healthcare professionals or at home by the patient or caregiver following comprehensive education and training. The intravenous administration time is 1 to 10 minutes, based on the patient's comfort level, and prophylaxis is administered once weekly. Healthcare resources used in conjunction with efanesoctocog alfa delivery include:

- Patient and caregiver education and training on intravenous injection technique
- Home infusion supplies (needles, syringes, alcohol swabs, sharps disposal containers)
- Cold chain storage (refrigeration at 2–8°C at home or clinic)
- Ongoing oversight and monitoring by an HTC.

Routine monitoring of FVIII activity levels for prophylactic dose adjustment is not necessary (ALTUVIII PI). If assessment of plasma FVIII activity is needed (e.g., prior to surgery), a validated activated partial thromboplastin time (aPTT)-based one-stage clotting assay is recommended. If bleeding is not controlled with efanesoctocog alfa and the expected FVIII activity plasma levels are not attained, an assay to determine if FVIII inhibitors are present should be undertaken.

Although inhibitor development was not detected in XTEND-1 or XTEND-Kids (von Drygalski *et al.*, 2023, Malec *et al.*, 2024), inhibitors could theoretically develop, as with any FVIII replacement therapy (Table 5). Post marketing, there has been cases of inhibitor development reported. In the rare event that inhibitors develop, patients would require inhibitors management strategies, which may include immune tolerance induction to eradicate the inhibitors (Srivastava *et al.*, 2020), or switching to alternative therapies such as emicizumab prophylaxis (Parikh *et al.*, 2022) or bypassing agents such as FEIBA for prophylaxis, treatment of bleeding episodes, and perioperative management (FEIBA PI).

Explain what other healthcare resources are used in conjunction with the comparator health technology:

Prophylaxis

Emicizumab is administered subcutaneously by the patient or caregiver at home. It may be administered QW, Q2W or Q4W. Healthcare resources used in conjunction with emicizumab delivery include patient and caregiver education and training on subcutaneous injection technique, home injection supplies (syringes, needles, alcohol swabs, sharps disposal containers), and cold chain storage.

Any breakthrough bleeding requires administration of EHL FVIII (or SHL FVIII) as an additional healthcare resource. As patients or caregivers may not have the skills to administer FVIII intravenously, this may require a hospital visit for administration, incurring additional healthcare costs and potential treatment delays.

EHL FVIII is administered twice weekly by intravenous injection for prophylaxis. Additional doses may be required to treat breakthrough bleeding. Healthcare resources used in conjunction with EHL FVIII delivery include patient and caregiver education and training on intravenous injection technique, home infusion supplies, cold chain storage, and ongoing oversight by HTC. Regular monitoring of FVIII activity levels (by one-stage clotting or chromogenic assays) is advised to guide dosing and infusion frequency.

Patients treated with EHL FVIII (or SHL VIII) may develop inhibitors. The same inhibitor management strategies described for efanesoctocog alfa are also applicable (i.e., immune tolerance induction, emicizumab prophylaxis, or bypassing agents).

Describe and explain any differences in the healthcare resources used in conjunction with the proposed health technology vs. the comparator health technology:

Treatment with efanesoctocog alfa prophylaxis is likely to require similar healthcare resources as emicizumab once patients and/or caregivers are trained to administer it at home. In terms of treating breakthrough bleeding, patients on efanesoctocog alfa prophylaxis are likely to be able to self-administer additional doses, whereas patients on emicizumab prophylaxis are less likely to have the skills to administer FVIII replacement to resolve a bleed. Therefore, patients on emicizumab may require more regular trips to hospital for the treatment of breakthrough bleeding, incurring additional healthcare resource use and cost compared with efanesoctocog alfa.

Prophylaxis with efanesoctocog alfa is likely to have a reduced injection burden compared with EHL FVIII, as efanesoctocog alfa is administered once weekly (approximately 52 injections/year) compared with twice weekly administration of EHL FVIII (approximately 104 injections/year). Both efanesoctocog alfa and EHL FVIII can both be self-administered following training. Patients treated with efanesoctocog alfa prophylaxis are also likely to have fewer breakthrough bleeds compared with EHL FVIII, which is expected to further reduce healthcare resource use through fewer additional FVIII doses and fewer associated hospital visits.

CLINICAL MANAGEMENT AFTER THE USE OF HEALTH TECHNOLOGY

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, after the use of the proposed health technology:

Patients receiving efanesoctocog alfa may be tested for inhibitors (via a blood test using the Bethesda assay) if the clinical response is not as expected, after intensive therapy, or before surgery, as previously discussed. Routine inhibitor screening is not required in the absence of clinical suspicion.

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, after the use of the comparator health technology:

Inhibitor testing is not required for emicizumab prophylaxis itself, as emicizumab is not a FVIII replacement product and does not include FVIII inhibitors. However, patients on emicizumab prophylaxis also require FVIII replacement for breakthrough bleeding and/or perioperative management, and inhibitor testing may be required under the same circumstances as for efanesoctocog alfa (i.e., if clinical response to FVIII is not as expected, after intensive FVIII therapy, or before surgery).

Patients receiving EHL FVIII prophylaxis may be tested for inhibitors under the same circumstances as for efanesoctocog alfa (i.e., if clinical response is not as expected, after intensive therapy, or before surgery). Routine inhibitor screening is not required in the absence of clinical suspicion.

Describe and explain any differences in the healthcare resources used after the proposed health technology vs. the comparator health technology:

Inhibitor development was not detected in XTEND-1 or XTEND-Kids (von Drygalski *et al.*, 2023; Malec *et al.*, 2024). While inhibitor development remains a theoretical risk with any FVIII replacement therapy, it is not expected to occur frequently with efanesoctocog alfa. The inhibitor testing protocols and healthcare resources required are the same for efanesoctocog alfa, EHL FVIII, and SHL FVIII (i.e., Bethesda assay when clinically indicated). Overall, healthcare resource utilisation for inhibitor monitoring is expected to be similar across all FVIII replacement products. However, given the lower breakthrough bleed rate observed with

efanesoctocog alfa compared with emicizumab and EHL FVIII, the frequency of inhibitor testing triggered by suboptimal clinical response may be lower with efanesoctocog alfa.

Insert diagrams demonstrating the clinical management algorithm with and without the proposed health technology:

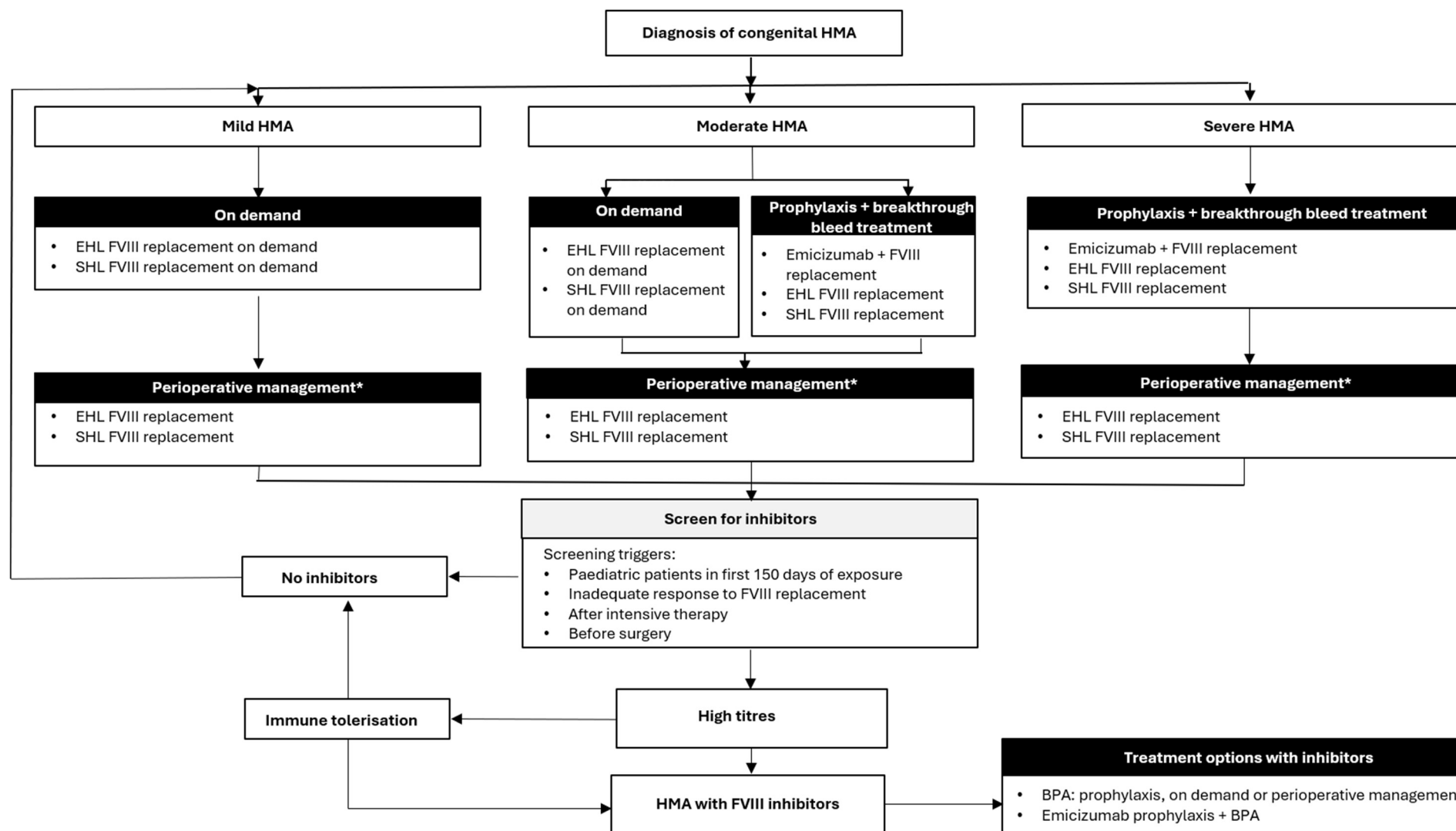


Figure 5 Current treatment algorithm for congenital haemophilia A without efanesoctocog alfa

**Perioperative management is required for major and minor surgery*

Abbreviations: BPA = bypassing agent; EHL = extended half-life; FVIII = factor VIII, HMA = haemophilia A, SHL = standard half-life

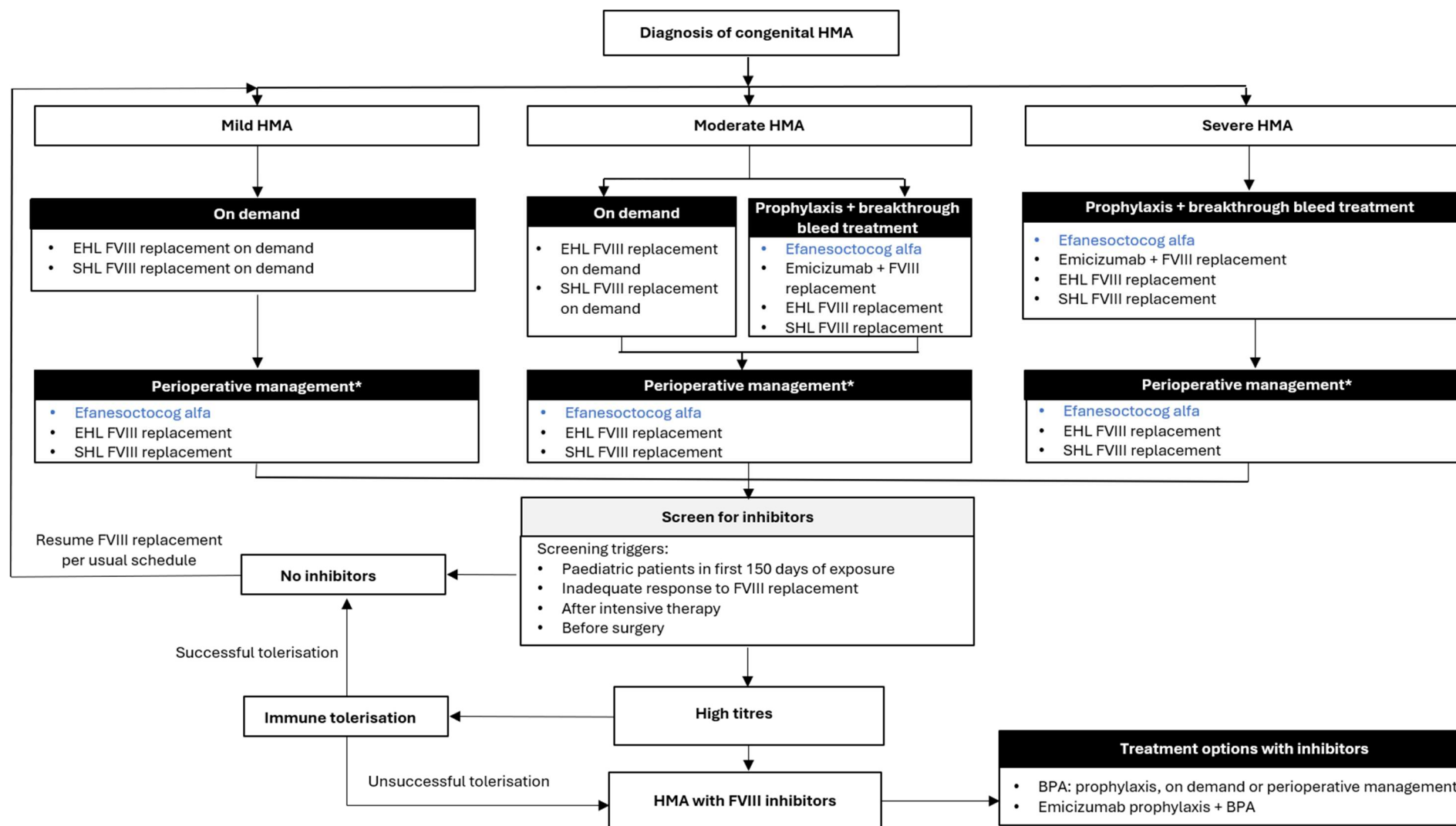


Figure 6 Treatment algorithm for congenital haemophilia A with efanesoctocog alfa

**Perioperative management is required for major and minor surgery*

Abbreviations: BPA = bypassing agent; EHL = extended half-life; FVIII = factor VIII, HMA = haemophilia A, SHL = standard half-life

Summary of Evidence

**Provide one or more recent (published) high quality clinical studies that support use of the proposed health service/technology.
At 'Application Form lodgement',**

No.	Type of study design*	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication
1	Phase 3 clinical trial	XTEND-1 (NCT04161495) Efanesoctocog Alfa Prophylaxis for Patients with Severe Hemophilia A	Patients aged ≥ 12 years with severe HMA treated with efanesoctocog alfa either as prophylaxis for 52 weeks (Group A; n = 133) or on-demand treatment for 26 weeks followed by prophylaxis for 26 weeks (Group B; n = 26). Efficacy, pharmacokinetics, immunogenicity and safety were assessed	Efanesoctocog Alfa Prophylaxis for Patients with Severe Hemophilia A New England Journal of Medicine	23 January 2023
2	Post-hoc analyses of Phase 3, non-randomised clinical trial	XTEND-1 (NCT04161495) Treatment of Bleeding Episodes With Efanesoctocog Alfa in Previously Treated Patients With Severe Hemophilia A in the Phase 3 XTEND-1 Study	Post-hoc analyses of XTEND-1 for bleeding episodes and the number of injections of efanesoctocog alfa required to treat the bleeding episodes	American Journal of Hematology Blood Research Journal Wiley Online Library	10 February 2025
3	Patient interviews from Phase 3, non-randomised clinical trial	XTEND-1 (NCT04161495) Patient Experience With Efanesoctocog Alfa for Severe Hemophilia A: Results From the XTEND-1 Phase 3 Clinical Study Exit Interviews	Exit interviews of 29 patients enrolled in XTEND-1 demonstrated that efanesoctocog alfa prophylaxis resulted in patient-relevant and meaningful improvements	Patient Experience With Efanesoctocog Alfa for Severe Hemophilia A: Results From the XTEND-1 Phase 3 Clinical Study Exit Interviews - Clinical Therapeutics	15 October 2024
4	HRQoL analysis of Phase 3, non-randomised clinical trial	XTEND-1 (NCT04161495) A Psychometric Analysis of the Haemophilia Quality of Life Questionnaire for Adults Physical Health Subscale and Total Scores: Data From the Phase 3 XTEND-1 Trial in Patients With Severe Haemophilia A	An analysis to evaluate the psychometric properties of the Haemophilia Quality of Life Questionnaire for Adults (Haem-A-QoL) and estimate clinically meaningful change thresholds using XTEND-1 data	A Psychometric Analysis of the Haemophilia Quality of Life Questionnaire for Adults Physical Health Subscale and Total Scores: Data From the Phase 3 XTEND-1 Trial in Patients With Severe Haemophilia A	6 March 2026
5	Prospective observational study/Phase 3, non-randomised clinical trial	Observational study: 242HA201/OBS16221; XTEND-1 (NCT04161495) Outcomes in participants switching from FVIII replacement therapy to efanesoctocog alfa prophylaxis in XTEND-1: a post hoc analysis	Paired assessment of patients from an observational study who were receiving prophylaxis with SHL or EHL FVIII prophylaxis to efanesoctocog alfa prophylaxis in XTEND-1 (n = 78)	Outcomes in participants switching from FVIII replacement therapy to efanesoctocog alfa prophylaxis in XTEND-1: a post hoc analysis	20 January 2026

No.	Type of study design*	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication
6	Phase 3, open-label, clinical trial	XTEND-Kids (NCT04759131) Efanesoctocog Alfa Prophylaxis for Children with Severe Hemophilia A	A phase 3, open-label study of patients aged <12 years with severe HMA (n = 74) that received prophylaxis with efanesoctocog alfa for 52 weeks. Efficacy, pharmacokinetics, immunogenicity and safety were assessed	Efanesoctocog Alfa Prophylaxis for Children with Severe Hemophilia A New England Journal of Medicine	17 July 2024
7	Post-hoc analyses of Phase 3, open-label clinical trial	XTEND-Kids (NCT04759131) Post hoc analysis of bleeding episodes and clinically relevant pharmacokinetic parameters among children <12 years old with severe hemophilia A receiving once-weekly efanesoctocog alfa prophylaxis in the XTEND-Kids phase 3 multinational trial	Post-hoc analyses of XTEND-Kids for bleeding episodes and the number of injections of efanesoctocog alfa required to treat the bleeding episodes	Post hoc analysis of bleeding episodes and clinically relevant pharmacokinetic parameters among children <12 years old with severe hemophilia A receiving once-weekly efanesoctocog alfa prophylaxis in the XTEND-Kids phase 3 multinational trial - Journal of Thrombosis and Haemostasis	21 July 2025
8	Matching adjusted indirect comparison of two Phase 3 clinical trials	XTEND-1 (NCT04161495)/HAVEN 3 (NCT02847637) Efanesoctocog Alfa Versus Emicizumab in Adolescent and Adult Patients With Haemophilia A Without Inhibitors	Matching adjusted indirect comparison of prophylaxis with efanesoctocog alfa and emicizumab in patients aged ≥12 years with severe HMA without inhibitors. Outcomes assessed were annualised bleeding rates for any, treated, and spontaneous bleeds	Efanesoctocog Alfa Versus Emicizumab in Adolescent and Adult Patients With Haemophilia A Without Inhibitors Advances in Therapy Springer Nature Link	22 November 2024
9	Matching adjusted indirect comparison of one Phase 3 clinical trial with meta-analyses of EHL and SHL FVIII	XTEND-1 trial, (NCT04161495) and Phase 3 trials of EHL and SHL FVIII Efanesoctocog Alfa versus Standard and Extended Half-Life Factor VIII Prophylaxis in Adolescent and Adult Patients with Haemophilia A without Inhibitors	Matching adjusted indirect comparison of prophylaxis with EHL and SHL FVIII and emicizumab in patients aged ≥12 years with severe HMA without inhibitors. Outcomes assessed were annualised bleeding rates for any, treated, and spontaneous bleeds	Efanesoctocog Alfa versus Standard and Extended Half-Life Factor VIII Prophylaxis in Adolescent and Adult Patients with Haemophilia A without Inhibitors Advances in Therapy Springer Nature Link	10 February 2025
10	Post-hoc analysis of Phase 3 trials	XTEND-1 (NCT04161495) & XTEND-Kids (NCT04759131) Perioperative Management With Efanesoctocog Alfa in Patients With Haemophilia A in the Phase 3 XTEND-1 and XTEND-Kids Studies	Analysis evaluated the efficacy and safety of efanesoctocog alfa for perioperative management during XTEND-1 (major surgery, n = 11; minor surgery; n = 15) and XTEND-Kids (major surgery; n = 2; minor; n = 8)	Perioperative Management With Efanesoctocog Alfa in Patients With Haemophilia A in the Phase 3 XTEND-1 and XTEND-Kids Studies - Klamroth - 2025 - Haemophilia - Wiley Online Library	18 March 2025

Identify yet-to-be-published research that may have results available in the near future (that could be relevant to your application).

	Type of study design*	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication***
1.	Long-term efficacy and safety study	Long-term Safety and Efficacy of Efanesoctocog Alfa (BIVV001) in Previously Treated Patients With Hemophilia A (XTEND-ed)	Patients who completed XTEND-1 (≥ 12 years) and XTEND-Kids (< 12 years), could continue efanesoctocog alfa 50 IU/kg QW prophylaxis in the ongoing, multicenter, open-label, long-term XTEND-ed study. The primary outcome was the incidence of FVIII inhibitor development and secondary outcomes included ABRs, efficacy for bleed treatment, and safety	Study Details NCT04644575 Long-term Safety and Efficacy of Efanesoctocog Alfa (BIVV001) in Previously Treated Patients With Hemophilia A ClinicalTrials.gov	Ongoing study

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