

# **MSAC Application 1751**

**Valoctocogene roxaparvovec for  
Haemophilia A**

# Application or referral for other medical service or health technology

## MSAC Application Number

1751

## Application title:

Valoctocogene roxaparvovec for haemophilia A

## Submitting organisation:

BIOMARIN PHARMACEUTICAL AUSTRALIA PTY LTD

## Submitting organisation ABN:

69159743496

## Application description

### Succinct description of the medical condition/s:

Haemophilia A is genetic FVIII (F8) gene resulting in a deficiency of the coagulation factor VIII (FVIII). As an X-linked congenital bleeding disorder, the vast majority of affected individuals are male with a reported incidence in Australia of approximately 11.5 per 100,000 males (Australian Haemophilia Centre Directors' Organisation [AHCDO] 2016). The characteristic phenotype in haemophilia is the bleeding tendency with severity of bleeding directly correlated to the level of clotting factor. In the most severe cases, bleeding episodes most commonly occur internally into the joints or muscles leading to painful, progressive and irreversible joint damage, however some bleeds can be life threatening, such as intracranial or gastrointestinal bleeds and require immediate treatment (Srivastava 2013). Bleeding may occur spontaneously without trauma or injury. Untreated, bleeding may result in permanent damage to muscles and joints, chronic pain, and death (AHCDO, 2016).

### Succinct description of the service or health technology:

ROCTAVIAN (valoctocogene roxaparvovec), is a gene therapy that uses an adeno-associated virus type 5 (AAV5), to deliver a healthy copy of the F8 gene. Following infusion with valoctocogene roxaparvovec into haemophilia A patients, the recombinant F8 gene is delivered to cell nuclei of several tissues. As the new F8 gene is under the control of a liver-specific promoter, only liver cells are able to activate transcription to make FVIII protein which is then secreted into the bloodstream (Ozelo 2022). As a gene therapy, valoctocogene roxaparvovec is provided as a single, one-time intravenous infusion.

## **Application contact details**

**Are you applying on behalf of an organisation, or as an individual?**

Organisation

**Is the applicant organisation the organisation you are representing in the HPP today?**

Yes

**Applicant organisation name:**

BIOMARIN PHARMACEUTICAL AUSTRALIA PTY LTD

## **Application details**

**Please select the program through which the health technology would be funded:**

National Blood Agreement

**Please provide justification for selecting the above program:**

Under the National Blood Agreement (NBA), valoctocogene roxaparvovec meets the definition of 'blood-related products' which are defined as "products used or intended for use for human therapeutic purposes which are alternative or complementary to the use of blood products" (e.g., FVIII replacement products).

**What is the type of service or health technology?**

Therapeutic

## PICO sets

PICO set	PICO set name
1	Valoctocogene roxaparvovec for haemophilia A
2	AAV5 test

### Application PICO Set 1: Valoctocogene roxaparvovec for haemophilia A

#### Population

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

Adults with severe haemophilia A without a history of FVIII inhibitors and pre-existing antibodies to AAV5, without active hepatitis or severe liver disease.

**Select the most applicable medical condition terminology (SNOMED CT):**

Haemophilia

#### Intervention

**Name of the proposed health technology:**

The proposed intervention is infusion of ROCTAVIAN™ (valoctocogene roxaparvovec), a gene therapy that uses an AAV5 vector to deliver a healthy copy of the F8 gene to the liver

#### 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 include identifying health care resources that are needed to be delivered at the same time as the comparator service:**

The nominated comparators to treatment with valoctocogene roxaparvovec are prophylactic FVIII replacement therapy and emicizumab.

#### Outcomes

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

Not applicable as valoctocogene roxaparvovec is not a test.

For outcome description of major and minor health outcomes for valoctocogene roxaparvovec, refer to PICO set.

### **Specified restrictions for funding**

**Please add one or more items, with specified restriction for funding, for each Population/Intervention:**

**Proposed item: AAAAA**

**Is the proposed item restricted:**

Yes - restricted

**Provide a short description of the restriction:**

Treatment of haemophilia A

**Please draft a proposed restriction to define the population and health technology usage characteristics that would define eligibility for funding:**

Adults with severe haemophilia A without a history of FVIII inhibitors and pre-existing antibodies to AAV5, without active hepatitis or severe liver disease.

**Proposed price of supply:**

0.00

**Indicate the overall cost per patient of providing the proposed health technology:**

0.00

**Provide details and explain:**

The cost of the valoctocogene roxaparvovec gene therapy will be determined and justified in the forthcoming applicant developed assessment report (ADAR). No other health care resources are used. The infusion will take place at the HTC, with no additional costs incurred in administering the treatment (ie covered within the operation of the HTC). Refer to Cost Information attachment for further details.

**How is the technology/service funded at present? (For example: research funding; State-based funding; self-funded by patients; no funding or payment):**

No funding

## **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

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

Valoctocogene roxaparvovec is expected to be associated with superior effectiveness (reduction in bleeds and improved quality of life) and non-inferior safety versus prophylactic treatment with FVIII therapy and emicizumab in patients with severe haemophilia A.

Relative to prophylactic treatment with FVIII therapy and emicizumab, valoctocogene roxaparvovec will reduce mean ABR due to constant FVIII expression and lack of trough related bleeding (Ozelo 2022, Mahlangu 2018). A matching adjusted indirect comparison (MAIC) demonstrated ABR for all bleeds was statistically significantly lower with valoctocogene roxaparvovec than emicizumab, and significantly higher proportions of patients had no treated joint bleeds and no treated bleeds than with emicizumab. Furthermore, valoctocogene roxaparvovec is expected to improve the quality of life of patients with severe haemophilia A compared with treatment with prophylactic treatment

with FVIII therapy and emicizumab, given the treatment burden associated with these therapies (FVIII infusions 2–4 times per week; emicizumab subcutaneous injections 1–4 times per month) versus a once-off treatment with valoctocogene roxaparvovec (Krumb 2021).

## Estimated utilisation

### **Estimate the prevalence and/or incidence of the proposed population:**

According to the Australian Bleeding Disorders Registry (ABDR) Annual Report, there are ≈2,500 people diagnosed with haemophilia A who require life-long care (NBA 2021). Of those, around 17% are adults with severe disease. Based on the historical trend, it is estimated that there are approximately 470 – 500 adult patients with severe haemophilia A in Australia during the first 4 years of proposed listing.

The proportion of patients meeting the proposed eligibility criteria is estimated based on the following:

- 75% do not have FVIII inhibitors: The cumulative incidence of inhibitor development in severe haemophilia A has been reported as 20 -30% (Srivastava 2013). The ABDR reports a point prevalence of 20% among all registered haemophilia A patients previously tested for the inhibitor. The disease severity has been reported to have a positive correlation with the inhibitor development (Wight and Paisley 2003). Therefore, the midpoint of the range reported in Srivastava et al. 2013 is applied.
- 76% do not have active hepatitis or severe liver disease: This estimate is based on the ADVANCE Working Group H3 study (Qvigstad 2018 ), a European multicentre, observational, noninterventional study (n = 532). This study was in a mixed haemophilia population (A and B; but predominantly haemophilia A [88%]) across all severity. The study also included patients aged 40 years old or above with mean age of 52 (no clear age correlation with prevalence was nonetheless observed).
- 74% of adults with severe haemophilia A (311/422) were using prophylactic factor VIII replacement therapy in 2020 in the ABDR.
- 64.3% do not have pre-existing antibodies to AAV5 based on a BioMarin study (Study 270-901; published in Klamroth 2022) which examined the prevalence of AAV5 antibodies among patients with haemophilia A. This global study (including Brazil, Russia, France, Italy, South Africa, Germany, Japan, USA and UK) reported a mean prevalence of 35.7% in adults; meaning 64.3% of patients would meet the proposed AAV5 negative eligibility criterion.

Combining these criteria, approximately 27% (75% x 76% x 74% x 64.3%) of the estimated 470-500 patients would become eligible for valoctocogene roxaparvovec. This hence translates to a prevalence of approximately 130 eligible patients, increasing to approximately 140 in 2027 (Year 4).

**Provide the percentage uptake of the proposed health technology by the proposed population:**

**Year 1 estimated uptake (%):**

TBC

**Year 2 estimated uptake (%):**

TBC

**Year 3 estimated uptake (%):**

TBC

**Year 4 estimated uptake (%):**

TBC

**Estimate the number of patients who will utilise the proposed technology for the first full year:**

An estimated prevalent pool of 130 patients exist who would meet proposed eligibility criteria.

**Optionally, provide details:**

BioMarin is engaging with AHCD0 and other key stakeholders to inform the likely uptake in the first full year and this will be presented in the forthcoming ADAR.

**Will the technology be needed more than once per patient?**

No, once only

## **Application PICO set 2: AAV5 test**

### **Population**

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

The proposed population is adults with severe haemophilia A without a history of FVIII inhibitors and without active hepatitis or severe liver disease. to determine access to valoctocogene roxaparvovec treatment (refer to valoctocogene roxaparvovec PICO set).

**Select the most applicable medical condition terminology (SNOMED CT):**

Haemophilia A

### **Intervention**

**Name of the proposed health technology:**

The name of the proposed health technology is AAV5 DetectCDx™ (generic name: AAV5 Total Antibody (TAb) Assay for Valoctocogene Roxaparvovec Eligibility in Haemophilia A).

## 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 include identifying health care resources that are needed to be delivered at the same time as the comparator service:**

There is currently no comparator to AAV5 DetectCDx™, and without this test, eligibility for valoctocogene roxaparvovec treatment cannot be determined and patients will continue with prophylactic treatment with FVIII therapy or emicizumab (as per the comparators in the valoctocogene roxaparvovec PICO set).

## Outcomes

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

The test informs eligibility for treatment with valoctocogene roxaparvovec.

## Specified restrictions for funding

**Please add one or more items, with specified restriction for funding, for each Population/Intervention:**

**Proposed item: AAAAA**

**Is the proposed item restricted:**

Yes - restricted

**Provide a short description of the restriction:**

Testing of AAV5 antibodies in patients with severe Haemophilia A

**Please draft a proposed restriction to define the population and health technology usage characteristics that would define eligibility for funding:**

Adults with severe haemophilia A without a history of FVIII inhibitors and without active hepatitis or severe liver disease

**Proposed price of supply:**

0.00

**Indicate the overall cost per patient of providing the proposed health technology:**

0.00

**Provide details and explain:**

██████████

**How is the technology / service funded at present? (For example: research funding; State-based funding; self-funded by patients; no funding or payment):**

Not funded.



## 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

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

Relative to the comparator: Compared with not testing, the AAV5 DetectCDx™ test is superior in detecting patients eligible for valoctocogene roxaparvovec. In turn, treatment with valoctocogene roxaparvovec provides superior outcomes relative to its comparators (see valoctocogene roxaparvovec PICO set).

## Estimated utilisation

**Estimate the prevalence and/or incidence of the proposed population:**

According to the Australian Bleeding Disorders Registry (ABDR) Annual Report, there are ≈2,500 people diagnosed with haemophilia A who require life-long care (NBA 2021). Of those, around 17% are adults with severe disease. Based on the historical trend, it is estimated that there will be approximately 470 – 500 adult patients with severe haemophilia A in Australia during the first 4 years of proposed listing.

It is expected that, before proceeding with AAV5 testing, patients are screened for the other two eligibility criteria for valoctocogene roxaparvovec, namely, a history of FVIII inhibitors and the absence of active hepatitis or severe liver disease. It is estimated that:

- 75% do not have FVIII inhibitors: The cumulative incidence of inhibitor development in severe haemophilia A has been reported as 20 -30% (Srivastava 2013). The ABDR reports a point prevalence of 20% among all registered haemophilia A patients previously tested for the inhibitor. The disease severity has been reported to have a positive correlation with the inhibitor development (Wight and Paisley 2003). A higher range estimate is hence applied.
- 76% do not have active hepatitis or severe liver disease: This estimate is based on the ADVANCE Working Group H3 study (Qvigstad 2018), a European multicentre, observational, noninterventional study (n = 532). This study was in a mixed haemophilia population (A and B; but predominantly haemophilia A [88%]) across all severity. The study also included patients aged 40 years old or above with mean age of 52 (no clear age correlation with prevalence was nonetheless observed).
- 74% of adults with severe haemophilia A (311/422) were using prophylactic factor VIII replacement therapy in 2020 in the ABDR.

Combining these criteria, approximately 42% (75% x 76% x 74%) of the estimated 470-500 patients are estimated to be potentially considered for AAV5 testing. This translates to a prevalence of approximately 200 eligible patients, increasing to 210 in 2027 (Year 4).

**Provide the percentage uptake of the proposed health technology by the proposed population:**

**Year 1 estimated uptake (%):**

TBC

**Year 2 estimated uptake (%):**

TBC

**Year 3 estimated uptake (%):**

TBC

**Year 4 estimated uptake (%):**

TBC

**Estimate the number of patients who will utilise the proposed technology for the first full year:**

An estimated prevalent pool of 200 patients exist who would meet proposed eligibility criteria.

**Optionally, provide details:**

It is estimated that there is a prevalent pool of approximately 200-210 patients who could be considered for AAV5 testing as a part of the eligibility assessment for valoctocogene roxaparvovec. BioMarin is engaging with AHCDO and other key stakeholders to inform the likely uptake in the first full year and this will be presented in the forthcoming ADAR.

**Will the technology be needed more than once per patient?**

No, once only

## **Consultation**

**List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the health technology/service:**

- Australian Haemophilia Centre Directors' Organisation (AHCDO)
- The Haematology Society of Australia & New Zealand (HSANZ)
- Thrombosis and Haemostasis Society of Australia and New Zealand (THANZ)

**List all appropriate professional bodies / organisations representing the group(s) of health professionals that may be impacted by the health technology/service:**

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**List the patient and consumer advocacy organisations or individuals relevant to the proposed health technology:**

- Haemophilia Foundation Australia (HFA)

**List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed service or health technology:**

- Australian Haemophilia Centre Directors' Organisation (AHCDO)
- The Haematology Society of Australia & New Zealand (HSANZ)
- Thrombosis and Haemostasis Society of Australia and New Zealand (THANZ)

## Regulatory information

**Would the proposed health technology involve the use of a medical device, in-vitro diagnostic test, radioactive tracer or any other type of therapeutic good?**

Yes

**Has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?**

No

**Is the therapeutic good classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?**

No

**Is the therapeutic good to be used in the service exempt from the regulatory requirements of the Therapeutic Goods Act 1989?**

No

**Is the therapeutic good classified by the TGA as for Research Use Only (RUO)?**

No

**Is the therapeutic good in the process of being considered by the TGA?**

Yes

**Please provide the TGA Application ID:**

PM-2021-04759-1-5

**Please provide the TGA submission date:**

22/09/2023