

MSAC Application 1778

**Fibroblast growth factor 23 (FGF-23)
testing for patients with a high pre-test
probability of X-linked hypophosphatemia
(XLH) to determine eligibility for
burosumab on the Pharmaceutical
Benefits Scheme (PBS)**

Application for MBS eligible service or health technology

MSAC Application Number:

1778

Application title:

Fibroblast growth factor 23 (FGF-23) testing for patients with a high pre-test probability of X-linked hypophosphatemia (XLH) to determine eligibility for burosumab on the Pharmaceutical Benefits Scheme (PBS)

Submitting organisation:

Department of Health and Aged Care

Application description

Succinct description of the medical condition/s:

Hypophosphatemic rickets is a condition in which, due to abnormal excess production of an endocrine hormone FGF23, there is excessive loss of phosphate in the urine that results in low serum phosphate. Because phosphate is an essential element in the formation of hydroxyapatite, the mineral that deposits on osteoid protein to produce a rigid skeleton, low phosphate levels produce under mineralisation of the skeleton, a condition called rickets or osteomalacia.

A small number of individuals, perhaps 300 in Australia, have developed osteomalacia because of phosphate deficiency due to excessive FGF23 production. In over 80% of cases this is due to an inactivation mutation in the PHEX gene that is an important negative regulator of the production of FGF23.

Succinct description of the service or health technology:

The application is to request public funding for the analysis of plasma or serum fibroblast growth factor 23 (FGF-23) for patients with a high pre-test probability of X-linked hypophosphatemic rickets to determine eligibility for burosumab.

Application details

Does the implementation of your service or health technology rely on a listing on the Pharmaceutical Benefits Scheme (PBS) and/or the Prostheses List?

Yes

Which list/schedule will the other health technologies be listed on? (if 'Yes' above)

Pharmaceutical Benefits Scheme

Is the application for a new service or health technology, or an amendment to an existing listed service or health technology?

New service

What is the type of service or health technology?

Investigative

Please select the type of investigative health technology: (if investigative)

Diagnostic pathology test

Application PICO set: FGF-23 biochemical testing for patients with a high pre-test probability of X-linked hypophosphatemic rickets

State the purpose(s) of the health technology for this PICO set and provide a rationale: (if investigative)

Purpose category:

Diagnosis

Purpose description:

To establish a diagnosis or disease (sub)classification in symptomatic or affected patients with suspected X-Linked hypophosphatemia. These patients will be identified by elevated (or inappropriately normal) serum or plasma FGF-23 levels above the mean of the assay-specific reference range in conjunction with other diagnostic findings in order to determine eligibility for treatment with burosumab.

Supporting documentation

Document type	Document file name
Application PICO set document	None – not required
Reference list	Haffner, D., <i>et al.</i> (2019) Clinical practice recommendations for the diagnosis and management of X-linked hypophosphataemia. <i>Nat Rev Nephrol</i> , 15: 435–455. https://doi.org/10.1038/s41581-019-0152-5 Sandy, J.L., <i>et al.</i> (2022), Clinical practice guidelines for paediatric X-linked hypophosphataemia in the era of burosumab. <i>J Paediatr Child Health</i> , 58: 762-768. https://doi.org/10.1111/jpc.15976

Population

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

Patients with a high pre-test probability of X-linked hypophosphatemic (XLH) rickets.

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

82236004

Intervention

Name of the proposed health technology:

Fibroblast growth factor 23 (FGF-23) biochemical testing

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:

No testing.

Outcomes

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

The proposed medical service (FGF-23 biochemical testing) will enable the diagnosis of X-linked hypophosphatemia, identified by elevated (or inappropriately normal) serum or plasma FGF-23 levels and in conjunction with other diagnostic findings. The diagnosis facilitates determination of eligibility for burosumab treatment.

Proposed MBS items

Please provide at least one proposed item with their descriptor and associated costs, for each Population / Intervention:

Proposed item	<system generated>
MBS item number (where used as a template for the proposed item)	XXXXX
Category number	Category 6
Category description	Pathology Services
Proposed item descriptor	<p>Fibroblast growth factor 23, quantification in serum or plasma if the service is requested by a specialist or consultant physician and the patient has:</p> <ul style="list-style-type: none"> (i) current radiographic X-ray evidence of rickets or for those with growth plate fusion historical radiographic X-ray evidence of rickets or current diagnosis of osteomalacia; and (ii) a high pre-test probability of X-linked hypophosphatemia; and (iii) a serum phosphate concentration below the age adjusted lower limit of normal; and (iv) renal phosphate wasting demonstrated by a ratio of tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR) according to age specific normal ranges using the second morning urine void and paired serum sample measuring phosphate and creatinine.
Proposed MBS fee	\$90
Indicate the overall cost per patient of providing the proposed health technology	<p>\$90, as above and based on fee at Royal Childrens' Hospital Melbourne</p> <p>https://www.rch.org.au/specimen-collection/Fibroblast Growth Factor 23 (FGF-23)/</p>
Please specify any anticipated out of pocket expenses	To be confirmed
Provide any further details and explain	The exact MBS item fee is to be determined.

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 or payments.

Please provide a cost break down attachment:

Document type	File name
Cost breakdown attachment	None – to be determined during assessment

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:

Patients require biochemical evidence of excessive FGF-23 or documented confirmation of PHEX pathogenic variant to access PBS support for burosumab to treat XLH rickets. The proposed MBS listing of the FGF-23 test will improve diagnostic accuracy for the purpose of identifying patients eligible for treatment with burosumab.

Estimated utilisation

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

Approximately 300 patients in Australia have developed rickets due to phosphate deficiency as a result of excessive FGF-23 production.

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

Year 1 estimated uptake (%):

100%

Year 2 estimated uptake (%):

100%

Year 3 estimated uptake (%):

100%

Year 4 estimated uptake (%):

100%

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

<100

Will the technology be needed more than once per patient?

No, once only

Provide references to support these calculations:

Document type	File name
Estimated utilisation references	Clinical expert opinion

Consultation

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

- Royal College of Pathologists of Australia (RCPA)
- Australian Pathology
- Public Pathology Australia

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

- Australian & New Zealand Bone and Mineral Society (ANZBMS)

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

- Royal College of Pathologists of Australia (RCPA)
- Australian & New Zealand Bone and Mineral Society (ANZBMS)
- Australasian Paediatric Endocrine Group (APEG)

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

Number of organisations listed:

- XLH Australia Incorporated
- Healthy Bones Australia
- Rare Voices Australia
- Genetic and Rare Disease Network
- The Bone Health foundation
- Musculoskeletal Australia

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

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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 - in vitro diagnostic test.

Has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TPG)? *(if 'Yes' above)*

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.

Please enter all relevant ARTG ID's:

ARTG ID	ARTG name

Is the intended purpose in this application the same as the intended purpose of the ARTG listing(s)?

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Provide details: *(if 'Yes' above)*

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

Yes.

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? *(if 'Yes' above)*

-

Please provide details of when you intend to lodge an ARTG inclusion application, or provide a rationale if you do not intend to lodge an ARTG inclusion application: *(if 'No' above)*

None required.

Please provide the TGA Application ID: *(if in the process of being considered by the TGA)*

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Please provide the TGA submission date (DD/MM/YYYY):

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Codependent details

Will a submission be made to the Pharmaceutical Benefits Advisory Committee (PBAC)?

No, the associated pharmaceutical burosumab is already included on the Pharmaceutical Benefits Scheme (PBS).

Please provide a rationale for the codependency and indicate how the proposed PBS restriction would reference the intervention(s) proposed for MSAC consideration:

The proposed FGF-23 biochemical test will be used to help determine eligibility for treatment with PBS listed burosumab.

The existing PBS Restriction for burosumab has clinical criteria that include:

- Patient must have a documented confirmation of PHEX pathogenic variant; OR
- Patient must have a confirmed diagnosis of X-linked hypophosphataemia demonstrated by the presence of all of the following: (i) a serum phosphate concentration below the age adjusted lower limit of normal; (ii) current or historical (for those with growth plate fusion) radiographic X-ray evidence of rickets; (iii) elevated (or inappropriately normal) serum or plasma FGF-23 levels of above the mean of the assay-specific reference range; (iv) renal phosphate wasting demonstrated by a ratio of tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR) according to age specific normal ranges using the second morning urine void and paired serum sample measuring phosphate and creatinine.

Will a submission be made to the Prostheses List Advisory Committee (PLAC)?

No.