

MSAC Application 1805

**Concizumab for routine
prophylaxis to prevent bleeding in
patients with haemophilia B**

Application for MBS eligible service or health technology

HPP Application number:

HPP200300

Application title:

Concizumab for routine prophylaxis to prevent bleeding in patients with haemophilia B.

Submitting organisation:

NOVO NORDISK PHARMACEUTICALS PTY. LIMITED

Submitting organisation ABN:

40002879996

Application description

Succinct description of the medical condition/s:

Haemophilia B (HMB) is a chronic bleeding disorder caused by deficiency or dysfunction of the coagulation protein factor IX (FIX). HMB patients experience spontaneous, painful bleeding episodes and prolonged, excessive haemorrhage following trauma or surgery. The development of neutralising anti-FIX antibodies (inhibitors) against exogenous clotting factor replacement therapy is one of the most serious and challenging complications of haemophilia, occurring in approximately 1—6% of patients with HMB, reducing treatment effectiveness. For Haemophilia B patients with inhibitors (HMBwI) there are no long-term prophylactic treatments approved in Australia and there is lack of easy-to-administer routine prophylactics in the HMBwI treatment landscape.

Succinct description of the service or health technology:

Concizumab is a humanised recombinant monoclonal antibody of the immunoglobulin G4 isotype; it is a novel, first in class, nonfactor prophylaxis treatment for HMB, with or without inhibitors, administered once daily subcutaneously using a prefilled pen device.

Concizumab acts independently from factor VIII (FVIII) and FIX by enhancing the initiation phase of coagulation through tissue factor pathway inhibitor (TFPI) sequestration, increasing factor Xa (FXa) production. The rationale behind TFPI

sequestration is that it extends the initiation phase of coagulation at sites of injury where tissue factor is exposed, thereby enhancing the remaining ability of the blood to form a clot, independent of the presence of endogenous FVIII or FIX, allowing HMBwI patients alike to receive prophylactic treatment.

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:

NOVO NORDISK PHARMACEUTICALS PTY. LIMITED

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:

National Blood Authority fund blood products

What is the type of service or health technology?

Therapeutic

PICO set

Concizumab for the prophylactic treatment of patients with Haemophilia B who have developed Factor IX inhibitors (HMBwI).

Population

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

This application is for the funding of concizumab for the prophylactic treatment of patients with Haemophilia B who have developed Factor IX inhibitors (HMBwI). Haemophilia B (HMB) is a chronic bleeding disorder caused by deficiency or dysfunction of the coagulation protein Factor IX (FIX). HMB is a serious and life-threatening condition in which patients experience spontaneous, painful bleeding episodes and prolonged, excessive haemorrhage following trauma or surgery. The development of neutralising anti-FIX antibodies (inhibitors) against exogenous clotting factor replacement therapy is one of the most serious and challenging complications of haemophilia, occurring in approximately 1—6% of HMB patients. The presence of circulating inhibitors partially or completely inactivates infused factor proteins, impairing their clinical efficacy and making the management of bleeding exceedingly difficult (Ragni 2017, Miller 2018). As a result, patients with HMBwI experience significant reductions in their HRQoL and pose an increased economic burden on healthcare systems.

Select the most applicable Medical condition terminology (SNOMED CT):

Haemophilia B with Factor IX inhibitors

Intervention

Name of the proposed health technology:

Concizumab

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:

Unlike Haemophilia A patients, there are no long-term prophylaxis treatment options available for patients with HMBwI in Australia. The proposed comparator is standard of care, which consists of:

- Short-term prophylaxis (up to 3 months) with the bypassing agent (BPA), NovoSeven® RT (rFVIIa)
- On demand treatment with the bypassing agent (BPA), NovoSeven® RT (rFVIIa)

Use of NovoSeven® RT (rFVIIa) by patients is heterogeneous and depends on the individual requirements of the patients. For patients with a high bleeding frequency, NovoSeven® RT (rFVIIa) can be used as prophylaxis, once daily for up to three

months to reduce the frequency of bleeding or can be used for surgical prophylaxis. NovoSeven® RT (rFVIIa) is otherwise used on demand in patients for the control of bleeding episodes.

Patients with inhibitors, particularly those with high-titre inhibitors (> 5 BU/mL), are at increased risk of uncontrollable haemorrhage, devastating joint damage and subsequent disability. For patients with low-titre inhibitors, effective management may be achieved with higher doses of FIX however, more than 80% of FIX alloantibodies are high-responding (DiMichele, Hoots et al. 2007). For these patients' use of BPAs is the primary treatment. Despite the availability of on demand and short-term prophylaxis, HMBwL patients still suffer from relatively poor clinical outcomes (D'Angiolella, Cortesi et al. 2018, Oladapo, Lu et al. 2018, Ragni, Berntorp et al. 2020).

There are currently no long-term prophylactic treatments available for patients with HMBwL as concizumab is the first and only long-term prophylaxis treatment approved for HMBwL. rFVIIa is the most appropriate comparator as patients with HMBwL currently manage bleeding episodes with on demand treatment or short-term prophylactic treatment with rFVIIa.

Concizumab will therefore replace on demand and short-term prophylactic treatment with rFVIIa (Royal, Schramm et al. 2002, Hoots and Nugent 2006, Collins, Faradji et al. 2010, Iorio, Marchesini et al. 2011, Manco-Johnson, Soucie et al. 2017, Castaman 2018, Miesbach, Kittler et al. 2020).

Outcomes

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

Currently there are no long-term prophylaxis treatments available to HMBwL patients. The introduction of concizumab to the HMBwL patient management algorithm will provide clinicians with a novel, long-term prophylaxis option. Concizumab also relieves the burden of treatment associated with iv administration as concizumab can be self-administered subcutaneously in the patient's home, resulting in a lower treatment burden which may have the potential to also improve treatment adherence and thereby achieve better clinical outcomes for patients with haemophilia (Hampton, Knoebl et al. 2022).

The following key health outcomes will be measured in assessing the clinical claim for concizumab:

Safety Outcomes: Safety and tolerability of concizumab treatment assessed by incidence and severity of adverse events

Primary effectiveness

- Reduction in number of bleeds over time (bleed rate)
- Prevention of bleeds

Secondary endpoints

- Responder status
- Other bleeding related outcomes such as: reduction in number of joint bleeds over time, reduction in number of target joint bleeds over time, reduces individual bleed rate compared to historical bleed rate and number of treated bleeds per month or year etc.
- HRQoL
- Joint health outcomes
- Chronic pain associated with haemophilia
- Number of missed days of work/activity/school

Healthcare resources

- Cost offsets
- Costs of delivering the intervention
- Costs of managing adverse events or breakthrough bleeding
- Cost per Quality Adjusted Life-Year gained

Specified restrictions for funding

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

Proposed item:

AAAAA

Is the proposed item restricted?

Yes - restricted

Provide a short description of the restriction:

For the prevention or reduction in the frequency of bleeding in patients with haemophilia B with inhibitors to FIX

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

Alhemo® is funded for the prevention or reduction in the frequency of bleeding in patients who meet the restrictions below:

Have a diagnosis of haemophilia B (congenital factor IX [FIX] deficiency)

Have inhibitors (antibodies) to FIX

Proposed price of supply:

REDACTED

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

REDACTED

Provide details and explain:

REDACTED

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

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:

The overall clinical claim is that concizumab is associated with superior health outcomes for HMBwL through improved efficacy (prevention and reduction in bleeds and improved quality of life) and at least non-inferior safety, if not superior safety, in comparison to treatment with NovoSeven® RT administered in either an on demand or short-term prophylactic manner.

The rationale for this claim are the results from the Explorer7 trial. The Explorer7 trial demonstrated that patients in the concizumab arm experienced effective prophylaxis, reduced bleeding, improved quality of life, reduced treatment burden and morbidity

and an overall preference for concizumab compared to BPAs (Thornburg and Duncan 2017, Lee, Cepo et al. 2019, Hampton, Knoebl et al. 2022).

Estimated utilisation

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

<5 patients

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

Year 1 estimated uptake (%):

REDACTED

Year 2 estimated uptake (%):

REDACTED

Year 3 estimated uptake (%):

REDACTED

Year 4 estimated uptake (%):

REDACTED

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

REDACTED

Optionally, provide details:

Will the technology be needed more than once per patient?

Yes, multiple times

Over what duration will the health technology or service be provided for a patient? (preferably a number of years):

Lifetime

Optionally, provide details:

What frequency will the health technology or service be required by the patient over the duration? (range, preferably on an annual basis):

Administered once daily

Optionally, provide details:

The recommended dosing regimen is a loading dose of 1 mg/kg concizumab given once on treatment day one. From day two until determination of individual maintenance dose an initial maintenance dose of 0.20 mg/kg concizumab is administered daily.

Consultation

List all entities that are relevant to the proposed service / health technology. The list can include professional bodies / organisations who provide, request, may be impacted by the service/health technology; sponsor(s) and / or manufacturer(s) who produce similar products; patient and consumer advocacy organisations or individuals relevant to the proposed service/health technology.

Entity who provides the health technology/service

Royal Australasian College of Physicians (RACP); Royal College of Pathologists of Australia (RCPA); and Australian Haemophilia Centre Directors' Organisation (AHCDO); Australian Haem Nurses Group AHNG

Entity who may be impacted by the health technology/service

There are currently no other products registered with a similar mechanism of action, indicated for use in HBwl. The only other nonfactor, antibody-based, subcutaneous therapy in haemophilia is Hemlibra

Patient and consumer advocacy organisations relevant to the proposed service/health technology

Haemophilia Foundation Australia (HFA)

Entity who produces similar products

Australian Red Cross Lifeblood; Australasian Society of Thrombosis and Haemostasis; Australian Centre for Blood Diseases; Australian Haemophilia Nurses' Group; ANZHSWCG; ANZPHG

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)? *(if 'Yes' above)*

Yes

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

Please enter all relevant ARTG IDs:

ARTG ID	ARTG name
466665	ConcizuTrace ELISA (CZM) - Clinical chemistry therapeutic drug monitoring IVDs