PHARMAC
TE PĀTAKA WHAIORANGA

**Specialist Advisory Committees**
**Objective advice to Pharmac**
www.pharmac.govt.nz

# Record of the Rare Disorders Advisory Committee Meeting held on 29 July 2026

Rare Disorders Advisory Committee records are published in accordance with the Terms of Reference for the Specialist Advisory Committees 2021.

**Note that this document is not necessarily a complete record of the Rare Disorders Advisory Committee meeting**; only the relevant portions of the meeting record relating to Rare Disorders Advisory Committee discussions about an application or Pharmac staff proposal that contain a recommendation are generally published.

The Rare Disorders Advisory Committee may:

(a) recommend that a pharmaceutical be listed by Pharmac on the Pharmaceutical Schedule and the priority it gives to such a listing;

(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or

(c) recommend that Pharmac decline to list a pharmaceutical on the Pharmaceutical Schedule.

Pharmac Advisory Committees make recommendations, including priority, within their therapeutic groups of interest.

The record of this Advisory Committee meeting will be reviewed by PTAC at an upcoming meeting.

Specialist Advisory Committees and PTAC may differ in the advice they provide to Pharmac, including recommendations' priority, due to the committees' different, if complementary, roles, expertise, experience, and perspectives.

Pharmac is not bound to follow the recommendations made below. Applications are prioritised by Pharmac against other funding options and progressed accordingly. The relative priority of any one funding choice is dependent on a number of factors, including (but not limited to) the recommendation of PTAC and/or Specialist Advisory Committees, the mix of other applications being assessed, the amount of funding available, the success of commercial negotiations and/or the availability of clinical data.

# Table of Contents


1. Attendance ..... 3
2. Summary of recommendations ..... 4
3. The role of Specialist Advisory Committees and records of meetings ..... 4
4. Welcome and introduction ..... 5
5. Pharmac Update ..... 5
6. Record of Rare Disorders Specialist Advisory Committee meeting held Tuesday, June 10, 2025 ..... 5
7. Previous action points/recommendations made ..... 5
8. Therapeutic Group and NPPA Review ..... 7
    - Idursulfase for Hunter syndrome ..... 7
    - Fortijuice for fatty-acid oxidation disorders ..... 7
    - Exceptional Circumstances Framework review update ..... 8
    - Named Patient Pharmaceutical Assessment (NPPA) funding update ..... 9
    - Horizon Scanning ..... 9
9. Palopegteriparatide for hypoparathyroidism without optimal response to conventional therapy ..... 10
    - Application ..... 10
    - Recommendation ..... 10
    - Discussion ..... 10
        - *Patient lived experience* ..... 10
        - *Māori impact* ..... 11
        - *Populations with high health needs* ..... 11
        - *Background* ..... 11
        - *Health need* ..... 11
        - *Health benefit* ..... 12
        - *Suitability* ..... 14
        - *Cost and savings* ..... 14
        - *Funding criteria* ..... 15
        - *Summary for assessment* ..... 15
10. Burosumab for X-linked hypophosphataemia (XLH) for children ..... 16
    - Application ..... 16
    - Recommendation ..... 17
    - Discussion ..... 17
        - *Patient lived experience* ..... 17
        - *Māori impact* ..... 18
        - *Populations with high health needs* ..... 18
        - *Background* ..... 18
        - *Health need* ..... 18
        - *Health benefit* ..... 20

*Suitability* ..... 21
*Cost and savings* ..... 21
*Funding criteria* ..... 22
*Summary for assessment* ..... 23
11. Burosumab for X-linked hypophosphatemia (XLH) for adults ..... 23
Application ..... 23
Recommendation ..... 23
Discussion ..... 24
*Patient lived experience* ..... 24
*Māori impact* ..... 25
*Populations with high health needs* ..... 25
*Background* ..... 25
*Health need* ..... 25
*Health benefit* ..... 26
*Suitability* ..... 28
*Cost and savings* ..... 28
*Funding criteria* ..... 28
*Summary for assessment* ..... 28
12. Pegvisomant as an adjunct treatment for acromegaly, following surgery and medical therapy ..... 29
Application ..... 29
Recommendation ..... 29
Discussion ..... 30
*Patient lived experience* ..... 30
*Māori impact* ..... 30
*Populations with high health needs* ..... 30
*Background* ..... 30
*Health need* ..... 31
*Health benefit* ..... 31
*Suitability* ..... 33
*Cost and savings* ..... 33
*Funding criteria* ..... 34
*Summary for assessment* ..... 34

## 1. Attendance

**Present**
Helen Evans (Chair)
Emma Glamuzina
James Cleland
Katherine Neas

Mercedes Burnside
Rhiannon Braund
Sarah McLean-Orsborn
Tim Stokes

**Observer – Invited Experts for part of the meeting**
Dr Marianne Elston
Associate Professor Craig Jefferies
Professor Ben Wheeler

## 2. Summary of recommendations

| | Pharmaceutical and Indication | Recommendation |
|---|---|---|
| 8.11. | Fortijuice for people with long-chain fatty-acid oxidation disorders, subject to Special Authority criteria | High priority |
| 9.4. | Palopegteriparatide for hypoparathyroidism without optimal response to conventional therapy | Decline |
| 10.5. | Burosumab for the treatment of X-linked hypophosphatemia for children, subject to Special Authority criteria | High priority |
| 11.5. | Burosumab for the treatment of X-linked hypophosphatemia for adults, subject to Special Authority criteria | Medium priority |
| 12.5. | Pegvisomant as an adjunct treatment for acromegaly, following surgery and medical therapy, subject to Special Authority criteria | Medium priority |

These recommendations were made within the context of rare disorders.

## 3. The role of Specialist Advisory Committees and records of meetings

3.1. This meeting record of the Rare Disorders Advisory Committee is published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) 2021 and Specialist Advisory Committees 2021.Terms of Reference describe, *inter alia*, the establishment, activities, considerations, advice, and the publication of such advice of Specialist Advisory Committees and PTAC.

3.2. Conflicts of Interest are described and managed in accordance with section 6.4 of the SAC Terms of Reference.

3.3. The Rare Disorders Advisory Committee is a Specialist Advisory Committee of Pharmac. The Rare Disorders Advisory Committee and PTAC and other Specialist Advisory Committees have complementary roles, expertise, experience, and perspectives. The Rare Disorders Advisory Committee and other Specialist Advisory Committees may therefore, at times, make recommendations for treatments for Rare Disorders that differ from PTAC's, including the priority assigned to recommendations, when considering the same evidence. Likewise, PTAC may, at times, make recommendations for treatments for Rare Disorders that differ from the Rare Disorders Advisory Committee's, or Specialist Advisory Committees may make recommendations that differ from other Specialist Advisory Committees'.

Pharmac considers the recommendations provided by both the Rare Disorders Advisory Committee and PTAC and any other relevant Specialist Advisory Committees when assessing applications for treatments for Rare Disorders.

## 4. Welcome and introduction

4.1. The Chair welcomed the Committee with a karakia.

4.2. The Committee acknowledged that several Observer – Invited Experts would be attending the meeting, online, to support the applications discussed.

## 5. Pharmac Update

5.1. The Committee noted the Pharmac Update.

5.2. The Committee acknowledged Dr Mercedes Burnside has recently been appointed to the Rare Disorders Advisory Committee and that recruitment for the Committee is ongoing.

5.3. The Committee acknowledged that several Endocrinologist Observer – Invited Experts were invited to attend the meeting for the discussions. This is an approach that was previously piloted with the 2025 Rare Disorders Advisory Committee and has since been implemented for PTAC and other Specialist Advisory Committee meetings. The Invited Experts will attend to provide their relevant expertise to support the Committee's considerations. Invited Experts will be given an opportunity to share their insights following the discussion lead presentation and participate in the Committee discussion to answer any questions at the invitation of the Chair. Invited experts will not be present when the Committee votes on a recommendation. Invited Experts complete a confidentiality agreement and a declaration of interest to participate in the meeting. Pharmac staff will consider how this approach could be developed and might support other meeting discussions in the future.

5.4. Pharmac staff shared with members that patient lived experience submissions were sought to support the applications being considered by the Committee. Rare Disorders New Zealand facilitated these submissions from relevant patient groups. Video or written submissions were provided in advance to share with the Committee as part of its preparation for the meeting.

5.5. The Committee acknowledged key updates from Pharmac:

5.5.1. The release of the 2026/27 Letter of Expectations

5.5.2. Conclusion of the Reset Programme

5.5.3. The establishment of the Programme Delivery Office

5.5.4. Consultation on the Exceptional Circumstances Framework Review is now closed

5.6. The Committee noted the establishment of the Timely Assessment Improvement Programme (TAP), a four-year programme that builds on the foundations of Pharmac's initial 12 month Reset Programme.

5.7. The Committee noted an update on the progress of the Rare Disorders Strategy 2024-34 and that Pharmac continues to support its implementation.

## 6. Record of Rare Disorders Specialist Advisory Committee meeting held Tuesday, June 10, 2025

6.1. The Committee reviewed the 10 June 2025 and agreed that the record be accepted.

## 7. Previous action points/recommendations made

7.1. The Committee noted the update provided by Pharmac staff on the status of funding applications since the last Rare Disorders Advisory Committee meeting in 2025.

7.2. The Committee noted the update provided by Pharmac on the actions undertaken since the last meeting.

7.3. The Committee noted that an action to refine the eligibility criteria for carglumic acid remained open and Pharmac would discuss this with relevant members outside the meeting.

7.4. The Committee noted that Pharmac was in the process of planning a procurement activity which could result in additional supplements for inherited metabolic disorders being funded by Pharmac, if they are cost neutral to currently funded options.

7.5. Members noted that the nutritional supplements available, and the needs change frequently, and that a panel-style arrangement could be suitable for these products for ongoing supply.

7.6. The Committee noted the treatments for rare disorders that had been funded since the last Committee meeting in 2025, including widening access to cystic fibrosis treatments for people aged two years to five years old, and funding a new treatment for people with cystic fibrosis six years old and above.

7.7. The Committee noted Pharmac's funding application pathway for medicines for rare disorders. Members noted that many rare disorder medicines would require new investment to be funded, as there are often no existing funded treatments that would be displaced to generate cost offsets. The Committee considered that this may present an additional challenge to funding medicines for rare disorders in New Zealand.

7.8. A member asked about treatment options for Fabry disease on Pharmac’s Options for Investment List and whether a procurement process could be undertaken for these. Pharmac staff noted that a competitive procurement process could be considered. However, Pharmac staff noted that funding treatments for Fabry disease would require additional investment, and that the availability of budget, along with priority of funding treatments for Fabry disease relative to the other medicines Pharmac could fund on its Options for Investment List would need to be considered before a process could be committed to.

7.9. Pharmac staff acknowledged the unmet health need of people with Fabry disease in New Zealand and noted that no procurement process was planned at this time.

7.10. The Committee noted that an application for givinostat had been received by Pharmac for Duchene Muscular Dystrophy. However, it was unable to be accepted at this time. Pharmac staff noted that Medsafe approval was not required at the time of application, but a commitment to seeking regulatory approval from Medsafe and supplying New Zealand was needed. This commitment was yet to be received for givinostat.

7.11. Members requested data showing how many medium- or high-priority recommendations from this Committee had subsequently been ranked and funded, and how this compared with other advisory committees. Pharmac staff agreed to consider how it could provide this analysis.

7.12. Members considered only a small number of medicines for rare disorders had been funded recently and noted a concern that if medicines were not able to be funded then suppliers may stop submitting funding applications.

7.13. The Committee noted that the Government has a rare disorders strategy, which aims to ensure that people with rare disorders in New Zealand are able to achieve quality care within New Zealand’s health system. It was noted that Pharmac is one of the accountable agencies for delivering this strategy.

7.14. The Committee considered it was important that applications for medicines for rare disorders continue to be submitted and assessed by Pharmac and ranked on its Options for Investment List so that as budget becomes available, they are able to be considered for funding against other medicines that could be funded.

7.15. Members raised that for some of the medicines for rare disorders on the Options for Investment List, the option of a biosimilar equivalent may be an option, which could increase the chance of medicines being funded by increasing cost-effectiveness.

7.16. Members considered that eculizumab for atypical haemolytic uremic syndrome (aHUS) was a high needs group with no funded alternatives and clinicians who manage these patients were unsure how this could be progressed to funding. It was noted that Pharmac had received an application for aHUS and this was under assessment with Pharmac's Assessment Directorate. Members considered that one of the challenges for the assessment of this medicine is that the comparator would be blood products or plasmapheresis, which are high cost but not funded by Pharmac, so would provide offsets to the wider health sector, however not to the Pharmaceutical budget.

7.17. The Committee noted the list of medicines for rare disorders currently being reviewed by other committees and the medicines currently funded in New Zealand for rare disorders

## 8. Therapeutic Group and NPPA Review

### Idursulfase for Hunter syndrome

8.1. The Committee noted that in 2016 idursulfase had been funded for people with Hunter syndrome, mucopolysaccharidosis II (MPS II) in the bridge to transplant setting. Pharmac staff noted that the application for the wider group of people with MPSII, including use outside of the bridge to transplant setting, had recently been reopened following correspondence with a clinician, despite receiving two previous decline recommendations being received from PTAC.

8.2. The Committee confirmed it did not consider this application needed to be reopened and that the application could be closed. Members noted there were a number of new treatments for MPS II on the horizon reporting positive results and recommended that these treatments should be considered for funding in the future. The Committee considered it would welcome funding applications for these treatments.

8.3. Members noted that for some people with MPSII it would be helpful to be able to consider idursulfase as a potential treatment, noting patient numbers would be very small. Pharmac staff noted that consideration via the Exceptional Circumstances Framework would continue to be an option. Members considered that a procurement process for idursulfase may be an option to reduce the cost of this treatment.

### Fortijuice for fatty-acid oxidation disorders

8.4. The Committee noted that an application had recently been received by Pharmac for the funding of Fortijuice for people with long-chain fatty-acid oxidation disorders who are nutritionally depleted and require a regimen that is high in calories, glucose and protein but contains no fat.

8.5. Members considered there would be a maximum of five patients at any one time in New Zealand who would be expected to require this treatment. Members considered patients would initially receive PolyCal and would move to Fortijuice if this was required.

8.6. Members considered that of these five patients, not all would end up needing Fortijuice, but it could be an important part of their emergency management plan.

8.7. The Committee considered that it would be appropriate to restrict access to Fortijuice to people with long-chain fatty-acid oxidation disorders who require an emergency regimen that is high in calories, glucose and protein but contains no fat.

8.8. The Committee considered that the current comparator for these people, without access to Fortijuice was intravenous nutrition. The Committee considered most individuals would require treatment for between three to seven days on average.

8.9. Members emphasised that Fortijuice would not be used as a substitute for people currently using Fortisip, or Ensure Plus, or other funded oral feeds who may have a preference for juice-based feeds as Fortijuice, being fat free, is not a nutritionally complete feed.

8.10. The Committee **recommended** Fortijuice be funded for people with long-chain fatty-acid oxidation disorders with a **high priority**, subject to Special Authority criteria.

8.11. In making this recommendation the Committee considered:

- The high unmet health need of people with long-chain fatty-acid oxidation disorders
- The effect on the whānau of people with long-chain fatty-acid oxidation disorders
- The lack of the currently funded treatments
- The availability of Fortijuice would reduce need for intravenous nutrition, and therefore potentially avoid hospital admission or reduce the length of stay.

8.12. The Committee noted further work is required to develop eligibility criteria for Fortijuice.

### Exceptional Circumstances Framework review update

8.13. The Committee noted the update on the review of the Exceptional Circumstances Framework review provided by Pharmac staff.

8.14. The Committee noted that Pharmac had recently undertaken the first round of public consultation on the review of the framework.

8.15. The Committee noted that feedback had been received from a range of stakeholders including clinicians, suppliers and consumer advocates.

8.16. The Committee noted the high-level themes of the feedback, including a framework that is simpler and easier to use and more transparent for applicants and Pharmac.

8.17. The Committee noted that feedback had been received about the consideration of rare disorders through the framework.

8.18. The Committee noted the timeframes for the remaining stages in review, including a second public consultation on a proposed outcome later in 2026.

8.19. Members shared their experience of having a strong relationship with the Exceptional Circumstances team which had helped their understanding of the current policy and improved outcomes for their patients. It was acknowledged that not all areas and specialties had strong relationships and good understanding of the current policy which may affect equitable outcomes or access to medicines funded via the exceptional circumstances framework.

8.20. Members shared that many patients with rare disorders would meet the current requirements of the exceptional circumstances framework but were unable to access treatment through that pathway due to the cost. Members considered it would be important to consider access for people with ultra-rare disorders as part of the review.

8.21. Members noted that they have received feedback that the low levels of funding of medicines for people with rare disorders in New Zealand meant that companies were

increasingly unwilling to bring their medicines to New Zealand or undertake clinical trials in New Zealand, which was an important avenue for treatment for some people.

## Named Patient Pharmaceutical Assessment (NPPA) funding update

8.22. Members considered the information provided by Pharmac regarding NPPA applications and outcomes for people with rare disorders over the last 12 months. Members noted that the data presented focused on people with ultra-rare disorders rather than the updated definition of 1 in 2000 people. Members noted NPPA applications for ultra-rare disorders are currently flagged in Pharmac's system as they are received and assessed. Members noted that the updated definition would include a significant number of conditions considered through the NPPA process, some of which may be better reviewed by other committees. Further work by Pharmac is required to consider the NPPA funding information that is relevant to the Rare Disorders Committee in line with the updated Rare Disorders definition.

8.23. Members noted the information presented regarding NPPA outcome by region and suggested it would be helpful to see information about the number of applications that were initially assessed as 'principles not met' that ultimately were approved.

8.24. Members noted that the proportion of NPPA applications approved within the rare disorders group was higher than for other therapeutic groups.

8.25. Members considered it would be helpful to have the data presented by domicile of patient as the National services submitted NPPA applications for people throughout the country.

8.26. Members considered many of the NPPA applications appeared to be rare manifestations of more common conditions. It was considered the exceptional circumstances framework was the appropriate funding pathway for these to be considered.

8.27. The Committee noted that for medicines with indications that are frequently approved via NPPA, Pharmac's preference was to list these on the Pharmaceutical Schedule subject to access criteria to reduce the workloads for applicants and Pharmac staff and provide greater certainty for people who need funded treatments, as well as a reduction of time to treatment.

8.28. Members raised that people with inherited metabolic disorders on a ketogenic diet who require ketone strips are currently restricted to 20 strips per prescription (10 with one repeat) despite needing to test ketones multiple times per day, resulting in a large number of prescriptions needing to be written and multiple visits to pharmacies for patients. Members considered a solution in the Pharmaceutical Schedule would be appropriate for this.

8.29. Members also noted that for people with rare disorders lifetime approvals were strongly preferred as the underlying conditions and treatments for these people would be lifelong.

8.30. Members also considered easier access for liquid formulations of funded medicines for children would also be helpful.

8.31. Members raised that adding continuous glucose monitors for people with congenital hyperinsulinism would be helpful as these are already approved via NPPA when they arise.

## Horizon Scanning

8.32. The Committee noted that Pharmac undertakes a range of regular horizon scanning activities as part of its usual activities, including seeking input from its clinical advisors.

8.33. The Committee noted that other countries such as Australia and the United Kingdom have different pathways for considering and funding high-cost medicines for people with rare disorders and noted the information provided by Pharmac on the medicines that have been funded through these pathways.

8.34. The Committee noted that Pharmac had assessed two gene therapies, both supplied by Novartis. Pharmac is currently working through how a gene therapy could be contracted and supplied within Pharmac's funding model, noting complexities including the high upfront cost of treatment. The Committee noted that once given, treatment is expected to provide benefit over a lifetime, but uncertainty remains about how long benefit will remain and any other health complexities that may arise in future. Members noted the need for infrastructure to be in place within Health New Zealand hospitals to allow gene therapies to be given.

## 9. Palopegteriparatide for hypoparathyroidism without optimal response to conventional therapy

9.1. Dr Marianne Elston Endocrinologist, Health New Zealand attended the discussion as an Observer – Invited Expert. Dr Elston left the meeting before the recommendation was made.

### Application

9.2. The Committee reviewed a clinician application for palopegteriparatide in the treatment of hypoparathyroidism without optimal response to conventional therapy

9.3. The application was received in response to Pharmac's 2025 rare disorders call for applications. Pharmac staff considered they met Pharmac's Policy principles for rare disorders. The supplier of palopegteriparatide provided information to support this application. The Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

### Recommendation

9.4. The Committee **recommended** that palopegteriparatide for hypoparathyroidism without optimal response to conventional therapy, within the context for treatments for rare disorders, **be declined**.

9.5. In making this recommendation, the Committee considered the substantial cost of the treatment, the limited evidence based derived from small clinical studies, and the uncertainty regarding the long-term impact of treatment on renal outcomes and other clinically important outcomes.

9.6. The Committee further considered that access to palopegteriparatide for individuals with exceptional clinical circumstances, such as rare genetic disorders could be considered through the Named Patient Pharmaceutical Assessment (NPPA) pathway.

9.7. The Committee considered that if updated evidence could be provided to address its uncertainties the application for palopegteriparatide for hypoparathyroidism without optimal response to conventional therapy could be reconsidered in future.

### Discussion

*Patient lived experience*

9.8. The Committee acknowledged and thanked individuals living with chronic hypoparathyroidism who shared their experiences with the Committee. The Committee considered that these submissions highlighted the substantial physical, emotional, and

practical burden associated with living with a chronic condition that requires lifelong management.

9.8.1. The individuals shared their journey to diagnosis, including delays to accessing specialists, and the effect of the treatments on their daily lives. The individuals shared how chronic hypoparathyroidism, despite treatment, has affected their ability to drive and socialise leaving them to feel isolated both professionally and privately. Individuals further described how the condition has had a severe financial toll on them, with the need to finance treatments and surcharges that are not paid for by the health system, as well as the need to move to achieve better access to healthcare or reduce housing costs.

9.8.2. In addition to the effect on them personally, the individuals described the effect on their whānau and people they live with, the lack of understanding of the condition, and the need to educate others about their symptoms that added to their mental burden.

9.8.3. Members noted that some individuals continue to experience persistent and disabling symptoms, including impacts on cognition, daily functioning, and ability to work, despite achieving normal serum calcium levels with conventional treatment. The Committee considered that the burden of disease and healthcare utilisation may therefore persist despite biochemical control and noted that further evidence regarding the long-term effects of palopegteriparatide on quality of life would be valuable.

*Māori impact*

9.9. The Committee noted there was no evidence that Māori experience differences in the underlying disease biology or expected treatment response for chronic hypoparathyroidism.

9.10. Members noted that most cases of chronic hypoparathyroidism are secondary to thyroid surgery. Members noted that Māori and Pacific peoples experience higher rates of thyroid disease and thyroid surgery and may therefore be disproportionately affected by hypoparathyroidism, although New Zealand-specific data are lacking.

*Populations with high health needs*

9.11. The Committee noted there was no evidence that Pacific peoples or other population groups experience differences in the underlying disease biology or expected treatment response for chronic hypoparathyroidism.

9.11.1. The Committee noted that a reduction in medication burden and monitoring requirements may provide particular suitability benefit for people with limited access to primary care, laboratory services, or specialist care.

*Background*

9.12. The Committee noted that palopegteriparatide had not previously been considered for funding in New Zealand and that no Named Patient Pharmaceutical Assessment (NPPA) applications had been identified.

9.13. The Committee noted the proposed target population was people with chronic hypoparathyroidism who remained inadequately controlled despite conventional therapy, including those with persistent biochemical abnormalities, recurrent acute presentations, renal complications, or hypercalciuria.

*Health need*

9.14. The Committee noted that chronic hypoparathyroidism is an incurable condition requiring lifelong treatment and is estimated to affect 30 people per 100,000 in New Zealand, resulting in approximately 1,500 people.

9.14.1. The Committee noted that approximately one-third of people with chronic hypoparathyroidism may remain inadequately controlled with conventional therapy.

9.14.2. The Committee noted that conventional therapy can correct hypocalcaemia but does not replace physiological parathyroid hormone or reliably prevent long-term renal complications.

9.14.3. Members noted that permanent hypoparathyroidism following thyroid surgery is uncommon, occurring in fewer than 2%. Members further noted that individuals with genetic causes of hypoparathyroidism may experience more severe disease and may be at greater risk of developing renal impairment due to the longer duration of disease.

9.15. The Committee noted that chronic hypoparathyroidism may result in acute complications including symptomatic hypocalcaemia, seizures, neuromuscular symptoms, emergency department presentations, and hospitalisations.

9.16. The Committee noted that long-term complications may include recurrent nephrolithiasis, nephrocalcinosis, chronic kidney disease, and neurological complications associated with basal ganglia calcification.

9.17. The Committee considered that the disease can have a substantial impact on quality of life through both acute symptoms and long-term complications.

9.18. The Committee noted there was limited New Zealand-specific information regarding the prevalence of inadequately controlled disease, rates of hospitalisation, nephrolithiasis, nephrocalcinosis, or progression to renal replacement therapy.

9.18.1. The Committee considered that estimates of disease burden and complications therefore rely largely on international data and may not fully reflect the New Zealand context.

9.19. The Committee noted considerable variability in disease control despite good treatment adherence, with some individuals requiring frequent biochemical monitoring to manage fluctuations in calcium levels.

*Health benefit*

9.20. The Committee noted that palopegteriparatide is administered as a subcutaneous injection with an initial dose of 18 micrograms daily and subsequent dose titration based on treatment response. The Committee noted that the goal of treatment with palopegteriparatide is to achieve and maintain normocalcaemia without the need for active vitamin D or high-dose calcium supplementation.

9.20.1. The Committee considered that the long-term benefits of treatment, including impacts on quality of life, renal outcomes, and healthcare utilisation, remained key areas of uncertainty.

9.21. The Committee noted the key evidence for palopegteriparatide was derived from the phase III PaTHway trial, a 26-week double-blind, placebo-controlled study involving 78 participants with chronic hypoparathyroidism, followed by an open-label extension. Participants received either once daily palopegteriparatide or placebo in addition to conventional therapy.

9.21.1. The Committee noted that at week 26, 79% of participants receiving palopegteriparatide achieved the composite primary efficacy endpoint compared with 5% of participants receiving placebo ($p<0.0001$) (Khan et al. J Bone Miner Res. 2023;38:14-25). The Committee noted that this endpoint comprised achievement of normocalcaemia together with independence from active vitamin D and high-dose calcium supplementation.

9.21.2. The Committee noted that 93% of participants receiving palopegteriparatide achieved independence from conventional therapy and that treatment was associated with normalisation of mean 24-hour urinary calcium excretion.

9.21.3. The Committee noted that improvements in patient-reported outcomes, including the Hypoparathyroidism Patient Experience Scale and SF-36 Physical Functioning score, were observed in favour of palopegteriparatide compared with placebo.

9.21.4. The Committee noted that efficacy appeared to be maintained during longer-term follow-up. At week 52, 81% of participants achieved the multicomponent efficacy endpoint and 95% achieved independence from conventional therapy (Clarke et al. J Clin Endocrinol Metab. 2024;110:951–60).

9.21.5. The Committee noted that, following 52 weeks of treatment in the open-label extension, 95% of participants remained on treatment. Among those who remained enrolled, 86% maintained normocalcaemia and 95% achieved independence from conventional therapy, defined as no active vitamin D use and calcium supplementation of 600 mg/day or less. The Committee further noted that no participants required active vitamin D therapy at 52 weeks (Rejnmark et al. Adv Ther. 2024;412500-18).

9.22. The Committee noted that palopegteriparatide was generally well tolerated, with most adverse events reported in clinical studies being mild to moderate in severity. The Committee further noted that no treatment-related discontinuations or emerging safety concerns were identified during the available follow-up period.

9.23. The Committee considered that uncertainty remained regarding the durability of treatment benefit, long-term renal outcomes, long-term safety, and the extent to which the observed improvements would translate into reductions in long-term complications and healthcare utilisation. Members noted that the available evidence was derived from small, industry-sponsored studies with limited long-term comparative follow-up, resulting in uncertainty regarding the long-term effectiveness and cost-effectiveness of treatment.

9.24. The Committee noted several limitations of the available evidence, including exclusion of people with advanced chronic kidney disease, limited ethnic diversity within study populations, and the potential for the comparator arm to not fully reflect optimised clinical practice. The Committee considered that these factors may limit the generalisability of the trial findings to the New Zealand population and to individuals with more severe disease.

9.24.1. The Committee noted that participants receiving recent thiazide therapy were excluded from the pivotal trial. Members considered that thiazide diuretics form part of the standard management for some individuals with chronic hypoparathyroidism because they may reduce urinary calcium excretion. The Committee considered that exclusion of these patients in the pivotal trial may have resulted in the comparator arm not fully reflecting optimised clinical practice, potentially favouring palopegteriparatide, although members considered that thiazides are not effective or well tolerated in all patients.

9.25. The Committee considered that the population included in the available evidence was less severe than the population described in the PICO. The Committee considered it uncertain whether the observed treatment effects would be representative of the relative benefits of palopegteriparatide compared with current treatments in the population of interest.

9.26. The Committee considered the overall quality of the evidence supporting palopegteriparatide to be moderate. Members noted that the available studies consistently demonstrated improvements in biochemical control and reduced dependence on conventional therapy; however, certainty was reduced by methodological limitations including industry sponsorship, a lack of independent replication, and reliance on open-label extension data for longer-term outcomes.

9.27. The Committee was made aware that progression to severe renal impairment and renal replacement therapy appears to be uncommon overall. However, Members considered that the risk may be higher in some subgroups, including individuals with genetic causes of hypoparathyroidism, and those with longstanding hypercalciuria. Members further noted that the long-term renal consequences of chronic hypoparathyroidism remain an important area of uncertainty.

9.28. The Committee noted that no clinical trial data were available for people with severe renal impairment (eGFR <30 mL/min/1.73m$^2$), despite this population being at greatest risk of progression to renal replacement therapy. Members considered that restricting treatment to people with better preserved renal function may exclude those most likely to benefit from any potential renal protective effects of treatment. However, the Committee noted that the magnitude of any benefit in this population remains uncertain due to the absence of evidence. The Committee noted that treatment adherence would be particularly important if palopegteriparatide were funded. Members considered that abrupt treatment discontinuation could place individuals at risk of severe hypocalcaemia and that this may be of particular concern for patients with difficulties accessing repeat prescriptions or maintaining regular treatment.

*Suitability*

9.29. The Committee noted that palopegteriparatide is self-administered as a once-daily subcutaneous injection and does not require infusion services, hospital administration, or specialised facilities.

9.30. The Committee noted that dose titration and biochemical monitoring are required during treatment initiation, including monitoring of serum calcium, phosphate, and renal function.

9.31. The Committee noted that the medication burden associated with conventional therapy can be substantial, with some individuals requiring multiple doses of calcium and active vitamin D each day. Members considered that reducing pill burden may provide meaningful benefits for some people living with chronic hypoparathyroidism.

*Cost and savings*

9.32. The Committee noted that palopegteriparatide would be associated with a substantial increase in pharmaceutical expenditure if funded. Members noted that estimates of the eligible population, uptake, and renewal rates were derived largely from supplier assumptions and international data.

9.33. The Committee further noted that proposed health system savings from reduced use of conventional therapies and delayed progression of chronic kidney disease were uncertain and dependent on assumptions that had not been validated in the New Zealand setting.

9.34. Members considered there was substantial uncertainty regarding the economic model, including the extrapolation of short-term clinical data to long-term outcomes, assumptions regarding quality-of-life gains, and the modelling of chronic kidney disease progression.

9.35. The Committee noted clinical advice that a treatment uptake of approximately 70% among eligible individuals was reasonable. Members noted that willingness to initiate treatment would likely vary between individuals, with some people potentially reluctant to commence a daily injectable treatment. The Committee considered that uptake would depend on individual preferences and perceptions of the potential benefits and burdens of treatment.

*Funding criteria*

9.36. The Committee considered that additional outcomes of clinical relevance to be evaluated should include urinary calcium excretion, rate of renal function decline, progression to end-stage kidney disease, and healthcare utilisation, including hospitalisations and emergency department presentations. Members noted that evidence for these longer-term outcomes remains limited.

9.37. The Committee considered that a six-month review following treatment initiation would be appropriate to assess treatment response. However, members considered that requiring complete independence from calcium supplementation and active vitamin D for ongoing treatment may be unnecessarily restrictive. The Committee noted that some individuals may achieve meaningful clinical benefit through reductions in hypercalciuria, lower supplement requirements, and improved disease control despite continuing to require low-dose conventional therapy.

9.38. The Committee considered that restricting eligibility to individuals with chronic hypoparathyroidism of at least 12 months duration was appropriate. Members noted that transient hypoparathyroidism following thyroid surgery is relatively common and most cases resolve within six months, with occasional recovery occurring between six and twelve months. The Committee considered that recovery beyond 12 months is uncommon and that a 12-month threshold would appropriately identify individuals with permanent disease who may benefit from treatment.

9.39. The Committee considered that the NPPA pathway would remain appropriate for a small number of individuals with exceptional clinical circumstances. Members noted that this may include some people with rare genetic forms of hypoparathyroidism who experience more severe disease, substantial impairment in quality of life, or progressive complications despite optimised conventional therapy. The Committee considered that the broader population with post-surgical hypoparathyroidism would not generally meet the threshold for exceptional circumstances.

*Summary for assessment*

9.40. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for palopegteriparatide if it were to be funded in New Zealand for hypoparathyroidism. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Committee's assessment at this time and may differ from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

| | |
|---|---|
| **P**opulation | Individuals with chronic hypoparathyroidism where the disease is inadequately controlled on conventional therapy, defined as:<br>• Calcium < 2.0 mmol/L or prior emergency room/urgent care visits related to hypoparathyroidism (in the previous 6 months), or prior hospitalisations related to hypoparathyroidism (in the previous 6 months), or<br>• Serum phosphate > 1.5 mmol/L (4.5 mg/dL), or<br>• History of nephrolithiasis, or<br>• History of nephrocalcinosis, or |

| | |
|---|---|
| | • Reduced kidney function (eGFR < 60 mL/min per 1.73m²), or<br>• Hypercalciuria (calcium excretion >7 mmol/24-hour). |
| **I**ntervention | Subcutaneous palopegteriparatide 18 mcg once daily with dose adjustments in 3 mcg increments thereafter every 7 days. The dose range is 6 to 60 mcg per day. The maintenance dose should be the lowest dose that achieves serum calcium within the normal range, without the need for active vitamin D or therapeutic doses of calcium. Treatment duration for affected individuals is anticipated to be indefinite. |
| **C**omparator(s) (NZ context) | Continuing conventional therapy, consisting of 0.5-2 mcg of active vitamin D and 800-1000 mg of dietary calcium per day |
| **O**utcome(s) | Outcomes observed in the PaTHway trial (palopegteriparatide vs standard calcium and active vitamin D supplementation):<br>Improved biochemical control, defined as normocalcaemia (2.07–2.64 mmol/L) with independence from active vitamin D and high-dose elemental calcium (>600 mg/day), with associated improvements in HRQoL (SF-36) observed between treatment arms.<br><br>Reduced rate of renal function decline observed in PaTHway trial assumed to be maintained in long-run, with this linked to reductions in rates of kidney function progression, mortality, and renal replacement therapy.<br><br>Other outcomes of clinical relevance with limited long-term evidence<br>- Urinary calcium excretion<br>- eGFR change<br>- Rate of progression to ESRD<br>- Health care resource use |
| *Table definitions:*<br>**P**opulation: The target population for the pharmaceutical, including any population defining characteristics (eg line of therapy, disease subgroup)<br>**I**ntervention: Details of the intervention pharmaceutical (dose, frequency, treatment duration/conditions for treatment cessation).<br>**C**omparator: Details the therapy(s) that the patient population would receive currently (status quo – including best supportive care; dose, frequency, treatment duration/conditions for treatment cessation).<br>**O**utcomes: Details the key therapeutic outcome(s), including therapeutic intent, outcome definitions, timeframes to achieve outcome(s), and source of outcome data. | |

## 10. Burosumab for X-linked hypophosphataemia (XLH) for children

10.1. Assoc Prof Craig Jefferies, Paediatric Endocrinologist, Health New Zealand and Professor Ben Wheeler, Paediatric Endocrinologist & Co-Director New Zealand Paediatric Surveillance Unit, attended the discussion as Observer – Invited Experts. Assoc Prof Jefferies and Professor Wheeler left the meeting before the recommendation was made.

### Application

10.2. The Committee reviewed a consumer and supplier application for burosumab in the treatment of X-linked hypophosphataemia (XLH) for children

10.3. These applications were received in response to Pharmac's 2025 rare disorders call for applications. Pharmac staff considered they met Pharmac's Policy principles for rare disorders.

10.4. The Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

## Recommendation

10.5. The Committee **recommended** that burosumab for the treatment of X-linked hypophosphataemia for children be listed with a **high priority** within the context of treatments for rare disorders subject to the following Special Authority criteria:

> **Initial application- (XLH)** from any relevant practitioner. Approvals valid for 12 months for applications meeting the following criteria:
>
> Both:
>
> 1. Patient has been diagnosed with X-linked hypophosphatemia; and
> 2. Patient's growth plates have not fused
>
> **Renewal—(XLH)** from any relevant practitioner. Approvals valid for 12 months for application meeting the following criteria:
>
> All of the following:
>
> 1. Patient has experienced a clinical benefit

10.6. In making this recommendation the Committee considered:

- The high unmet health need of children with XLH
- The effect on the whānau of children with XLH
- The poor suitability of the currently available treatments
- Burosumab treatment offers a clinically meaningful benefit
- Burosumab treatment would significantly reduce the need for orthopaedic surgery.

## Discussion

*Patient lived experience*

10.7. The Committee received a large number of patient lived experience submissions providing the experience of the families of children with XLH and the effect on their daily lives, and wider family.

10.8. The Committee also received submissions from the Australian and New Zealand Society of Paediatric Endocrinology and Diabetes Bone and Mineral Working Group, the New Zealand Paediatric Endocrine Society Incorporated and XLH Australia in support of the application.

10.9. The families shared the high burden that conventional treatment has placed on them, and their experiences in navigating the New Zealand health service. This includes numerous specialist appointments, as well as painful and repeated orthopaedic surgeries.

10.10. Some individuals note that this has driven them to explore the option of moving abroad to seek treatment. For those that have moved abroad and received burosumab treatment, the submissions outline how burosumab treatment has resulted in improved quality of life, including reduced pain, and improved mobility and energy levels, however this has come at the cost of moving away from family to access treatment. For those that have moved and received burosumab treatment from a very young age, the family reports that burosumab treatment has meant that their child has had no symptoms and is growing normally.

10.11. The families have also highlighted that living with XLH has had a negative effect on the children's psychological health, with some experiencing a loss of confidence and feeling different to their peers.

10.12. Overall, the submissions highlighted that XLH is a multigenerational, debilitating condition that severely affects the health of children with the disease and significantly affects the lives of their families too, causing distress to caregivers.

10.13. The Committee expressed its sincere gratitude to the individuals and patient group for their submissions and recognised the courage of sharing their personal stories and experiences.

*Māori impact*

10.14. The Committee discussed the impact of funding burosumab for the treatment of XLH on Māori health areas of focus | Hauora Arotahi and Māori health outcomes. The Committee considered that while there is a lack of evidence to support an ethnic disparity in the prevalence of XLH, the Committee considered that Māori would be disproportionately impacted by barriers to diagnosis and subsequently accessing endocrinology clinics for specialist treatments.

*Populations with high health needs*

10.15. The Committee discussed the health need(s) of XLH among Māori, Pacific peoples, disabled peoples including tāngata whaikaha Māori, and other populations identified by the Government Policy Statement on Health 2024-2027 to have high health needs. The Committee discussed the impact of funding burosumab and considered:

10.15.1. Individuals in rural areas would have additional barriers to accessing specialist clinics for diagnosis and treatment. The Committee considered that some parents do not regularly bring their children, who may appear clinically well, to appointments due to the burden that places on their whānau, paid employment and the child's schooling.

10.15.2. Pacific peoples would be disproportionately impacted by barriers to diagnosis and subsequently accessing endocrinology clinics for specialist treatments.

*Background*

10.16. The Committee noted that burosumab and other treatments for XLH have not been considered previously.

10.17. The Committee noted a consumer application for burosumab for the treatment of adults with XLH was considered separately at the meeting.

*Health need*

10.18. The Committee noted XLH is a rare metabolic bone disorder caused by pathogenic variants in the phosphate-regulating endopeptidase homologue X-linked (*PHEX*) gene, which is mainly expressed in bones (osteoblasts and osteocytes) and teeth (odontoblasts and cementoblasts). The pathogenesis of XLH is complex and not fully understood. Many features of the disease can be explained by increased secretion of the phosphaturic hormone fibroblast growth factor 23 (FGF-23) from bone (Haffner et al. Nat Rev Nephrol. 2025;21:330-54).

10.19. The Committee considered the disorder usually presents during the first two years of life, typically presenting with delayed walking, an abnormal waddling gait, lower-limb deformity and decreased growth velocity. The Committee noted a recent survey conducted in New Zealand and Australia reported that despite a family history in most cases, delayed diagnosis was common, with 49% diagnosed after two years of age (Sandy et al. Bone. 2023:173:116791).

10.20. The Committee noted the clinical consequences of XLH can include rickets, osteomalacia, bone pain, leg deformities, premature fusion of the cranial sutures and disproportionate short stature that usually develops during the

first 2 years of life. Patients also show hypomineralisation of teeth and are prone to tooth abscesses and periodontitis (Haffner et al. 2025).

10.21. The Committee noted a New Zealand and Australia based study that reported that the most common clinical characteristics included leg bowing (89%), bone and joint pain (68%), abnormal gait (57%) and short stature (49%). There was a significant burden of orthopaedic disease and surgeries and a high rate of complications of nephrocalcinosis and hyperparathyroidism (32% and 20% respectively) (Sandy et al. 2023).

10.22. The Committee noted a recent prevalence survey conducted by the New Zealand Paediatric Surveillance Unit estimated a minimum prevalence of 1.60 per 100,000 persons aged under 18 years in New Zealand. However, the authors considered this estimate to be an underestimation of the true prevalence due to incomplete reporting, variable clinician awareness of XLH, delayed or historical underdiagnosis (Sandy et al. 2023).

10.23. The Committee noted a New Zealand and Australia based study that suggests that the prevalence of XLH in Māori children is higher than in among other ethnicities, accounting for 31% of identified cases, despite comprising approximately 18% of the New Zealand population (Sandy et al. 2023). However, the Committee considered there was a lack of data to determine an ethnic disparity in the prevalence of XLH due to the small number of participants.

10.24. The Committee noted the challenges associated with the manifestations of XLH can limit the ability to perform basic activities of daily living, including walking, dressing, and personal hygiene. They also reduce the ability of children with XLH to participate in age-appropriate physical activities, which are important for childhood development (Cheung et al. 2021).

10.25. The Committee considered the high carer burden associated with this condition, with caregivers required to wake frequently during the night to administer treatment, and to accompany children to specialist medical appointments which can involve several hours of travel in addition to the appointment itself. The Committee considered that regular appointments can be disruptive to the family's daily routine, and difficult to manage around existing commitments, such as work or caring for other children.

10.25.1. The Committee also considered that the health-related quality of life of caregivers. may also be affected by the condition.

10.26. The Committee was made aware that XLH has an effect on the entire whānau with some individuals choosing not to have children to prevent the condition being passed to their children.

10.27. The Committee considered some children can appear clinically well and may not be regularly reviewed by endocrinologists as caregivers may be reluctant to travel for appointments when children appear relatively well. However, these children are expected to experience severe skeletal impacts in the future.

10.28. The Committee considered that the current treatments of phosphate and vitamin D supplementation aimed to ameliorate the symptoms of the disease, through improved growth and ricket signs in children. However, these treatments could have secondary effects such as aggravating renal phosphate wasting, increasing urinary calcium excretion with risks of nephrocalcinosis and may increase FGF-23 secretion. The Committee considered there was little evidence of long-term positive benefit from the currently funded treatments.

10.28.1. The Committee considered that while conventional treatment minimises acute hospital admissions, it does not prevent the skeletal consequences of the disease including severe short stature and limb deformities.

10.29. The Committee were made aware that administration of conventional treatment can impact children's relationships with their parents and mental health, due to their unpalatable flavour and frequency of dosing.

10.30. The Committee considered children currently undergo multiple, complex and painful orthopaedic surgeries that aim to minimise the skeletal impacts of the disease however this was not performed with curative intent. The Committee considered this had a significant health related quality of life impact on children and resulted in lifelong scarring and impacts on mobility at a young age.

*Health benefit*

10.31. The Committee noted CL301, a randomised, active-controlled, open-label phase III trial (n=61) (Imel et al. Lancet. 2019;393:2416-27) that reported the following results:

- At week 40 the burosumab group had a significantly greater improvement in Radiographic Global Impression of Change (RGI-C) global score compared to conventional therapy (least squares mean +1·9 [SE 0·1] with burosumab vs +0·8 [0·1] with conventional therapy; difference 1·1, 95% CI 0·8–1·5; p<0·0001).

10.32. The Committee noted the CL301 open label extension where individuals continued on burosumab treatment or crossed over to burosumab treatment (Ward et al. JBMR Plus. 2024;8:ziad001) that reported the following results:

- There were improvements in both groups in the RGI-C rickets total score, RGI-C lower limb deformity score, and mean height Z-score.
- Phosphate metabolism normalised rapidly in the crossover group and persisted in the continuation group, mean serum alkaline phosphatase decreased in both groups.

10.32.1. The Committee considered individuals included in the study may be more clinically severe based on their ricket score than those in the New Zealand population.

10.33. The Committee noted CL201, a randomised, open-label, dose-finding, phase II trial (n=52) (Carpenter et al. N Engl J Med 2018;378:1987-98) reported the following results:

- Mean total Thacher rickets severity score (TRSS) decreased from 1.9 at baseline to 0.8 every-2-week dosing, from 1.7 at baseline to 1.1 at week 40 with every-4-week dosing (P<0.001 for both comparisons); these improvements persisted at week 64.
- Improvements in fasting serum phosphorus levels, renal tubular phosphate reabsorption, and serum phosphatase levels.
- The mean standing-height z score increased in both groups, with greater improvement seen at all time points with every-2-week dosing (an increase from baseline of 0.19 at week 64) than with every-4-week dosing (an increase from baseline of 0.12 at week 64). Physical ability improved and pain decreased.

10.34. The Committee noted CL205, a multicentre open label phase II trial (n=13) (Whyte et al. Lancet Diabetes Endocrinol. 2019;7:189-99)

10.35. The Committee noted Linglart et al. Lancet Diabetes Endocrinol. 2026;14:475-84 that reported results in children younger than 1 year of age. The study reported that burosumab is safe and effective in this age range.

10.36. The Committee noted the following studies:

- Padidela et al. Calcif Tissue Int 2021;108:622-33
- Ward et al. J Clin Endocrinol Metab. 2022;107:e3241-e53.
- Wang et al. J Clin Endocrinol Metab. 2023;109:293-302.

- Linglart et al. J Clin Endocrinol Metab. 2022; 107:813-24.
- Klein et al. Pediatr Nephrol. 2024;39:3221-31.
- Jarvis et al. Bone Rep. 2024:24:101819.
- Ward et al. J Bone Miner Res. 2025;40:1332-42.
- Wang et al. Front Endocrinol (Lausanne). 2024 :15:1414509.

10.37. The Committee considered that the earlier children are treated, the larger the health benefit they would receive.

10.38. The Committee considered overall the quality of evidence was high, however the studies included small numbers of individuals due to the rarity of the disease.

10.39. The Committee considered that the data are generalisable to the New Zealand population.

10.40. Overall, based on the evidence reviewed and patient lived experiences submitted, the Committee considered there would be a significant positive impact on the health-related quality of life for children with XLH receiving burosumab, including a reduction in the significant pain and skeletal deformities, and the need for extensive orthopaedic surgeries.

10.41. The Committee further considered burosumab treatment would improve functional outcomes and participation in daily activities, including school attendance, self-care, and physical activity.

10.42. The Committee considered that burosumab treatment was well tolerated, and the main side effects were localised hypersensitivity reactions that were not severe in nature.

*Suitability*

10.43. The Committee considered burosumab would offer significant suitability advantages and benefits compared to the current standard of care treatments. The current treatments require frequent administration, including during the night, which can disrupt sleep for both the child and their caregiver.

10.44. The Committee additionally considered the current treatments were challenging to administer and had poorer adherence due to the very poor taste profile.

10.45. The Committee considered that burosumab treatment would reduce the healthcare appointment related burden for individuals and their whānau, with a reduction in the frequency of biochemical testing and ultrasound scans, as well as a reduction in the need for painful orthopaedic surgery.

10.46. The Committee were made aware of the clinical challenges of conventional treatment, including dosing calculations and reconstitution of the medicines. The Committee were made aware that errors in dosing can result in lifelong disabilities and the need for renal transplantation.

10.47. The Committee considered the subcutaneous injection may be a challenge to some individuals with needle phobia.

*Cost and savings*

10.48. The Committee considered the patient number estimates to be reasonable.

10.49. The Committee considered there was approximately 20 children in New Zealand who would benefit from burosumab treatment. The Committee were made aware that there would not be more than 30 children who would receive burosumab treatment.

10.50. The Committee were made aware that older children (over three years of age) have extensive skeletal deformities, whilst these have not yet developed in younger children. The Committee were made aware that the remodelling of the bones takes a long period of time, and some may not recover. The Committee considered there would be up to a 90% reduction in the need for orthopaedic surgery if individuals commence burosumab treatment at an early age, and consequent health sector related costs for the surgery, hospital stays and recovery.

10.51. The Committee considered it would be appropriate for children to be treated as soon as they were diagnosed, with the aim of treating children from the age of 12 months if possible.

10.52. The Committee considered that as first teeth are formed prior to initiation of burosumab treatment there would be need for ongoing dental care, however this would be reduced compared to conventional therapy.

10.53. The Committee considered children routinely develop renal impairment and require extended renal dialysis or treatment due to conventional treatment. The Committee considered burosumab treatment would reduce the renal consequences and the renal ultrasound scans required to monitor for nephrocalcinosis, which currently occur once yearly on average.

10.54. The Committee considered individuals would currently receive three monthly phosphate, calcium creatine, alkaline phosphatase, parathyroid hormone, urinary calcium and creatinine testing, however this may occur more frequently in some individuals.

10.55. The Committee considered there would be an initial increase in biochemical monitoring as a child initiates burosumab treatment to reach a stable dose, before reducing monitoring to three to six monthly.

10.56. The Committee considered uptake of burosumab would be very high for individuals who regularly access specialised services.

10.57. The Committee considered overall there was evidence that the health benefit was long lasting and did not wane after five years on treatment.

10.58. The Committee were made aware of anecdotal evidence that conventional therapy in addition to burosumab treatment has not been necessary in the Australian healthcare setting.

10.59. The Committee considered it was appropriate to assume an average burosumab dose of 0.8mg/kg in children.

10.60. The Committee considered it was reasonable to assume growth plate closure of 14 years for girls and 15 years for boys.

10.61. The Committee considered that the health state occupancy, and the magnitude of the treatment benefit assumptions were reasonable given the available evidence.

*Funding criteria*

10.62. The Committee considered most children were not diagnosed until at least six months of age, due to the high levels of circulating phosphate during this time period. The Committee considered individuals should initiate treatment upon diagnosis.

10.63. In the context that adults are funded for burosumab treatment, the Committee considered that children who initiate treatment prior to growth plate fusion should remain on burosumab treatment as adults if they experience a clinical benefit. This differs from the consideration of adults who would initiate burosumab treatment as a second line therapy.

*Summary for assessment*

10.64. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for burosumab if it were to be funded in New Zealand for XLH. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Committee's assessment at this time and may differ from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

| | |
|---|---|
| Population | Patient has been diagnosed with X-linked hypophosphataemia, and patient's growth plates have not fused. |
| Intervention | 0.8 mg/kg body weight as a subcutaneous injection every 2 weeks<br>Treatment is expected to continue until skeletal maturity, with periodic reassessment of clinical response and biochemical parameters. |
| Comparator(s) | Oral phosphate and active vitamin D (such as calcitriol). |
| Outcome(s) | Reduced rickets and osteomalacia, dental abscess formation and improvements in growth in children. |
| Table definitions: Population, the target population for the pharmaceutical; Intervention, details of the intervention pharmaceutical; Comparator, details the therapy(s) that the patient population would receive currently (status quo – including best supportive care); Outcomes, details the key therapeutic outcome(s) and source of outcome data. | |

## 11. Burosumab for X-linked hypophosphatemia (XLH) for adults

11.1. Assoc Prof Craig Jefferies, Professor Ben Wheeler and Dr Marianne Elston attended the discussion as Observer – Invited Experts. Assoc Prof Jefferies, Professor Wheeler and Dr Elston left the meeting before the recommendation was made.

### Application

11.2. The Committee reviewed a consumer application for burosumab in the treatment of X-linked hypophosphatemia (XLH) for adults.

11.3. The consumer application was received in 2022 and progressed following the supplier application being received in 2026 for burosumab in the treatment of children with XLH, indicating it is willing to supply burosumab to the New Zealand market. Pharmac staff considered the application met Pharmac's Policy principles for rare disorders.

11.4. The Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

### Recommendation

11.5. The Committee **recommended** that burosumab for treatment of X-linked hypophosphatemia for adults be listed with a **medium priority** within the context of treatments for rare disorders subject to the following Special Authority criteria:

> **Initial application –** X-linked hypophosphataemia (XLH) from any relevant practitioner. Approvals valid for 12 months for applications meeting the following criteria:
> 1. Either of the following:
>  1.1. Patient has documented confirmation of PHEX pathogenic variant, or
>  1.2. Patient must have a diagnosis of X-linked hypophosphataemia, and
> 2. Any of the following:
>  2.1. Patient has had insufficient response or refractory to conventional therapy (defined as active vitamin D and oral phosphate supplementation), defined as either:
>  2.1.1. presence of either radiographic evidence of osteomalacia, nonhealing complete fractures, or nonhealing incomplete fractures after 1 year of therapy
>  2.1.2. the development of hyperparathyroidism or nephrocalcinosis; or

2.1.3. Patient has experienced intolerable side effects from treatment with active vitamin D an oral phosphate supplementation;

**Renewal application –** X-linked hypophosphataemia (XLH) only from a relevant specialist or any other practitioner on the recommendation of a relevant specialist. Approvals valid for 12 months for applications meeting the following criteria:

1. Patient has experienced a clinical benefit

11.6. In making this recommendation the Committee considered:

- The high health need of adults with XLH that is not met by current conventional treatment
- The high-quality trial data that supports a clinically meaningful benefit from burosumab treatment
- Burosumab treatment is well tolerated
- Many of the skeletal complications of XLH occur during childhood which would not be ameliorated by burosumab treatment in adults

## Discussion

*Patient lived experience*

11.7. The Committee received submissions from Australian and New Zealand Society of Paediatric Endocrinology and Diabetes Bone and Mineral Working Group (ANZSPED BMWG) in support of the application.

11.8. The Committee received a large number of patient lived experience submissions providing the experience of the adults with XLH.

11.8.1. Individuals shared the significant impacts of living with XLH on their lives including the need to seek expensive dental care that is not subsidised which has resulted in a significant financial burden on the individual and their whānau.

11.8.2. Individuals described the high level of pain experienced from the skeletal impacts of the disease, and the need for daily high-strength pain medication to manage this. The medication and pain burden has resulted in individuals being unable to work or participate in family life. The ongoing physical impacts have also affected the individual's mobility.

11.8.3. Some individuals also shared their experience of being both a patient with XLH and a parent to a child with XLH. The individuals noted the high burden of attending a large volume of clinic appointments, the immense emotional toll on medical surgeries and the knowledge of the pain of the disease from a personal experience. Where individuals or their whānau had moved internationally to seek treatment, they note that adults, who did not receive burosumab treatment as children, who have received burosumab now experience no pain, which has been transformative to their lives. They hope that one day they may be able to return back to New Zealand to receive funded burosumab treatment.

11.8.4. In addition to the physical effects of the condition individuals also noted the significant impact on their mental health and quality of life.

11.9. The Committee expressed its thanks to the individuals and patient group for their submissions and recognised how challenging it is to share their personal experiences.

*Māori impact*

11.10. The Committee discussed the impact of funding burosumab for the treatment of XLH on Māori health areas of focus | Hauora Arotahi and Māori health outcomes. The Committee considered that while there is a lack of evidence to support an ethnic disparity in the prevalence of XLH, the Committee considered that Māori would be disproportionately impacted by barriers to diagnosis and subsequently accessing endocrinology clinics for specialist treatments.

*Populations with high health needs*

11.11. The Committee discussed the health need(s) of XLH among Māori, Pacific peoples, disabled peoples including tāngata whaikaha Māori, and other populations identified by the Government Policy Statement on Health 2024-2027 to have high health needs. The Committee discussed the impact of funding burosumab and considered:

11.11.1. Pacific peoples would be disproportionately impacted by barriers to diagnosis and subsequently accessing endocrinology clinics for specialist treatments.

*Background*

11.12. The Committee noted that burosumab for the treatment of children with XLH where their growth plates have not fused was also discussed at the meeting.

*Health need*

11.13. The Committee noted it has discussed the genetic basis of XLH when considering burosumab for the treatment of children with XLH. The Committee considered that while the presentation of the disease varied between children and adults, the genetic basis and prevalence did not.

11.14. The Committee considered presentation in adults differs, with adults presenting with pseudo fractures due to osteomalacia as well as osteoarthritis, enthesopathies, spinal stenosis, hearing loss, depression and reduced quality of life. The pathogenesis of osteoarthritis and enthesopathies and to what extent these are sequelae of certain primary manifestations of XLH is poorly understood.

11.15. The Committee noted that adults may also require surgical correction for the limb deformities incurred during childhood, and experience hypomineralisation of teeth which are prone to tooth abscesses and periodontitis (Haffner et al. Nat Rev Nephrol. 2019;15:435–55). A review of adults entering the XLH International Registry reported 71.8% reported skeletal symptoms/manifestations, and high numbers reported problems with dentition including 75.9% with abscesses Haffner et al. 2019).

11.16. The Committee noted a study that reported the quality of life in adults living with XLH is altered and significantly worse than that of axial spondylarthritis, which is associated with a low quality of life. It also reported that structural lesions and especially enthesopathies are associated with a lower quality of life (Che et al. Eur J Endocrinol. 2016;174:325-33).

11.17. The Committee considered XLH is commonly treated with frequent doses of oral phosphate supplements and active vitamin D, referred to as ‘conventional treatment.’

11.18. The Committee considered treatment goals in adults are to normalise alkaline phosphatase levels, heal fractures, improve bone pain and enhance physical function.

11.19. The Committee considered there was moderate to weak evidence to support conventional therapy, which does not address the underlying pathogenesis of XLH.

11.20. The Committee considered that, similarly to children, conventional treatment is associated with adverse effects, including hyperparathyroidism (that can require

surgery) and nephrocalcinosis. It was also noted that conventional treatment is poorly tolerated owing to gastrointestinal adverse effects and the need for frequent dosing (Haffner et al. 2019). The Committee were made aware that many discontinue treatment, as the treatment is intolerable due to the side effects and complications.

11.21. The Committee considered that biochemical deterioration can be associated with symptom flare, and that serum phosphate levels do not always correlate with symptoms. The Committee considered many symptom flares result from chronic skeletal complications including skeletal impacts that arose in childhood.

11.22. The Committee were made aware that there was a lack of wrap around care to support children transitioning to adult endocrinology services. The Committee was made aware that commonly only those with the most severe forms of XLH and with skeletal deformities may continue to be reviewed by adult endocrinology services due to the burden of the conventional treatment, and lack of efficacy to resolve symptoms that occurred in childhood.

11.23. The Committee were made aware that there was a range of XLH severity that was observed in adults, with some less severe phenotypes experiencing little impact on daily life, whereas others experienced severe mobility disabilities and could not work.

11.24. The Committee considered that many adults with XLH are also caregivers for their parents, family members or children with XLH.

11.25. The Committee noted a study that reported caregivers of people with XLH reported better quality of life than non-caregivers in all EQ-5D dimensions except for anxiety/depression (EQ-5D score of 0.467 vs 0.356 for non-caregivers). The study reported that this might be due to the person with better quality of life taking on a caregiver role in families where there is more than one person with XLH, (Pinedo-Villaneuva et al. JBMR Plus. 2025;9:ziaf078).

11.26. The Committee noted a UK study that caregivers of adults with XLH (n = 13) reported their private life, leisure, and psychological well-being were affected but not the feeling of being burdened or their self-esteem by providing care.

*Health benefit*

11.27. The Committee noted NCT02526160, a randomised, double-blind, placebo-controlled, phase III trial, in 124 adults with XLH that reported the following trial results:

11.27.1. The Committee noted Insogna et al. J Bone Miner Res. 2018;33:1383-93 that reported trial results at 24 weeks

- 94.1% of participants treated with burosumab attained significant mean serum phosphate levels above the lower limit of normal vs 7.6% compared to placebo ($p < 0.001$).
- Burosumab significantly reduced the Western Ontario and the McMaster Universities Osteoarthritis Index (WOMAC) stiffness subscale vs placebo (least squares [LS] mean ± standard error [SE] difference, -8.1 ± 3.24; p = 0.0expl12).
- At week 24, 43.1% (burosumab) and 7.7% (placebo) of baseline active fractures were fully healed; the odds of healed fracture in the burosumab group was 16.8-fold greater than that in the placebo group ($p < 0.001$).

11.27.2. The Committee noted Portale et al. Calcif Tissue Int. 2019;105:271-84 that reported the following results of the open label extension to the study at 48 weeks:

- Serum phosphorus concentrations remained normal in 83.8% with those receiving burosumab throughout the trial and were normalized in 89.4% who received burosumab after placebo.
- At week 48, 63.1% of baseline fractures/pseudo fractures were fully healed with burosumab vs 35.2% with those receiving burosumab after placebo.
- In both groups, burosumab was associated with clinically significant and sustained improvement from baseline to week 48 in scores for patient-reported outcomes of stiffness, pain, physical function, and total distance walked in 6 min.

11.27.3. The Committee noted 96-week results from the open label extension were reported in Briot et al. RMD Open. 2021;7:e001714.

11.27.4. The Committee noted the majority of trial participants were women and had a mean age of 40 years of age.

11.27.5. The Committee considered that most had initiated conventional therapy prior to the age of 18 and were receiving pain medication at baseline. In addition, the majority had received prior surgery. Therefore, the Committee considered the trial population were a severely affected group that influenced trial outcomes.

11.27.6. The trial evidence was of high quality and generalisable to the New Zealand population.

11.28. The Committee noted real world evidence was reported in Bubbear et al. Calcif Tissue Int. 2025 Sep 18;116(1):122 and Kumar et al. JBMR Plus, Volume 9, Issue Supplement_5, 2025, Pages v39–v46.

11.29. The Committee noted the following publications:

- Schindeler et al. Front Endocrinol (Lausanne). 2020:11:338
- Bouzemane et al. J Clin Endocrinol Metab. 2024;109:e488-e94.
- Florenzano et al. J Bone Miner Res. 2025;40:973-86
- Fratzl-Zelman et al. J Bone Miner Res. 2022;37:1665-78
- Insogna et al. J Bone Miner Res. 2019;34:2183-91
- Fukishima et al. Cureus. 2025;17:e90480
- Day et al. Bone Rep. 2024:23:101814
- Bandir et al. Front Endocrinol (Lausanne). 2025:16:1665649.
- Brandi et al. Calcif Tissue Int. 2022;111:409-18
- Dodamani et al. Arch Endocrinol Metab. 2024:68:e230242
- Kiafzezi et al. Calcif Tissue Int. 2024;115:229-41
- Ali et al. J Clin Endocrinol Metab. 2025;110:1767-80

11.30. The Committee considered overall burosumab treatment was well tolerated.

11.31. The Committee considered overall burosumab provided a clinically meaningful health benefit for adults with XLH, as well as an increase in health-related quality of life related to physical and mental well-being.

11.32. The Committee considered the health benefit results from the clinical trial data were maintained over time to at least 18 months (open label extension and real-world evidence), with additional registry data from 2017 being collected.

*Suitability*

11.33. The Committee considered current conventional treatment was a burden on patients, due to tolerability and suitability factors such as pill frequency burden and poor taste profile.

11.34. The Committee considered some individuals with mild symptoms may not wish to initiate treatment with a subcutaneous injection.

*Cost and savings*

11.35. The Committee considered it was reasonable to use the body weight from the clinical trials for dosing calculations.

11.36. The Committee considered it was reasonable to assume an average dose of 1 mg/kg burosumab.

11.37. The Committee considered if children with XLH were treated with burosumab from diagnosis, the severe unmet health need of adults with XLH would be reduced, as burosumab treatment prevents many of the skeletal and tooth deformities which affects the quality of life of adults.

11.38. The Committee considered individuals would not receive concomitant conventional therapy with burosumab treatment.

11.39. The Committee considered the patient number estimates realistic and likely uptake estimates to be reasonable.

11.40. The Committee considered it was reasonable to assume a reduction in associated morbidities (for example fractures) of approximately 80-100% and improved health related quality of life (HRQoL) based on mapping of WOMAC scores. The Committee considered there was no direct evidence to assume a reduction in mortality.

*Funding criteria*

11.41. The Committee considered that individuals who initiated first line burosumab treatment as children (prior to growth plate fusion) should continue to receive burosumab treatment as adults according to the intent of the Special Authority criteria for children.

11.42. The Committee considered individuals who did not receive burosumab treatment as children (prior to growth plate fusion) should trial conventional therapy as first line treatment.

*Summary for assessment*

11.43. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for burosumab if it were to be funded in New Zealand for adults with XLH. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Committee's assessment at this time and may differ from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

| | |
|---|---|
| Population | Patient has been diagnosed with X-linked hypophosphataemia and has not received sufficient benefit from conventional treatment with oral phosphate supplements and active vitamin D. |
| Intervention | Burosumab, administered via subcutaneous injection every four weeks.<br>Starting dose of 1.0 mg/kg (rounded to the nearest 10 mg) with dose reduction or escalation as required, up to a maximum of 90 mg. |

| | |
|---|---|
| | Treatment duration is ongoing provided treatment is well-tolerated and the individual is experiencing a treatment benefit. |
| Comparator(s) | Continued use of conventional therapy (oral phosphate and active vitamin), despite insufficient response, or no conventional therapy. |
| Outcome(s) | Normalisation of serum phosphate levels (94.1% vs. 7.6% in those receiving placebo) ($p < 0.001$) (Insogna et al. J Bone Miner Res. 2018;33:1383-93).<br>Improved health-related quality of life through improvements in clinical outcomes:<br>• Significantly improved McMaster Universities Osteoarthritis Index (WOMAC), Brief Pain inventory-Short Form (BPI-SF) and Brief Fatigue Inventory (BFI) and 6 min walk test (6MWT) scores vs. placebo (Briot et al. RMD Open. 2021;7:e001714).<br>• Increased fracture healing vs. placebo (at week 24, 43.1% vs. 7.7% of baseline active fractures were fully healed) (Insogna et al. 2018).<br>• Significant increase in biochemical markers of bone formation and resorption compared with placebo (Insogna et al. 2018).<br><br>Potential reductions in morbidities (e.g. fractures, dental abscesses). |
| Table definitions: Population, the target population for the pharmaceutical; Intervention, details of the intervention pharmaceutical; Comparator, details the therapy(s) that the patient population would receive currently (status quo – including best supportive care); Outcomes, details the key therapeutic outcome(s) and source of outcome data. | |

## 12. Pegvisomant as an adjunct treatment for acromegaly, following surgery and medical therapy

12.1. Dr Marianne Elston Endocrinologist, Health New Zealand attended the discussion as an Observer – Invited Expert. Dr Elston left the meeting before the recommendation was made.

### Application

12.2. The Committee reviewed the application for pegvisomant as an adjunct treatment for acromegaly, following surgery and medical therapy

12.3. The Committee noted that two clinician applications for pegvisomant for the treatment of acromegaly were received in March 2024 and April 2026 (in response to Pharmac's 2025 rare disorders call for applications), and that supporting documentation was subsequently provided by the supplier in May 2026. Pharmac staff considered they met Pharmac's Policy principles for rare disorders.

12.4. The Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

### Recommendation

12.5. The Committee **recommended** that pegvisomant as an adjunct treatment for acromegaly, following surgery and medical therapy be listed with a **medium priority** within the context for treatments for rare disorders, subject to the following Special Authority criteria:

> **Initial application** – (acromegaly) from any relevant practitioner. Approvals valid for 12 months for applications meeting the following criteria:
>
> All of the following:
> 1. Patient has acromegaly; and
> 2. Patient has elevated IGF-1 levels above the age-adjusted upper limit of normal; and
> 3. Patient has had an inadequate biochemical response, intolerance, or contraindication to maximal tolerated doses of somatostatin analogue therapy such as octreotide, with or without cabergoline.

**Renewal** – (acromegaly) from any relevant practitioner. Approvals valid without further renewal for applications meeting the following criteria:
Both of the following:

1. Patient has had a reduction in IGF-1 levels from baseline or normalisation of IGF-1; and
2. Treatment with pegvisomant is considered to be clinically appropriate and continued benefit is demonstrated.

12.6. In making these recommendations, the Committee noted the following:

12.6.1. Acromegaly is associated with a significant reduction in life expectancy and substantial morbidity, including cardiovascular disease, diabetes, sleep apnoea, musculoskeletal complications, and psychological distress.

12.6.2. The Committee noted that there is an unmet health need for people whose disease remains uncontrolled despite currently funded treatment options, and that pegvisomant offers a clinically meaningful treatment option that can improve biochemical control and reduce the burden of disease.

## Discussion

*Patient lived experience*

12.7. The Committee noted that patient lived experience information had been sought with support from Rare Disorders New Zealand; however, no submissions were received prior to the meeting.

*Māori impact*

12.8. The Committee discussed the impact of funding pegvisomant for the treatment of acromegaly on Māori health areas of focus | Hauora Arotahi and Māori health outcomes. The Committee noted that no New Zealand-specific data were available regarding the incidence, burden or outcomes of acromegaly in Māori. However, given that acromegaly is associated with cardiovascular disease, diabetes, sleep apnoea, osteoarticular complications, and malignancy risk, and that Māori and Pacific peoples experience established inequities in many of these conditions, delayed diagnosis and acromegaly-related morbidity may disproportionately affect these populations.

*Populations with high health needs*

12.9. The Committee noted that acromegaly is a rare condition and that evidence describing disease burden, treatment outcomes, and potential inequities in health outcomes among Māori, Pacific peoples, disabled people including tāngata whaikaha Māori, and other populations identified in the Government Policy Statement on Health 2024–2027 is limited.

*Background*

12.10. The Committee noted that funded treatment options for acromegaly currently include octreotide (funded in 2010 and 2012), long-acting octreotide (funded in 2021), and lanreotide (funded in 2025).

12.11. The Committee noted that surgery remains the preferred first-line treatment for acromegaly where feasible; however, the Committee further noted that surgical cure is not possible for all people, particularly for those with unresectable or invasive tumours.

12.11.1. The Committee noted that current treatment options for persistent disease include somatostatin analogues, cabergoline, and radiotherapy, but that a proportion of people remain biochemically and clinically uncontrolled despite these treatments.

12.11.2. The Committee further noted that radiotherapy is generally reserved as a later treatment option due to its delayed onset of action and risk of long-term adverse effects, including hypopituitarism.

12.11.3. The Committee considered that there is an unmet health need for people with persistent acromegaly whose disease is inadequately controlled despite currently funded treatment options.

*Health need*

12.12. The Committee noted that acromegaly is a rare, chronic endocrine disorder caused by excess growth hormone and insulin-like growth factor 1 (IGF-1), most commonly due to a pituitary somatotroph adenoma (Katznelson, et al. J Clin Endocrinol Metab. 2014;99(11):3933-51).

12.12.1. The Committee noted that acromegaly is associated with substantial morbidity and excess mortality (Bolfi, et al. Eur J Endocrinol. 2018;179(1):59-71), including cardiovascular, metabolic, respiratory, musculoskeletal, and neoplastic complications (Melmed, et al. Nat Rev Endocrinol. 2025;21(11):718-37);(Giustina, et al. J Clin Endocrinol Metab. 2020;105(4):dgz096).

12.12.2. The Committee further noted that common manifestations include progressive changes in appearance, enlargement of the hands and feet, sweating, headache, visual disturbance, obstructive sleep apnoea, carpal tunnel syndrome, and joint pain, and that delays in diagnosis can result in irreversible complications, impaired quality of life and premature mortality.

12.12.3. The Committee noted that uncontrolled acromegaly can cause substantial changes in physical appearance which may contribute to psychological distress, and that effective treatment may provide important psychosocial benefits in addition to improving biochemical and clinical control.

12.13. The Committee further noted the impact of the condition on family, whānau and caregivers, particularly in the context of delayed diagnosis, long-term complications, and the ongoing burden of treatment and disease management.

12.14. The Committee considered that there remains an unmet health need for some people with acromegaly, noting that not all patients are suitable candidates for surgery and that a proportion of patients experience persistent or recurrent disease despite treatment with currently funded medicines.

12.15. The Committee noted that acromegaly is a rare disorder, with an estimated incidence of 4–6 new cases per million people annually (The New Zealand Acromegaly Society; Information Booklet Series, 2018). The Committee considered expert estimates that approximately 500 people may be living with acromegaly in New Zealand, around one quarter of whom require medical treatment. The Committee further noted that approximately 60 people remain inadequately controlled following surgery, and that only a small proportion of these individuals remain uncontrolled despite treatment with somatostatin analogues and/or cabergoline.

*Health benefit*

12.16. The Committee noted that pegvisomant is a growth hormone receptor antagonist that reduces circulating IGF-1 levels and is administered as an initial subcutaneous loading dose followed by daily subcutaneous injections, with dose titration according to treatment response.

12.17. The Committee noted evidence from the ACROSTUDY registry, a large multinational real-world study involving 2,221 people with acromegaly treated with pegvisomant for a median of 9.3 years (Fleseriu, et al. Eur J Endocrinol. 2021;185(4):525-38).

12.17.1. The Committee noted sustained improvements in biochemical disease control over time. The Committee noted that IGF-1 normalisation increased from approximately 11% at treatment initiation to 54% at one year and over 60% from five years onwards, with approximately 62% of participants achieving normalised IGF-1 levels at their last assessment.

12.17.2. The Committee further noted pegvisomant was generally well tolerated, with treatment-related discontinuations occurring infrequently (1.3%), clinically significant liver enzyme elevations reported in approximately 3% of participants, and no reported cases of liver failure.

12.17.3. The Committee noted that the ACROSTUDY evidence was generally applicable to the proposed New Zealand population in terms of age and treatment setting. However, the Committee noted that the study population was predominantly Caucasian/European (approximately 92%), which may limit the generalisability of the findings to Māori, Pacific peoples and other ethnic groups in New Zealand.

12.17.4. The Committee considered the evidence to be of moderate to high quality, noting supportive long-term real-world data from ACROSTUDY, but also noted uncertainty regarding generalisability to the New Zealand population.

12.18. The Committee noted the results of a landmark randomised, double-blind, placebo-controlled trial (Trainer, et al. N Eng J Med. 2000;342:1171-77), which evaluated pegvisomant 10 mg, 15 mg or 20 mg daily compared with placebo in 112 adults with active acromegaly over 12 weeks. The Committee noted most participants had previously received surgery, radiotherapy and/or medical therapy.

12.18.1. The Committee noted that pegvisomant was associated with statistically significant, dose-dependent reductions in serum IGF-1 from baseline compared with placebo. The Committee noted mean IGF-1 reductions were 26.7% with pegvisomant 10 mg, 50.1% with pegvisomant 15 mg, and 62.5% with pegvisomant 20 mg, compared with 4.0% with placebo ($P<0.001$ for each pegvisomant group vs placebo).

12.18.2. The Committee noted that IGF-1 normalisation was achieved in 54% of participants receiving pegvisomant 10 mg, 81% receiving pegvisomant 15 mg and 90% receiving pegvisomant 20 mg, compared with 10% of participants receiving placebo.

12.18.3. The Committee noted that biochemical improvements were accompanied by improvements in clinical manifestations of acromegaly, including reductions in soft-tissue swelling, excessive perspiration, fatigue, and overall symptom burden.

12.18.4. The Committee noted that pegvisomant was generally well tolerated over the 12-week treatment period, with a smaller incidence of adverse events across pegvisomant and placebo groups. Common adverse events included mild injection-site reactions. The Committee noted that no clinically meaningful change in pituitary tumour volume was observed over the 12-week study period, although the short duration of follow-up limited assessment of longer-term tumour progression.

12.19. The Committee noted a recent narrative review of 45 studies (Brue, et al. Rev Endocr Metab Disord. 2026;27(1):109-122), which found that pegvisomant consistently achieved high rates of IGF-1 normalisation across both clinical trials and real-world practice, with evidence suggesting improvements in quality of life and several acromegaly-related comorbidities. The Committee further noted that reported IGF-1

normalisation rates were typically 60–80% in real-world studies and up to 89% in clinical trials.

12.20. The Committee also noted the following studies:

- Buchfelder, et al. Eur J of Endocrinol. 2018;179(6):419-27
- Leonart, et al. Endocrine. 2019;63:18-26
- Ma, et al. BMC Endocrine Dis. 2020;20(1):126
- Kaparounaki, et al. Eur J Endocrinol. 2025;193(5):S83-S94
- Pirchio, et al. J Endocrinol Invest. 2023;46(5):1027-38
- Quock, et al. J Comp Eff Res. 2025;14(9):e250080
- Feola, et al. J Clin Endocrinol Metab. 2019;104(7):2892-2902

12.21. The Committee considered that improved biochemical control of acromegaly is expected to improve symptoms such as soft tissue swelling and obstructive sleep apnoea and that similar benefits would be anticipated with pegvisomant in patients with uncontrolled disease despite funded treatments. The Committee further noted that some established complications, particularly osteoarthritis, may be irreversible, highlighting the importance of early diagnosis and effective disease control.

*Suitability*

12.22. The Committee noted that pegvisomant is administered daily as a subcutaneous injection and requires reconstitution, refrigeration, and administration within six hours of preparation.

12.22.1. The Committee considered that these requirements, together with the need for patient training, regular IGF-1 monitoring, and liver function monitoring, may increase treatment burden for some patients.

12.22.2. The Committee noted expert advice that pegvisomant would require patient education and training for self-administration by subcutaneous injection, although this is increasingly common with biologic therapies.

*Cost and savings*

12.23. The Committee considered that better disease control may reduce healthcare utilisation, including general practice and hospital visits, resulting in benefits for the wider health system.

12.24. The Committee considered that uptake and adherence to pegvisomant are likely to be high, noting real-world evidence demonstrating sustained reductions in IGF-1 levels over time (Fleseriu, et al. Eur J Endocrinol. 2021;185(4):525-38). The Committee considered that the significant morbidity associated with uncontrolled acromegaly is likely to support treatment adherence.

12.25. The Committee considered that achieving biochemical control of acromegaly is likely to reduce healthcare resource utilisation through improvements in comorbidities, including reduced requirements for sleep clinic appointments, sleep studies, and continuous positive airway pressure (CPAP) machine use where sleep apnoea resolves following treatment.

12.26. The Committee considered that improved biochemical control may reduce the risk and long-term consequences of diabetes and cardiovascular disease, which are important contributors to healthcare utilisation in people with acromegaly.

12.27. The Committee was made aware that the eligible population for pegvisomant would be approximately 5% of total acromegaly population.

12.28. The Committee considered that where ongoing tumour shrinkage or tumour control was required, pegvisomant may be added to existing treatment, whereas pegvisomant may be used as monotherapy if clinically appropriate.

12.29. The Committee considered that the health benefits observed with pegvisomant in the ACROSTUDY are likely to reflect the comparative health benefits of the pegvisomant relative to the available alternatives.

*Funding criteria*

12.30. The Committee was made aware that a small proportion of patients remain inadequately controlled despite surgery and currently funded medical therapies. Members considered that, of approximately 500 people with acromegaly in New Zealand, fewer than one-quarter would be expected to require pegvisomant, with the eligible population likely representing a relatively small number of patients with persistent disease despite existing treatment options.

12.31. The Committee considered that surgery would remain the first-line treatment. The Committee considered that pegvisomant would likely be used as an adjunct treatment for patients whose disease remains inadequately controlled despite surgery and treatment with somatostatin analogues. The Committee further noted that, unlike somatostatin analogues, pegvisomant does not directly reduce tumour size or inhibit tumour growth.

12.32. The Committee was made aware that first-line use of pegvisomant in place of octreotide or cabergoline would be uncommon but may be appropriate in rare circumstances, such as when a person is intolerant to treatment, has a small residual tumour not cured by surgery, or has a psychiatric condition that precludes the use of cabergoline.

12.33. The Committee was made aware that patients receiving octreotide who experience no clinical benefit would typically discontinue treatment and move to an alternative therapy where available. However, given the limited treatment options currently available in New Zealand, treatment may be continued where there is evidence of partial benefit.

12.34. The Committee considered that pegvisomant would most commonly be used as combination therapy alongside existing treatment, with relatively few patients expected to receive pegvisomant monotherapy unless treatment-limited adverse effects occurred with other therapies.

12.35. The Committee considered that concomitant use of pegvisomant, octreotide, and cabergoline would be uncommon. Treatment combinations would be determined on a case-by-case basis, taking into account treatment response, adverse effects, and tumour characteristics.

12.36. The Committee was made aware that introduction of pegvisomant may allow reduction or discontinuation of other therapies in some patients, particularly where adverse effects are experienced, and biochemical control has been achieved. However, octreotide may be continued where tumour control is required.

*Summary for assessment*

12.37. The Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for pegvisomant if it were to be funded in New Zealand for treatment for acromegaly, following surgery and medical therapy. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Committee's assessment at this time and may differ

from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

| | |
|---|---|
| **P**opulation | Adults with acromegaly with persistent biochemical disease (defined as elevated age-adjusted IGF-1) following surgery (if appropriate), whose disease remains inadequately controlled despite optimised medical therapy with a somatostatin analogue (SSA) therapy and/or cabergoline, or who have intolerance/ contraindications to one or both of these agents. |
| **I**ntervention | Pegvisomant 10-30mg once daily (dose titrated to IGF-1 levels) administered as a subcutaneous injection, either:<br>• as monotherapy<br>• in combination with SSA and/or cabergoline<br>Treatment with pegvisomant to be discontinued if:<br>• the person has not experienced a clinically meaningful reduction in IGF-1 after an adequate titration period (~6 months)<br>• liver function tests show transaminase levels exceeding five times the upper limit of normal, or<br>• if there is disease progression |
| **C**omparator(s)<br>(NZ context) | Standard of care including:<br>• continued SSA therapy (octreotide) with or without cabergoline<br>• radiotherapy<br>• no medical treatment |
| **O**utcome(s) | Biochemical disease control status (controlled vs uncontrolled), defined by normalisation of IGF-1 levels, and its associated impacts on:<br>• cardiovascular and metabolic morbidity<br>• sleep apnoea and other complications<br>• health-related quality of life benefit<br>• mortality |

*Table definitions:*

**P**opulation: The target population for the pharmaceutical, including any population defining characteristics (eg line of therapy, disease subgroup)

**I**ntervention: Details of the intervention pharmaceutical (dose, frequency, treatment duration/conditions for treatment cessation).

**C**omparator: Details the therapy(s) that the patient population would receive currently (status quo – including best supportive care; dose, frequency, treatment duration/conditions for treatment cessation).

**O**utcomes: Details the key therapeutic outcome(s), including therapeutic intent, outcome definitions, timeframes to achieve outcome(s), and source of outcome data.