PHARMAC
TE PĀTAKA WHAIORANGA

Pharmacology and Therapeutics
Advisory Committee
Objective advice to Pharmac

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Record of the Pharmacology and Therapeutics Advisory Committee Meeting

Held on 13 November & 14 November 2025

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1. Attendance:

PTAC members:
Rhiannon Braund (Chair)
Brian Anderson
Elizabeth Dennett
Helen Evans
James Le Fevre
John Mottershead
Liza Lack
Matthew Dawes
Matthew Strother
Robyn Manuel
Stephen Munn

Apologies:
Bruce King

2. The role of PTAC, Specialist Advisory Committees and meeting records

2.1. This meeting record of PTAC is published in accordance with the Pharmacology and Therapeutics Advisory Committee (PTAC) Terms of Reference 2021, and Specialist Advisory Committees Terms of Reference 2021.

2.2. The PTAC Terms of Reference describe, *inter alia*, the establishment, activities, considerations, advice, and the publication of such advice of PTAC and Specialist Advisory Committees.

2.3. Conflicts of Interest are described and managed in accordance with sections 6.4 of both the PTAC Terms of Reference and Specialist Advisory Committee Terms of Reference.

2.4. PTAC and Specialist Advisory Committees have complementary roles, expertise, experience, and perspectives. PTAC may therefore, at times, make recommendations that differ from Specialist Advisory Committees', including the priority assigned to recommendations, when considering the same evidence. Likewise, Specialist Advisory Committees may, at times, make recommendations that differ from PTAC's, or from other Specialist Advisory Committees', when considering the same evidence.

Pharmac considers the recommendations provided by both PTAC and Specialist Advisory Committees when assessing applications.

3. Summary of Recommendations

	Pharmaceutical and Indication	Recommendation
8.3	Nivolumab (in combination with cisplatin and gemcitabine) for the first line treatment of unresectable or metastatic urothelial carcinoma	Declined
9.3	Semaglutide for treatment of insufficiently controlled type 2 diabetes, subject to Special Authority criteria	High Priority
10.3	Anifrolumab for severe Systemic Lupus Erythematosus (SLE), subject to Special Authority criteria identifying a wider population	High Priority

10.5	Anifrolumab for severe Systemic Lupus Erythematosus (SLE), subject to Special Authority criteria identifying a narrower population	Low Priority
11.3	Bevacizumab for severe hereditary haemorrhagic telangiectasia, subject to Special Authority criteria	High Priority
12.3	Pembrolizumab subcutaneous formulation for all currently funded indications of intravenous pembrolizumab, subject to Special Authority criteria	Cost Neutral
13.3	Vedolizumab subcutaneous formulation for the maintenance treatment of ulcerative colitis and Crohn's disease, subject to Special Authority criteria	Cost Neutral
14.3	Biosimilar – tocilizumab	Cost savings
15.3	Tezepelumab for chronic rhinosinusitis with nasal polyps, subject to Special Authority criteria	High Priority

4. Record of PTAC meeting held 15 August 2025

The Committee reviewed the record of the PTAC meeting held on 15 August 2025.

The Committee accepted the record.

5. Action Points

There are no current action points.

6. Pharmac Update

6.1. The Committee noted the Pharmac Update.

6.2. The Committee acknowledged the introduction of new Pharmac staff and ongoing leadership changes, including the new Chief Executive who started at Pharmac in mid-September.

6.3. The Committee noted an update about the organisation reset programme and acknowledged that more information can be found on the Pharmac Website.

6.4. The Committee noted an update on work underway to revise Pharmac's vision and strategy, providing feedback from PTAC's perspective.

6.5. The Committee noted the Cabinet decision and outcome of the Medical Device Review and the new Letter of Expectation for Medical Devices sent to Pharmac and Health New Zealand. Members noted work underway to support the transition and implementation of the review outcome.

6.6. The Committee noted updates on the societal perspectives workstream, further work regarding Rule 8.1b to consider expansion to include adolescent population, and updates to the Rare Disorders Policy, which now aligns with the Aotearoa New Zealand Rare Disorders Strategy.

6.7. The Committee noted the following updates and progress to the record processes:

6.7.1. 30-day provisional recommendation pilot

6.7.2. The Committee noted the removal of second committee reviews, with targeted reviews to be used as required, and supported the use of direct engagement with Discussion Leads to resolve outstanding issues.

6.8. The Committee noted the proposed publishing of agenda summaries for all Advisory Committee meetings.

7. Specialist Advisory Committee Record

7.1. June 2025 Rare Disorders Advisory Committee

7.1.1. PTAC reviewed the records of the Rare Disorders Advisory Committee meeting held on the 10 June 2025

7.1.2. PTAC noted the records including the Advisory Committee's recommendations

7.2. June 2025 Cardiovascular Advisory Committee

7.2.1. PTAC reviewed the records of the Cardiovascular Advisory Committee meeting held on the 27 June 2025

7.2.2. PTAC noted the records including the Advisory Committee's recommendations

7.3. June 2025 Diabetes Advisory Committee

7.3.1. PTAC reviewed the records of the Diabetes Advisory Committee meeting held on the 26 June 2025

7.3.2. PTAC noted the records including the Advisory Committee's recommendations

7.4. June 2025 Immunisation Advisory Committee

7.4.1. PTAC reviewed the records of the Immunisation Advisory Committee meeting held on the 26 June 2025

7.4.2. PTAC noted the records including the Advisory Committee's recommendations

7.5. May 2025 Cancer Treatments Advisory Committee

7.5.1. PTAC reviewed the records of the Cancer Treatments Advisory Committee meeting held on the 02 May 2025

7.5.2. PTAC noted the records including the Advisory Committee's recommendations

7.6. June 2025 Interim Medical Devices Advisory Group

7.6.1. PTAC reviewed the records of the Interim Medical Devices Advisory Group meeting held on the 09 June 2025

7.6.2. PTAC noted the records including the Advisory Group's recommendations

8. Nivolumab for unresectable or metastatic urothelial carcinoma, first line

Application

8.1. The Committee reviewed the application for nivolumab (in combination with cisplatin and gemcitabine) for unresectable or metastatic urothelial carcinoma in first line.

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

Recommendation

8.3. The Committee **recommended** that nivolumab (in combination with cisplatin and gemcitabine) for the treatment of unresectable or metastatic urothelial carcinoma in first line be **declined**.

8.4. The Committee considered the following when making their recommendations:

- The high health need of individuals with unresectable or metastatic urothelial carcinoma
- The marginal health benefit that nivolumab provides compared to standard of care
- Uncertainty in the overall survival benefit

Discussion

Māori impact

8.5. The Committee discussed the impact of funding nivolumab (in combination with cisplatin and gemcitabine) for unresectable or metastatic urothelial carcinoma in first line on Māori health areas of focus | Hauora Arotahi and Māori health outcomes. The Committee considered that Māori had a higher incidence of bladder cancer between 2019-2023 (5.73 per 100,000 age-standardised to the World Health Organization's standard world population) compared with for European/ other (5.37 per 100,000 age-standardised to the World Health Organization's standard world population) (Cancer data webtool, Te Whatu Ora) with a worse prognosis, with later stage diagnosis. The Committee considered that worse prognosis may be due to barriers to diagnosis, access to primary and secondary care, as well as accessing treatment following diagnosis. The Committee noted that data collection did not accurately reflect stage of disease, and therefore considered it is likely Māori represent a higher proportion of late-stage disease. The Committee considered it is likely the proportion is likely similar to other smoking related cancers including lung cancer.

Populations with high health needs

8.6. The Committee discussed the health need(s) of unresectable or metastatic urothelial carcinoma 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 nivolumab (in combination with cisplatin and gemcitabine) and noted:

8.6.1. The Committee noted that Pacific peoples had a lower incidence of bladder cancer compared to European/Other (3.94 vs 5.37 per 100,000 people age-standardised to the World Health Organization's standard world population), however likely had a worse prognosis, with later stage diagnosis (Cancer data webtool, Te Whatu Ora). The Committee considered that lower incidence may be due to barriers to diagnosis, access to primary and secondary care, as well as accessing treatment following diagnosis. The Committee noted that data collection did not accurately reflect stage of disease, considered Pacific peoples may represent a higher proportion of late-stage disease.

Background

8.7. The Committee noted it had previously considered pembrolizumab for the first line treatment of locally advanced or metastatic urothelial carcinoma in people not eligible for cisplatin. The application for first line treatment was declined in 2018 citing poor strength and quality of currently available evidence. CTAC also recommended this application be declined on the same grounds in 2019.

8.8. The Committee noted pembrolizumab for second line treatment was previously reviewed and has been funded since September 2024. Atezolizumab for the same indication is currently being considered for decline following public consultation.

Health need

8.9. The Committee noted that it had previously considered the health need of individuals with urothelial cancer in 2018.

8.10. The Committee noted urothelial (transitional cell) carcinoma is the predominant histological type of bladder cancer, accounting for more than 90% of bladder cancers (Lerner, S. P. UpToDate, 2024).

8.11. The Committee noted that urothelial carcinoma prevalence data is not publicly reported, and there is a paucity of published evidence specific to the New Zealand context, however general bladder cancer prevalence data is available. In 2020, there were 468 bladder cancer registrations, resulting in a rate per 100,000 of 4.77 (CI 4.55, 4.99) (Health NZ Cancer Web Tool, accessed 17/09/2025).

8.12. The Committee considered that Māori and Pacific peoples likely had a worse prognosis, with later stage diagnosis. The Committee considered that lower incidence for Pacific peoples may be due to barriers to diagnosis, access to primary and secondary care, as well as accessing treatment following diagnosis. The Committee noted that data collection did not accurately reflect stage of disease, and therefore considered it is likely Māori and Pacific peoples represent a higher proportion of late-stage disease. The Committee considered it is likely the proportion is likely similar to other smoking related cancers including lung cancer.

8.13. The Committee noted the current clinical management of previously untreated urothelial carcinoma in people eligible for cisplatin therapy typically consists of a platinum-based chemotherapy regime in combination with gemcitabine/cisplatin (GC) or methotrexate/vinblastine/doxorubicin/cisplatin (MVAC). Other possible therapies include high dose MVAC (HDMVAC) or paclitaxel/cisplatin/gemcitabine (PCG).

8.14. The Committee considered renal impairment is common in individuals with urothelial cancer and noted that cisplatin was not recommended for individuals with a glomerular filtration rate ≤60 ml/minute. The Committee considered these individuals would receive carboplatin, however noted the survival gain was less compared to cisplatin.

Health benefit

8.15. The Committee noted Checkmate 901, a randomised, phase III, multinational, open-label trial (N=608), that compared nivolumab with GC every three weeks for up to six cycles followed by nivolumab monotherapy with GC alone (van der Heijden et al. NEJM 2023;389:1778-89).

8.15.1. The Committee noted the study was comprised of two parts, with the second part of the study still ongoing.

8.15.2. The Committee noted the median overall survival (OS) was 21.7 months (95% CI 18.6-26.4) for nivolumab compared to 18.9 months (95% CI 14.7-22.4) for

GC. The percentage OS at 24 months was 46.9% nivolumab compared to 40.7% for GC. The Committee noted the hazard ratio (HR) for death was 0.78 (95% CI 0.63-0.96) P=0.02.

8.15.2.1. The Committee noted that HR is an instantaneous risk of death at any point in time whereas the OS is a cumulative result that is impacted by other factors including when events occurred and when patients are being censored. The Committee considered the Kaplan Meier curves for OS do not separate until approximately 12 months, which increased at 24 months, however noted that there was a low number of individuals in the study by this time point.

8.16. The Committee noted the median progression free survival (PFS) was 7.9 months (95% CI 7.6-9.5) for nivolumab, compared to 7.6 months (95% CI 6.1-7.8) for GC. The HR for death was 0.72 (95% CI 0.59-0.88) P=0.001.

8.16.1. The Committee considered there was evidence that there is a high correlation between PFS and OS for urothelial carcinoma. The Committee considered numerically the PFS was not greater in the nivolumab group however the HR for disease progression or death was statistically significant.

8.16.2. The Committee considered the baseline characteristics between the two arms of the study were similar.

8.16.3. The Committee noted as there were two primary outcomes in the study, the significance was split between OS and PFS.

8.16.4. The Committee considered the safety profiles were similar between the nivolumab and GC groups, however the treatment related adverse events were more likely to lead to discontinuation in the nivolumab group (21.1% vs 17.4% respectively).

8.16.5. The Committee noted there was no difference in the quality of life between the participants in the groups at any time point.

8.16.6. The Committee noted that GC as a comparator aligns with the New Zealand standard of care.

8.16.7. The Committee considered that the trial achieved longer survival with GC alone than had been achieved in previous studies.

8.16.8. The Committee considered the ethnicities of trial population did not reflect the New Zealand population.

8.17. The Committee noted three meta-analyses:

- Yanagisawa et al. Cancer Immunol Immunother. 2025;74:76
- Xie et al. Ther Adv Med Oncol. 2025;17:17588359251357527
- Di Civita et al. Curr Oncol. 2024;31:4713-27

8.18. The Committee considered that across the analyses enfortumab vedotin and pembrolizumab were reported to have the best OS and/or PFS when comparing immune checkpoint inhibitor treatments for urothelial carcinomas. The Committee considered it would welcome an application for enfortumab vedotin for this indication.

Suitability

8.19. The Committee noted that treatment with nivolumab would increase the number of infusions for individuals with urothelial carcinoma compared to GC alone. The Committee

noted that this could be further increased if dosing was every two weeks rather than every four weeks. The Committee noted there is a subcutaneous version of nivolumab available which would be of particular benefit to those experiencing health inequities, including those who find it difficult to access infusion clinics.

Cost and savings

8.20. The Committee considered that the number of individuals receiving subsequent therapy is similar between the Checkmate 901 trial and New Zealand population. The Committee considered that very few would receive subsequent surgery and treatment with radiotherapy would likely be higher than in the trial. The Committee noted several of the subsequent treatments are not funded in New Zealand for example enfortumab vedotin.

8.21. The Committee considered individuals would receive pembrolizumab in second line if nivolumab was funded in first line. The Committee considered there was evidence to suggest benefit from an alternative immune checkpoint inhibitor following progression, however there was limited evidence in sequencing immune checkpoint inhibitors for urothelial carcinoma. The Committee considered the health benefit of the immune checkpoint inhibitor is reduced in each subsequent line of therapy, with an approximate 3-month survival benefit in receiving the therapy in first line compared to later lines.

8.22. The Committee considered there may be a small population (5-10%) who receive a reduced dose of GC to be eligible for treatment with an immune checkpoint inhibitor, who would not have received a GC otherwise. The Committee considered this group would likely receive a similar health benefit compared to those that are cisplatin eligible from the nivolumab therapy. The Committee considered there was emerging evidence that immune checkpoint inhibitors are as effective at lower doses than indicated.

8.23. The Committee considered 55% would be cisplatin eligible.

8.24. The Committee considered the following estimates reasonable; that 90% of urothelial carcinomas originate in the bladder,25% of patients with bladder cancer with muscle-invasive disease will either present with or develop metastatic disease and that 44% of patients would be cisplatin eligible. The Committee considered it may be more appropriate to use the number of bladder cancer deaths as starting point to estimate the number of people with muscle invasive disease.

8.25. The Committee considered the uptake in first line therapy would not be changed if nivolumab were funded.

8.26. The Committee considered that there would be a population who would receive single agent chemotherapy followed by pembrolizumab in second line. The Committee considered that if nivolumab were funded in first line there would be a decrease in the number receiving pembrolizumab in second line.

8.27. The Committee considered there was evidence that weight and flat based dosing for nivolumab are similar in terms of efficacy and safety (Long et al. Ann Oncol. 2018;29:2208-13, Campo Le Brun et al. Cancer. 2025;131:e35679, Samlowski et al. Cancer Med. 2023;12:2378-88).

8.28. The Committee considered there was a lack of evidence to assess the dosing in individuals with a higher body mass index. The Committee considered there was emerging evidence that individuals who are classified as obese have better health outcomes when treated with immune checkpoint inhibitors, however may also experience more adverse events (Cortellini et al. J Immunother Cancer. 2019;7:57, Cortellini et al. Eur J Cancer. 2020:128:17-26).).

Funding criteria

8.29. The Committee considered ECOG scoring was not objectively measurable. The Committee considered it would be more appropriate to restrict funding to those receiving cisplatin.

Summary for assessment

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

Population	Unresectable or metastatic urothelial cancer: • Eligible to receive cisplatin therapy (including GFR of ≥60 ml/minute) • No previous systemic chemotherapy for unresectable or metastatic urothelial carcinoma
Intervention	Intravenous (IV) nivolumab 360 mg with gemcitabine-cisplatin chemotherapy every 3 weeks for up to six cycles, followed by nivolumab monotherapy at a dose of either 480 mg every 4 weeks, or 240 mg every 2 weeks until disease progression, unacceptable toxic effects, withdrawal of consent, or up to a maximum of 2 years.
Comparator(s)	Gemcitabine–cisplatin alone every 3 weeks for up to six cycles
Outcome(s)	**Median Overall Survival (OS)** Nivolumab 21.7 months (95% CI 18.6-26.4) vs. gemcitabine-cisplatin 18.9 months (95% CI 14.7-22.4), HR for death: 0.78 (95% CI 0.63-0.96) P=0.02 **Median Progression-free survival** Nivolumab 7.9 months (95% CI 7.6-9.5) vs. gemcitabine-cisplatin 7.6 months (95% CI 6.1-7.8), HR for death: 0.72 (95% CI 0.59-0.88) P=0.001
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.	

9. Semaglutide (Ozempic) for treatment of insufficiently controlled type 2 diabetes

Application

9.1. The Committee reviewed the application for semaglutide (Ozempic) for the treatment of insufficiently controlled type 2 diabetes mellitus

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

Recommendation

9.3. The Committee **recommended** that semaglutide for insufficiently controlled type 2 diabetes mellitus be listed with a **high priority**, subject to the following Special Authority criteria:

> Initial application from any relevant practitioner. Approvals valid without further renewal unless notified for applications meeting the following criteria:
> All of the following:
>
> 1. Patient has type 2 diabetes; and

2. Target HbA1c (of 53 mmol/mol or less) has not been achieved despite the regular use of ALL of the following funded blood glucose lowering agents for a period of least 6 months, where clinically appropriate: empagliflozin, metformin, and vildagliptin; and
3. Any of the following:
    3.1. Patient has pre-existing cardiovascular disease or risk equivalent (see note a)*; or
    3.2. Patient has an absolute 5-year cardiovascular disease risk of 15% or greater according to a validated cardiovascular risk assessment calculator*; or
    3.3. Patient has a high lifetime cardiovascular risk due to being diagnosed with type 2 diabetes during childhood or as a young adult*; or
    3.4. Patient has diabetic kidney disease (see note b)*.

Notes: * Criteria intended to describe patients at high risk of cardiovascular or renal complications of diabetes.

1. Pre-existing cardiovascular disease or risk equivalent defined as: prior cardiovascular disease event (i.e. angina, myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, transient ischaemic attack, ischaemic stroke, peripheral vascular disease), congestive heart failure or familial hypercholesterolaemia.
2. Diabetic kidney disease defined as: persistent albuminuria (albumin:creatinine ratio greater than or equal to 3 mg/mmol, in at least two out of three samples over a 3-6 month period) and/or eGFR less than 60 mL/min/1.73m^2 in the presence of diabetes, without alternative cause identified.
3. Funded GLP-1a treatment is not to be given in combination with [empagliflozin / empagliflozin with metformin hydrochloride] unless receiving (empagliflozin or empagliflozin in combination with metformin hydrochloride] for the treatment of heart failure.

9.4. In making this recommendation, the Committee considered:

9.4.1. The high health need of individuals with insufficiently controlled T2DM, with a substantial proportion of patients not achieving target HbA1c levels.

9.4.2. The unmet treatment need for individuals with sub-optimal glycaemic control despite current therapies.

9.4.3. The disproportionately higher prevalence of T2DM among Māori and Pacific peoples, contributing to significant health inequities.

9.4.4. The therapeutic advantages of semaglutide, including superior HbA1c reduction and weight reduction compared to currently funded treatments.

Discussion

Māori impact

9.5. The Committee discussed the impact of funding semaglutide for the treatment of insufficiently controlled type 2 diabetes mellitus (T2DM) on Māori health areas of focus | Hauora Arotahi and Māori health outcomes.

9.5.1. The Committee noted that the Diabetes and Cardiovascular Subcommittees have previously acknowledged the extensive evidence showing that Māori experience a higher disease burden of diabetes, resulting in disproportionately worse outcomes, and experience a higher rate of mortality attributable to T2D than the general population.

Background

9.6. The Committee noted that PTAC has provided advice for tirzepatide (Mounjaro) for inadequately controlled type 2 diabetes in August 2025. At the time, the Committee

recommended that tirzepatide be listed with a medium priority, subject to Special Authority criteria.

Health need

9.7. The Committee noted that the health needs of individuals with inadequately controlled T2DM were recently considered by PTAC in August 2025 during its discussion of tirzepatide for the same indication.

9.8. The Committee reiterated that treatment in individuals with T2DM improves cardiovascular and renal outcomes, and noted there remains an unmet health need among those with sub-optimal glycaemic control despite current therapies.

9.9. The Committee noted that while HbA1c is widely used as an indicator of long-term glycaemic control, it reflects an average glucose level and does not capture day-to-day variability or post-prandial glucose excursions, which are important contributors to cardiovascular risk. Members considered that HbA1c can vary by ethnicity, and therefore HbA1c thresholds may not represent equivalent glycaemic burden across all population groups, including Māori and Pacific Peoples.

Health benefit

9.10. The Committee noted that the overall quality of the applicable evidence was reasonable, comprising of well-conducted head-to-head trials with appropriate methodology. However, the Committee also noted limitations, including relatively short follow-up periods and that SUSTAIN-7 included only participants with preserved or relatively preserved renal function, which may restrict applicability to the broader population.

9.11. The Committee noted SUSTAIN-7 (Pratley et al. Lancet Diabetes Endocrinol. 2018;6(4):275-286), a phase 3b, open-label trial conducted across 194 hospitals in 16 countries. The Committee noted that 1,201 participants with T2DM on metformin monotherapy, were randomly assigned in a 1:1:1:1 ratio to receive semaglutide (0.5 mg or 1.0 mg) or dulaglutide (0.75 mg or 1.5 mg) as weekly maintenance doses.

9.11.1. The Committee noted baseline characteristics were similar between treatment groups, and pre-trial doses of metformin were maintained throughout the trial.

9.11.2. The Committee noted that at week 40, mean HbA1c reduction from baseline was 1.5 percentage points with semaglutide 0.5 mg, compared with 1.1 percentage points with dulaglutide 0.75 mg, estimated treatment difference (ETD) of -0.40; 95% CI: -0.55 to -0.25; p<0.0001.

9.11.3. The Committee noted for semaglutide 1.0 mg versus dulaglutide 1.5 mg, HbA1c reductions were 1.8 and 1.4 percentage points respectively (ETD -0.41; 95% CI: -0.57 to -0.25; p<0.0001).

9.11.4. The Committee noted the glycaemic targets, weight loss responses and composite endpoints all achieved statistical significance.

9.11.5. The Committee noted similar rates of adverse events in both treatment groups, 68% and 69% for semaglutide 0.5 mg and 1.0 mg respectively, and 62% and 74% for dulaglutide 0.75 mg and 1.5 mg respectively.

9.11.6. The Committee noted the limitations of the trial, including its open-label design, restriction of participants to those receiving metformin with relatively preserved renal function, reduced generalisability to the wider type 2 diabetes population in New Zealand, and the short study duration, in which weight loss in the semaglutide 1.0 mg arm had not yet plateaued.

9.11.7. The Committee noted that semaglutide demonstrated superior improvements in glycaemic control and reductions in bodyweight compared with dulaglutide, and that safety profiles and adverse events were similar between treatment groups.

9.12. The Committee noted SUSTAIN-10 (Capehorn, et al. Diabetes Metab. 2020;46(2):100-9), a phase 3b, open-label trial conducted across 11 European centres involving 577 participants, randomised in a 1:1 ratio to receive either semaglutide (maintenance dose of 1.0 mg once weekly) or liraglutide (maintenance dose of 1.2 mg daily). The Committee noted that participants with T2DM were inadequately controlled despite treatment with oral anti-hyperglycaemic agents (either metformin, sulfonylureas, or SGLT-2i).

9.12.1. The Committee noted a mean baseline HbA1c of 8.2%, with a mean reduction at week 30 of 1.7% for semaglutide and 1.0% for liraglutide. The Committee noted an ETD of -0.69% (95% CI: -0.82 to -0.56).

9.12.2. The Committee noted a mean baseline for bodyweight of 96.9kg, with a mean reduction at week 30 of -5.8 kg for semaglutide and -1.9 kg. The Committee noted an ETD of -3.83 kg (95% CI: -4.57 to -3.09). The Committee noted that changes in HbA1c and weight had not plateaued in the semaglutide group.

9.12.3. The Committee noted 288 participants per arm were required to achieve 90% power to confirm superiority for both endpoints.

9.12.4. The Committee noted the treatment-emergent adverse events (TEAEs) were similar between groups in both frequency and severity. However, the Committee noted discontinuation rates were higher in the semaglutide group (11.4%), compared to liraglutide (6.6%), likely due to a higher incidence of gastrointestinal adverse events with semaglutide (7.6% vs. 3.8%). The Committee noted gastrointestinal adverse events included nausea, diarrhoea, vomiting, constipation, and abdominal pain, consistent with semaglutide's mechanism of slowing gastrointestinal transit.

9.12.5. The Committee noted that the trial was limited by its open-label design, short duration, and the absence of evaluation for semaglutide 0.5 mg and liraglutide 1.8 mg.

9.12.6. The Committee noted that semaglutide demonstrated superior glycaemic and weight reduction over 30 weeks compared with liraglutide, with a similar safety profile, although discontinuations were higher in the semaglutide group due to gastrointestinal adverse events.

9.13. The Committee noted that the age and ethnic distribution in the SUSTAIN-7 and SUSTAIN-10 trials were not representative of New Zealand population, with a mean trial age of 56 years versus 65–74 years in New Zealand, and a predominantly Caucasian study population.

9.13.1. The Committee noted the concomitant therapies administered in these trials were broadly consistent with the treatment paradigm in New Zealand.

9.14. The Committee noted there are no head-to-head trials of tirzepatide versus semaglutide for weight reduction in people with obesity or overweight and T2DM. The Committee noted an indirect treatment comparison, comparing SURMOUNT-2 (tirzepatide) and STEP-2 (semaglutide) (Hankosky, et al. Diabetes Obes Metab. 2025;27(7):3757-65).

9.14.1. The Committee noted that ≥5% weight reduction was achieved more frequently with tirzepatide 15 mg (OR 1.76; p=0.035), and that HbA1c reductions were also greater with tirzepatide (mean reductions of 0.47% with 10 mg and 0.56% with 15 mg; p<0.001).

9.14.2. The Committee acknowledged limitations of the evidence, including reliance on comparisons across different studies rather than direct trials, and the use of higher weight-loss doses for both agents.

9.15. The Committee noted a comparative systematic review and network meta-analysis evaluating the effectiveness of GLP-1 receptor agonists (RAs) on glycaemic control (Yao, et al. BMJ. 2024;384:e076410). The Committee noted the PTAC Committee reviewed this publication in August 2025 while evaluating tirzepatide. The Committee noted that tirzepatide is a dual GIP/GLP-1 RA, whereas semaglutide is a GLP-1 only agonist, and therefore members were cautious about making direct comparisons between the two agents due to their differing mechanisms of action.

9.15.1. The Committee noted that tirzepatide demonstrated the greatest HbA1c reduction among all GLP-1 RAs included in the analysis, with a mean difference of -2.10% (95%CI: -2.47 to -1.74) compared to placebo. The Committee noted that CagriSema (semaglutide/cagrilintide) resulted in the highest weight loss (mean difference -14.03 kg (95% CI: -17.05 to -11.0).

9.15.2. The Committee noted that gastrointestinal side effects were common in all GLP-1 RAs, especially with high doses.

9.16. The Committee noted that, in the absence of long-term data, it is difficult to accurately extrapolate clinical outcomes beyond the reported follow-up periods. The Committee noted in SUSTAIN-10, the treatment effect of semaglutide had not yet plateaued, adding further uncertainty to long-term projections. The Committee noted that semaglutide was superior to comparator treatments over the available study periods, and considered it likely to be at least non-inferior in the longer term, although sustained benefit may depend on continued use and could be influenced by adverse effects.

9.16.1. Committee members noted that, in circumstances where treatment is discontinued, substantial rebound weight gain has been observed. Members considered that the relative rebound effect would not differ between GLP-1 RAs. Members considered that the rebound effect may complicate extrapolation of long-term outcomes, as projections assuming sustained benefit may not be valid if treatment is ceased or adherence is inconsistent.

Suitability

9.17. The Committee noted the shelf life of semaglutide is 36 months, and once opened, the semaglutide pen does not require refrigeration and can be stored at room temperature for up to 42 days.

9.17.1. The Committee noted in comparison, liraglutide has a shelf life of 30 months, and can be stored for 1 month at room temperature, and the shelf life of dulaglutide is 2 years and once opened can be stored at room temperature for up to 14 days.

9.18. The Committee noted that weekly injections (semaglutide, dulaglutide) are likely to be preferred by many people due to the reduced dosing frequency. However, the Committee also noted that some individuals may prefer a daily injectable option (such as liraglutide), for example, if they find a daily routine easier to remember.

9.19. The Committee noted anecdotal reports of potential behavioural patterns associated with GLP-1 RA use, including reports of individuals not taking the medicine as prescribed. The Committee considered that practices such as ‘micro-dosing’, sharing pens, or trialling doses informally may occur, and noted the potential implications of such behaviours for treatment effectiveness, safety and equitable access.

9.20. The Committee noted that in SUSTAIN-10, semaglutide was associated with a higher incidence of gastrointestinal adverse events compared with liraglutide, whereas this

difference was less evident in the SUSTAIN-7 trial against dulaglutide. The Committee considered that, given dulaglutide is currently the predominant GLP-1 RA funded in New Zealand (80% of patients), the gastrointestinal side-effect profile of semaglutide is unlikely to be appreciably different in clinical practice.

9.21. The Committee noted that switching from currently funded treatments to semaglutide would require appointments with treating clinicians, which may present barriers for people with limited access to primary care, or those living rurally. The Committee noted that switching could generally be undertaken during routine follow-up and that people currently using liraglutide may benefit form the shift to a weekly administration schedule.

Cost and savings

9.22. The Committee noted the estimated pharmaceutical costs associated with semaglutide, the funded comparator treatments, dulaglutide and liraglutide, and tirzepatide as a potential comparator under consideration for funding.

9.23. The Committee noted the projected growth in the number of people receiving GLP-1 receptor agonists, with total GLP-1 RA use expected to continue increasing through 2030, with rising dulaglutide use and a corresponding decline in liraglutide use based on current forecasts, if there were to be no changes to the currently available therapies. The Committee further noted that uptake of GLP-1 RA therapies has been rapid, with an annual increase of approximately 19% between 2022 and 2024, expected to slow to 11% in 2026 and 2.3% by 2030.

9.24. The Committee noted that while GLP-1 RA therapies incur health-system costs, including GP visits for initiation and titration and management of adverse events, these costs may be offset by reductions in diabetes-related complications.

9.25. The Committee noted the potential shifts in GLP-1 RA therapy pricing with the entry of generic products, and acknowledged one generic brand of liraglutide already registered in New Zealand. The Committee considered that generic availability is likely to reduce the price of currently funded comparator treatments relative to semaglutide.

9.26. The Committee noted that uptake of semaglutide may be enhanced due to brand-name familiarity, but that this would not impact the size of the overall eligible group.

Funding criteria

9.27. The Committee noted, if funded, semaglutide for T2DM would be used in place of currently funded GLP-1 RA therapies. The Committee noted it would be used as a second-line agent following an SGLT2i.

Summary for assessment

9.28. The Committee considered that the below summarises its interpretation of the most appropriate PICO table (population, intervention, comparator, outcomes) information for semaglutide if it were to be funded in New Zealand for inadequately controlled type 2 diabetes mellitus (T2DM). This PICO table captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO table is based on the Committee's assessment at this time and may differ from that requested by the applicant. The PICO table may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	New Zealand patients eligible for dulaglutide or liraglutide under the current Special Authority criteria.
Intervention	Semaglutide: 0.25 mg–1.0 mg, once weekly. Treatment is expected to continue indefinitely, unless it is determined that the individual is no longer deriving clinical benefit or is unable to tolerate the therapy.
Comparator(s) (NZ context)	Dulaglutide 1.5 mg (once a week, subcutaneous injection) Liraglutide 1.2-1.8 mg (once daily, subcutaneous injection)
Outcome(s)	Improved glycaemic control (HbA1c) Reduction in cardiovascular events and renal complications

Table definitions:

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

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

Comparator: 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).

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

10. Anifrolumab for severe systemic lupus erythematosus (SLE)

Application

10.1. The Committee reviewed the anifrolumab for severe systemic lupus erythematosus

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

Recommendation

10.3. The Committee **recommended** that anifrolumab for severe systemic lupus erythematosus (for the wider group) be funded with a **high priority** subject to the following Special Authority criteria:

Initial application (Active systemic lupus erythematosus)

Applications from a rheumatologist or clinical immunologist. Approvals valid without further renewal unless notified for applications meeting the following criteria:

1. Patient has documented diagnosis of severe systemic lupus erythematosus (SLE); and
2. Patient has persistent disease activity as supported by a SLE Disease Activity Index 2000 (SLEDAI-2K) score of at least 6 points; and
3. Patient is receiving immunosuppressant medication, with treatment received for at least 12 weeks unless contraindicated/intolerant necessitating treatment withdrawal, with either:
   - 3.1 Minimum dose of methotrexate 20 mg per week; or
   - 3.2 Azathioprine 100 mg per day; or
   - 3.3 Mycophenolate 1000 mg per day; or
4. Patient is currently receiving prednisolone or equivalent ≥ 5mg per day, with treatment received for at least 4 weeks, unless contraindicated/intolerant necessitating treatment withdrawal; and
5. Patient must not have either:
   - 5.1 Severe active lupus nephritis; or
   - 5.2 Severe active central nervous system systemic lupus erythematosus

10.4. In making this recommendation the Committee considered:

- The high health need of individuals with severe systemic lupus erythematosus
- The reduction in steroids for individuals who receive anifrolumab
- The health benefit of anifrolumab for the individuals who were represented in the trial population

10.5. The Committee **recommended** that anifrolumab for severe systemic lupus erythematosus (for a more severe group) be funded with a **low** recommendation subject to the following Special Authority criteria:

Initial application (Active systemic lupus erythematosus)

Applications from a rheumatologist or clinical immunologist. Approvals valid without further renewal unless notified for applications meeting the following criteria:

1. Patient has documented diagnosis of severe systemic lupus erythematosus (SLE); and
2. Patient has persistent disease activity as supported by a SLE Disease Activity Index 2000 (SLEDAI-2K) score of at least 10 points; and
3. Patient is currently receiving hydroxychloroquine, with treatment received for at least 12 weeks, unless contraindicated/intolerant necessitating treatment withdrawal; and
4. Patient is receiving immunosuppressant medication, with treatment received for at least 12 weeks unless contraindicated/intolerant necessitating treatment withdrawal, with either:
   - 4.1 Minimum dose of methotrexate 20mg per week; or
   - 4.2 Azathioprine 100 mg per day; or
   - 4.3 Mycophenolate 1000 mg per day; and
5. Patient is currently receiving prednisolone or equivalent ≥ 5 mg per day, with treatment received for at least 4 weeks, unless contraindicated/intolerant necessitating treatment withdrawal; and
6. Patient must not have either:
   - 6.1 Severe active lupus nephritis; or
   - 6.2 Severe active central nervous system systemic lupus erythematosus

10.6. In making this recommendation the Committee considered:

- The high health need of individuals with a severe systemic lupus erythematosus whose disease has progressed following corticosteroid and immunosuppressant treatment.
- The individuals would be represented in the clinical trial populations however would have more severe and treatment-refractory disease than many trial participants.
- The lack of subgroup analysis for this group of individuals in the trial and uncertainty if these individuals would receive similar or greater clinical benefit from the treatment.

10.7. The Committee recommended the Rheumatology Advisory Committee review this application and both Special Authority criteria as well as provide advice on the Special Authority renewal criteria.

Discussion

Māori impact

10.8. The Committee discussed the impact of funding anifrolumab for severe systemic lupus erythematosus (SLE) on Māori health areas of focus and Māori health outcomes. The Committee noted Māori have approximately twice the incidence and prevalence compared with Europeans/others.

10.9. The Committee noted Lao et al. Rheumatology. 2024;63:1560-7 that reported that Māori with SLE had worse all-cause mortality and SLE specific mortality than other ethnic groups

Populations with high health needs

10.10. The Committee discussed the health need(s) of SLE 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 anifrolumab and noted:

10.10.1. Pacific peoples have the highest incidence and prevalence of SLE, with incidence rates approximately four times higher, and prevalence three times higher than Europeans/others. Asian populations also have approximately twice the incidence and prevalence compared with Europeans/others.

Background

10.11. The Committee noted it had recently considered belimumab for lupus nephritis in November 2023, and recommended funding with a high priority.

10.12. The Committee noted it had considered quinacrine for the treatment of SLE. The Committee recommended the application be declined in November 2020, and 2024. The application was subsequently declined for funding in July 2024.

10.13. The Committee noted rituximab is funded for severe, refractory SLE.

Health need

10.14. The Committee noted it had recently reviewed the health need for SLE in November 2020.

10.15. The Committee noted Lao et al. Rheumatology. 2024;63:1560-7, a nationwide retrospective cohort analysis which used linked administrative health datasets to identify cases of SLE in New Zealand between 2005 and 2021. The study reported that compared to the general population, SLE patients were four times more likely to die (standardised mortality ratio: 95% CI: 3.7, 4.3), with SLE the leading cause of death.

10.16. The Committee noted Lao et al. Lupus. 2023;32:1019-27 that reported

- The average age-adjusted rate of incidence and prevalence of SLE in 2010–2021 was reported to be 2.1 and 42.1 per 100,000 people in New Zealand, which was reported to be comparable to rates observed in European countries.
- Women account for 83.8**%** of people with SLE in New Zealand.
- Women have the highest rate of incidence in younger age groups while men have a higher rate of incidence in older age groups
- Pacific peoples have the highest incidence and prevalence of SLE, with incidence rates about four times higher and prevalence about three times higher than Europeans/others. Māori and Asian populations also have approximately twice the incidence and prevalence compared with Europeans/others.

10.17. The Committee noted in severe SLE, standard of care is 'triple therapy', consisting of antimalarials, immunosuppressants, and corticosteroids. In refractory severe SLE, rituximab is used in the hospital setting, only when the disease has relapsed despite receiving the standard of care.

10.18. The Committee considered it is challenging to objectively score the severity of SLE overtime, due to the relapsing, remitting nature of the disease.

10.19. The Committee considered scoring was also challenging due to the differing presentations of SLE, including affecting single, multiple or combinations of organs, as well as factors including damage to organs, and comorbidities. The Committee considered the varying clinical presentation of the disease can confound the assessment of disease activity.

10.20. The Committee noted the supplier provided data regarding quality of life, that reported individuals with SLE have a worse quality of life, across domains including physical function, bodily pain, social function and mental health.

10.21. The Committee considered there was no gold standard of scoring for SLE. The Committee noted current scoring systems include the British Isles Lupus Assessment (BILAG)-2004 index, the Physician Global Assessment (PGA), the Systemic Lupus International Collaborating Clinics-American College of Rheumatology Damage Index (SDI). The Committee noted the Systemic Lupus Erythematosus Disease Activity Index

2000 (SLEDAI-2K) score was commonly used in clinical trials and in practice in New Zealand.

10.22. The Committee noted a score of ≥10 is severe, whilst ≤4 is low activity. The Committee noted that a reduction in SLEDAI-2K scoring of four points is clinically significant.

10.23. The Committee considered that SLEDAI-2K is the basis of scoring for two goals of SLE treatment: Definition of Remission in SLE (DORIS) defined as a SLEDAI -2K score of 0 and Lupus Low Disease Activity State (LLDAS) defined as a SLEDAI-2K score of ≤4. The Committee considered DORIS is the goal for the treatment of SLE, however infrequently achieved, whereas LLDAS is a key interim target that signals a reduction in disease flaring and damage accrual.

Health benefit

10.24. The Committee noted the MUSE phase two trial of 48 weeks duration (n=305), and the three-year trials long term extension (MUSE -LTE). The Committee noted Furie et al. Arthritis Rheumatol. 2017;69:376-86 that reported the following results:The primary end point (SRI[4] response with sustained reduction of oral corticosteroids at week 24) anifrolumab (34.3% for 300 mg and 28.8% for 1,000 mg) than placebo (17.6% of 102) (P = 0.014 for 300 mg and P = 0.063 for 1,000 mg, versus placebo).

10.24.1. At week 52, anifrolumab treated group achieved greater responses in SRI(4) (40.2% versus 62.6% [P < 0.001] and 53.8% [P = 0.043] with placebo, anifrolumab 300 mg, and anifrolumab 1,000 mg, respectively).

10.24.2. The Committee noted Chatham et al. Arthritis Rheumatol. 2021;73:816–25 that reported the following results from the open label extension study:

10.24.2.1. Approximately 64.9% of patients with a baseline SLEDAI-2K score ≥6 achieved a ≥4-point reduction, and 27.9% with a baseline SLEDAI-2K score >0 achieved a SLEDAI-2K score of 0 at week 160.

10.24.3. The Committee considered the individuals in the trial were young and predominantly female.

10.24.4. The Committee noted those with a central nervous system involvement were excluded.

10.24.5. The Committee noted the average SLEDAI-2K score was 11, and therefore the population represented a group with severe SLE.

10.24.6. The Committee noted there was an increase in herpes zoster infections.

10.24.7. The Committee noted individuals treated with anifrolumab had a greater response to treatment rate (≥4 SLEDAI-2K score decrease) compared to placebo. The Committee considered this was a clinically meaningful decrease.

10.24.8. The Committee noted the open label LTE trial reported anifrolumab treatment maintains a beneficial effect over the three years, with a maintained improvement in SLEDAI-2K score whilst on treatment.

10.25. The Committee noted TULIP-1, a randomised, double-blind, placebo-controlled, parallel group, phase III study (n=457) that compared anifrolumab at two different doses (300 mg vs 150 mg) in addition to standard of care treatment.

10.25.1. The Committee noted Furie et al. Lancet Rheumatol. 2019;1:e208-e219 that reported the following results at 52 weeks of treatment:

10.25.1.1. SRI-4 response of 4 at week 52 with the pre-specified analysis reporting the following results: anifrolumab 36%, placebo 40% and difference of -4.2% (95% CI -14.2, 5.8), P=0.412. The amended analysis reported 47%, 43% and a difference of -3.9% (95% CI -6.3, 14.1), P=0.455 for anifrolumab and placebo respectively.

10.25.1.2. SLEDAI-2K change from baseline to week 52 (least squares mean) was -6.0 for anifrolumab compared to -5.3 for placebo, with a difference of -0.7 (95% CI -1.6, 0.2).

10.25.2. The Committee noted the primary end point (four-point change in SLEDAI-2K score) was not statistically significant. The Committee noted that the authors considered this may not accurately reflect treatment effect, as the trial classified individuals who had received a non-steroidal drug during the trial as non-responders, which the authors considered unreasonable.

10.25.3. The Committee noted the secondary endpoints, that included other SLE scoring such as BICLA scoring, was statistically significant.

10.26. The Committee noted TULIP-2 a randomised, double-blind, placebo-controlled, parallel group, phase III study (n=365) that compared anifrolumab (300 mg) to placebo in addition to standard of care treatment.

10.26.1. The Committee noted Morand et al. NEJM 2020;382:211-21 that reported the following results at 52 weeks for treatment:

10.26.1.1. BICLA response (at week 52) of 86/180 (47.8%) for anifrolumab and 57/182 (31.5%) for placebo with a difference of 16.3% (95% CI 6.3, 26.3), P=0.001.

10.26.1.2. Glucocorticoid reduction to target dose (sustained from week 40-52) of 45/87 (51.5%) for anifrolumab, 25/83 (30.2%) for placebo with a difference of 21.2% (95% CI 6.8, 35.7), P=0.01

10.26.1.3. BILAG annualised flare rate through week 52 was 0.43 for anifrolumab, 0.64 for placebo with a rate ratio of 0.67 (95% CI 0.48, 0.94), P=0.08

10.26.2. The Committee noted the primary endpoint (BICLA score) was statistically significant, as well as the secondary endpoint (four-point change in SLEDAI-2K score [SRI-4]). The Committee noted the primary endpoint was amended; this was informed by the results of the TULIP-1 trial.

10.27. The Committee noted the TULIP long term extension (LTE) study, a pooled analysis of the TULIP-1 and TULIP-2 trials (n=547). The Committee noted that this study lacked statistical testing. The Committee noted all individuals received 300mg anifrolumab during the LTE.

10.28. The Committee noted Kalunian et al. Arthritis Rheumatol. 2023;75:253-65 that reported results following three years of follow up.

10.29. The Committee noted Morand et al Ann Rheum Dis. 2025;84:777-88 that reported a post hoc analysis of the TULIP-1/2 trials and LTE.

10.29.1. After 4 years of treatment (at Week 208), 36.9% of anifrolumab-treated patients versus 17.1% of placebo-treated patients were in LLDAS (odds ratio [OR], 2.7; 95% CI, 1.3-5.5; P = 0.0081); 30.3% versus 18.3% were in DORIS (OR, 1.9; 95% CI, 1.0-3.9; P = 0.0663).

10.29.2. Time to first LLDAS and DORIS favoured anifrolumab versus placebo (LLDAS: hazard ratio, 1.56; 95% CI, 1.18-2.09; P = 0.0024; DORIS: hazard ratio, 1.50; 95% CI, 1.04-2.22; P = 0.0373).

10.29.3. Cumulative time in LLDAS and DORIS was greater with anifrolumab than that with placebo (P = 0.0004 and P = 0.0032, respectively).

10.30. The Committee noted in both the TULIP-1 and 2 trials the population were young and predominantly female. The Committee noted the average SLEDAI-2K score was 11, and therefore the population represented a group with severe SLE.

10.31. The Committee noted anifrolumab treatment resulted in a greater reduction in SLEDAI-2K score than placebo in the first 52 weeks that was maintained over the LTE period.

10.32. The Committee considered anifrolumab had a steroid sparing effect, with individuals treated with anifrolumab receiving a lower cumulative steroid dosage over the study and LTE period.

10.33. The Committee noted there was no difference in the overall mortality between individuals treated with anifrolumab or placebo, however considered the trial period was short and therefore a difference would not be expected in this time period.

10.34. The Committee noted there was an increase in the herpes zoster, and identification of latent tuberculosis infections in individuals in the first year treated with anifrolumab compared to placebo. The Committee considered there was currently no recommendations regarding vaccination prior to treatment with anifrolumab.

10.35. The Committee considered overall the side effect profile of anifrolumab was well tolerated.

10.36. The Committee considered anifrolumab treatment was associated with a higher rate of individuals achieving LLDAS, and DORIS compared with placebo. The Committee considered that the 2023 update of the EULAR recommendations for the management of SLE (Fanouriakis et al. Ann Rheum Dis. 2024;83:15-29), and considered that achieving these treatment targets - ideally remission, or alternatively, state of low disease activity - has been extensively validated and shown to reduce the risk for damage and other adverse outcomes in patients with SLE. The Committee considered, based on the EULAR 2023 update and other studies, that an improvement in these treatment targets are likely to result in long-term outcomes, which would include reduced organ damage, reduced mortality and improvement quality of life. The Committee noted that the percentage achieving LLDAS or DORIS increased over time with anifrolumab treatment.

10.37. The Committee noted a meta-analysis by Mahmoud et al. Rheumatology & Autoimmunity, 2025;5;285-96 that included the TULIP trial, and reported that anifrolumab improved reductions in SRI-4 and SRI-8 scores, as well as decreasing the number of SLE flares compared to placebo.

10.38. The Committee noted an open label, real world use study by Tani et al. J Rheumatol. 2024 Nov 1;51:1096-101, that investigated the compassionate use of anifrolumab (N=26) in individuals who had progressed after belimumab (80%) or rituximab (19%) treatment. The Committee noted there was an improvement in SLEDAI-2K score following four weeks of treatment, with approximately 80% achieving LLDAS status at six months.

10.39. The Committee noted there was a large scale observational, multicentre study evaluating effectiveness and safety of anifrolumab in active SLE patients (REVEAL) over five years that is due to report its findings in 2031.

10.40. The Committee considered overall anifrolumab treatment was associated with an increase in the percentage of people achieving DORIS or LLDAS, as well as being steroid

sparing, with a tolerable side effect profile. The Committee further considered it had positive effects on the quality of life of individuals with SLE.

10.41. The Committee considered the treatment benefits of anifrolumab were maintained over the one-year treatment period and three-year LTE (four years total).

10.42. The Committee overall considered the data was generalisable to the New Zealand population for the less severe population. The applicability of the data to the more severe population group was uncertain.

Suitability

10.43. The Committee noted that anifrolumab is administered every four weeks via intravenous infusion. The Committee considered this may increase pressures on already overburdened infusion services, as well as represent an additional treatment burden for individuals who have to travel to infusions centres.

Cost and savings

10.44. The Committee considered that the population suggested by the supplier of anifrolumab were more clinically unwell, than the entry criteria in the TULIP or MUSE trials (SLEDAI-2K ≥10 compared to SLEDAI-2K ≥6). The proposed population would also have been more heavily treated, requiring prior use of triple therapy before eligibility, whereas trial participants had only received monotherapy of either an immunosuppressant or corticosteroid.

10.45. The Committee considered it was uncertain what the effect size would be in individuals who are receiving triple therapy and have a SLEDAI-2K ≥10, as this group includes people with more severe and treatment-refractory disease than seen in the trial population. The Committee was not aware of a sub-group analysis for this population, and therefore considered it was uncertain whether people with more severe disease on triple therapy would experience similar or greater benefit from anifrolumab compared to trial results. However, the Committee emphasised that an absence of data does not equate to an absence of effect. The Committee also noted that patients with high interferon gene signatures showed similar outcomes in the trial, and these patients are likely to have more severe disease.

10.45.1. The Committee considered the treatment effect in this more severe population remains uncertain when considering the expected benefits for both the intervention and comparator arms.

10.46. The Committee considered the funding of one antibody treatment for SLE would not be appropriate when considering both anifrolumab and belimumab, as these treatments had different mechanisms of action and were indicated for different forms of lupus (nephritis vs SLE).

10.47. The Committee considered individuals may require Quantiferon gold testing, as well as guidance on preventative treatments for herpes zoster.

10.48. The Committee considered individuals treated with anifrolumab may be more prone to infections including pneumonia.

10.49. The Committee noted the proportion of individuals achieving LLDAS and DORIS during the trial or LTE period increased over time.

10.50. The Committee considered that there was no evidence of treatment waning during the trial or LTE period, but there was uncertainty regarding the long-term treatment effect beyond the four years of trial data. The Committee noted that approximately 3% of

patients developed anti-drug antibodies, a relatively low proportion when considering potential impacts on long-term efficacy.

10.51. The Committee considered the standard of care treatment may experience treatment waning, or individuals may require increases in the dose of corticosteroids to achieve similar clinical results.

10.52. The Committee considered that both LLDAS and DORIS were important endpoints and should be incorporated into modelling the effects of anifrolumab. The Committee noted that using only LLDAS in an economic model would fail to fully capture the impact of treatment on achieving DORIS (remission), and the change in treatment outcomes of individuals over time.

10.53. The Committee noted only 2-2.9% of individuals treated with anifrolumab were considered non-responders to treatment, compared to 5.4% in the placebo group. The Committee considered that individuals not responding to treatment would require a bespoke treatment plan based on their individual needs and would likely receive high-dose oral corticosteroids.

10.54. The Committee noted approximately 15.1% of individuals withdrew from TULIP-1 or TULIP-2 in the first year of the trial. The Committee noted of this 2% discontinued due to lack of efficacy. The Committee considered overall 25-30% of individuals withdrew from the trial/s over the four-years (trial and LTE period) for reasons including adverse effects or lack of efficacy.

10.55. The Committee noted a publication by Pitsigavdaki et al Ann Rheum Dis. 2024;83:464-74., that reported the results from a ten-year retrospective study. The Committee noted the study reported a positive correlation between the time spent in DORIS or LLDAS and the better the survival outcomes, and reduction in organ damage.

10.56. The Committee considered incidence of SLE was decreasing, whilst prevalence was increasing – potentially due to improved detection and survival. The Committee noted Lao et al. Lupus. 2023;32:1019-27 reported a decrease in incidence of SLE from 3.1 to 1.6 per 100,000 from 2010 to 2021 in New Zealand. The Committee considered the 2021 data was the most appropriate figure to use for modelling. The Committee considered there would be a prevalent population.

10.57. The Committee considered it was reasonable to assume approximately 15.83% of individuals with SLE have a SLEDAI-2K score ≥10. The Committee considered there was evidence that the proportion of individuals may be higher than this estimate.

10.58. The Committee considered SLEDAI-2K scoring was not consistently used by all rheumatologists in New Zealand. The Committee considered that there would be an increase in the number of rheumatologists who utilise the scoring system as it is becoming an important measure for monitoring disease outcomes and the number of treatments that require a baseline score increase. The Committee considered the scoring was quick and easy to use, and not a barrier to access.

10.59. The Committee considered the uptake of the treatment would be high.

10.60. The Committee considered it would be appropriate to use the mean health sector costs when considering resource use. The Committee noted that resource use is likely to be affected by treatment in areas such as specialist visits, medical investigations, emergency department visits and hospitalisations, but there was uncertainty regarding he extent to which primary care costs will be impacted.

10.61. The Committee considered that improvement in LLDAS and DORIS are likely to affect health related quality of life, The Committee considered that improvement in LLDAS and DORIS are likely to affect health related quality of life, but was uncertain as to the extent

to which SDI scores or evidence about flares could be used separately from this to reflect changes in quality of life.

Funding criteria

10.62. The Committee considered individuals with lupus nephritis and neuropsychiatric manifestations of SLE should be excluded, as per the trial entry criteria, as the health benefit data from the trials could not be reasonably extrapolated in these groups.

10.63. The Committee considered it was not reasonable to restrict access to only individuals receiving triple therapy and considered the trial criteria of receiving either an immunosuppressant or corticosteroid to be more appropriate.

10.64. The Committee considered there was a lack of evidence to support the use of anifrolumab for retreatment following disease progression.

10.65. The Committee noted that the Canadian Health Technology Assessment Agency recommended annual renewal criteria whereby individuals should continue receiving anifrolumab if they are on ≤7.5mg of prednisone daily or have achieved a ≥50% reduction in oral corticosteroid use compared to baseline, and their BILAG/ SLEDAI-2K scores showed improvement or remain stable. The Committee recommended the Rheumatology Advisory Committee review and propose annual renewal criteria for the New Zealand population

Summary for assessment

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

	Population with more severe and treatment-refractory disease (as proposed in supplier application)	**Population reflecting TULIP-1, TULIP-2 and TULIP LTE trials (wider group)**
Population	People with severe SLE with a SLEDAI-2K score ≥ 10 despite standard of care	People with SLE with a SLEDAI-2K score ≥ 6 despite standard of care
	People with active lupus nephritis or central nervous system SLE not included	
Intervention	Anifrolumab 300mg intravenous infusion over a 30-minute period, every 4 weeks in addition to standard of care.	
Comparator(s) (NZ context)	Standard of care is a triple therapy consisting of some combination of: a glucocorticoid, an antimalarial, and/or an immunosuppressant.	Received either an oral glucocorticoid, or an immunosuppressant
Outcome(s)	Improved SLEDAI-2K, as evidenced by a pooled analysis of TULIP-1, TULIP-2 and TULIP LTE trials (Kalunian et al. 2023). Relevant outcomes include: 1) Disease activity improvement/ worsening as measured by SLEDAI, which is reflected in two goals of treatment: DORIS and LLDAS 2) Improved health related quality of life 3) Reduced irreversible organ damage, as measured by SDI 4) Improved overall survival 5) Reduction in flare rate, severity, and duration.	Improved SLEDAI-2K, as evidenced by a pooled analysis of TULIP-1, TULIP-2 and TULIP LTE trials (Kalunian et al. 2023). Relevant outcomes include: 6) Disease activity improvement/ worsening as measured by SLEDAI, which is reflected in two goals of treatment: DORIS and LLDAS 7) Improved health related quality of life 8) Reduced irreversible organ damage, as measured by SDI 9) Improved overall survival 1) Reduction in flare rate, severity, and duration.

Table definitions:

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

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

Comparator: 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).

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

11. Bevacizumab for severe hereditary haemorrhagic telangiectasia

Application

11.1. The Committee reviewed the clinician and consumer applications for intravenous (IV) bevacizumab for people with severe hereditary haemorrhagic telangiectasia (HHT).

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

Recommendation

11.3. The Committee **recommended** that the listing of bevacizumab be widened to include the treatment of severe hereditary haemorrhagic telangiectasia (HHT) with a **high priority**, subject to the following Special Authority criteria:

> Initial application — hereditary haemorrhagic telangiectasia (HHT)
> Applications from any relevant practitioner. Approvals valid without further renewal unless notified.
> Both:
>
> 1. Patient has been diagnosed with hereditary haemorrhagic telangiectasia (HHT); and
> 2. Patient has severe disease defined as having at least one of the following:
>
> 2.1. Significant epistaxis with an epistaxis severity score of 7 or greater, or NOSE HHT score of 2 or greater; or
>
> 2.2. Requirement for greater than 2,000 mg IV elemental iron in a calendar year; or
>
> 2.3. Red blood cell transfusion dependence; or
>
> 2.4. Multiple liver arteriovenous malformations (AVMs) precipitating a serious hepatic or cardiopulmonary complication (eg high-output cardiac failure or ischemic cholangiopathy); and
>
> 3. Patient has trialled (if appropriate) and received insufficient benefit from other funded therapies recommended for HHT in international treatment guidelines (eg moisturising topical therapies, ablative therapies and/or tranexamic acid).

11.4. In making this recommendation, the Committee considered that there is:

11.4.1 Strong evidence of the high health need of people with severe HHT who experience significant, ongoing bleeding

11.4.2 Evidence including a good-quality retrospective study to support clinically significant and meaningful health benefits from intravenous (IV) bevacizumab for severe HHT (ie improved quality of life, increased haemoglobin, reduced need for iron and red blood cell transfusions, and improvements in high-output cardiac failure [if present]).

11.5. The Committee considered that Pharmac staff could consider applying renewal criteria to bevacizumab for HHT if appropriate based on further advice or information. This could be similar to renewal criteria used for those receiving bevacizumab for severe HHT via the Named Patient Pharmaceutical Assessment (NPPA) pathway, or based on additional advice from relevant specialists and/or Specialist Advisory Committees (eg haematologists, gastroenterologists, ear nose and throat [ENT] specialists).

Discussion

Māori impact

11.6. The Committee discussed the impact of funding bevacizumab for the treatment of HHT on Māori health areas of focus and Māori health outcomes. The Committee noted that

relevant considerations have been previously described in August 2024 and February 2025, and raised no specific new considerations.

Impact on Pacific peoples, disabled people, tāngata whaikaha Māori, and other people who have been underserved by the health system

11.7. The Committee noted that relevant considerations about the impact of HTT on groups who are underserved by the health system have been previously described in August 2024 and February 2025, and raised no specific new considerations.

Background

11.8. The Committee noted that Pharmac and PTAC have previously considered two iron products for the treatment of HHT:

11.8.1 Ferric carboxymatose (Ferinject) for people with HHT with serum ferritin 50 mcg/L or less or transferrin saturation 20% or less – widening access. In August 2024, PTAC recommended the application be declined.

11.8.2 Ferric derisomaltose (Monofer) for people with HHT to prevent iron deficiency/anaemia – new listing. In February 2025, PTAC recommended it be listed with a high priority.

11.9. The Committee noted that bevacizumab is currently funded and has been considered on many previous occasions for a range of predominantly cancer indications. Refer to the application tracker for further information.

11.10. The Committee noted that a subset of patients with severe HHT have received funded bevacizumab via the Named Patient Pharmaceutical Assessment (NPPA) pathway.

Health need

11.11. The Committee noted that the health needs of people with HHT has been discussed previously in August 2024 and February 2025. The Committee reiterated that those with severe HHT have a high health need due to any of the following: recurrent epistaxis, gastrointestinal (GI) bleeding, anaemia, iron deficiency, high output cardiac failure (HOCF) which is more likely in those with liver arteriovascular malformations, AVMs), and an increased risk of stroke (possibly related to pulmonary AVMs). The Committee noted that HHT is associated with a reduced life expectancy (Donaldson et al. Neurology. 2015;84:1886-93) and reduced quality of life (QOL) (Zarrabeitia et al. Health Qual Life Outcomes. 2017; 15:19).

11.11.1 The Committee noted the high frequency of iron and/or red blood cell (RBC) transfusions for severe HHT, which can be associated with complications including infusion reactions, transfusion-transmitted infections or RBC alloimmunisation.

11.11.2 The Committee noted that the applications described the lived experiences of people with severe HHT and considered these were very compelling. Members considered that having an effective disease-modifying treatment funded for severe HHT would be highly valuable for individuals and families with HHT.

Health benefit

11.12. The Committee noted that bevacizumab is a VEGF-inhibitor and the first disease modifying treatment to be considered by Pharmac for severe HHT. The Committee noted that bevacizumab is Medsafe approved although its approved indications do not include HHT (ie unapproved use).

11.13. The Committee noted that bevacizumab would be administered as an intravenous (IV) with four to six cycles given as induction followed by maintenance to prevent recurrent

bleeding every four to 12 weeks. The Committee noted that internationally, maintenance might be given continuously or as needed.

11.14. The Committee noted that the basis of the evidence for bevacizumab in severe HHT comes from the international, multicentre InHIBIT-Bleed study (Al-Samkari et al Haematologica 2021;106;2162). This retrospective study included 238 patients aged >18 years treated with IV bevacizumab for HHT-associated bleeding (epistaxis, GI bleeding, or both) from 2011 until 2019 at 12 treatment centres across four countries (predominantly USA).

11.14.1 The Committee noted that selected participants had significant anaemia pre-treatment with a mean haemoglobin (Hb) of 8.6 g/dL (and were treated for anaemia) or significant epistaxis with a mean Epistaxis Severity Score (ESS) of 6.75 (and were treated for epistaxis).The Committee noted that outcomes with bevacizumab were assessed in participants compared with those during the six months prior to being prescribed bevacizumab.

11.14.2 The mean Hb increased by 3.2 g/dL (95% confidence interval [95% CI]: 2.9-3.4, P<0.0001) from baseline and mean ESS decreased by 3.37 points (95% CI: -3.69 to -3.05; P<0.0001) from baseline following bevacizumab treatment. The Committee noted that the decrease in ESS was substantially higher than the minimal clinically important difference (MCID) for ESS of 0.71 (Yin et al. Laryngoscope. 2016;126:1029-32).

11.14.3 The Committee noted that the median number of RBC units transfused decreased from 6.0 (interquartile range [IQR the 6 months pretreatment to 0.0 (IQR, 0.0 6 months after treatment (P<0.0001).

11.14.4 The Committee considered that the study reported no waning of effects after 12 months but considered that this was a relatively short duration and that it was somewhat unclear whether these benefits would be maintained long term.

11.15. The Committee noted the prospective, double-blind, multicentre randomised (1:1) phase II BABH trial which included 24 adults with clinically confirmed HHT requiring at least four units of RBC transfused in three months prior, related to epistaxis or digestive bleeding (Dupuis-Girod et al. J Intern Med. 2023;294:761-74). Participants received bevacizumab intravenously (IV) 5 mg/kg every 14 days for a total of six injections (25 mg/mL) or IV sodium chloride (0.9%) solution, for six months.

11.15.1 The primary endpoint was the number of RBC units transfused per patient that decreased by at least 50% between the three-month period before treatment and the period from the third to sixth months after the beginning of treatment, which was reported in 63.6% (7/11) bevacizumab compared with 33.3% (4/12) placebo (P = 0.22). The Committee noted that there was a numerical decrease despite this not being statistically significant.

11.15.2 The Committee noted there was also an increase in Hb (Mean Hb 88 and 100 g/L with bevacizumab, respectively at inclusion and at six months vs 84 and 85 g/L with placebo, respectively [P = 0.02]).

11.15.3 Members noted that the lack of a reduction in requirement for RBC transfusion in the placebo group supported the reported response in InHIBIT-Bleed.

11.16. The Committee noted evidence of improvement in HOCF in severe HHT with normalisation of cardiac index reported in 20 of 24 participants at three months and considered that this was quite a striking benefit (Dupuis-Girod et al. JAMA 2012;307:948-55).

11.17. The Committee noted that the network meta-analyses conducted by Taha et al. (Eur Arch Otorhinolaryngol. 2025;282:2821-32) and Chen et al. (Front Pharmacol. 2023 12:14:1089847) reported limited findings and a small reduction in ESS, respectively. Members considered that both reviews excluded InHIBIT-Bleed and therefore reflected a small number of underpowered, prospective, placebo-controlled studies. The Committee also noted that Li et al. (Int Forum Allergy Rhinol. 2025;15:803-17) reported a favourable outcome based on different eligibility criteria, however, members considered that this analysis did not provide additional insight beyond that already reported in InHIBIT-Bleed.

11.18. The Committee also noted the following:

- Albitar et al. Mayo Clin Proc. 2020;95:1604-12
- Guilhem et al. PLoS One. 2017;12:e0188943
- Dupuis-Girod et al. Ther Adv Hematol. 2025:16:20406207241300828
- Iyer et al. Mayo Clin Proc. 2018; 93:155-66
- Dupuis-Girod et al. Eur J Med Genet. 2022;65:104575
- Al-Samkari et al. Haemophilia. 2020;26:1038-45
- Al-Samkari H. Blood. 2021;137:888-95
- Halderman et al. Am J Rhinol Allergy. 2018;32:258-68

11.19. The Committee noted the following safety considerations from the evidence base:

11.19.1 Increased risk of hypertension with bevacizumab in severe HHT means that some individuals would be expected to require antihypertensive medication

11.19.2 Individuals receiving bevacizumab for severe HHT might experience fatigue or proteinuria

11.19.3 VEGF inhibitors such as bevacizumab might impair wound healing in severe HHT and were not permitted to be initiated in some studies whilst a participant was recovering from a surgical procedure

11.19.4 There is possibly a small increased risk of venous thromboembolism (VTE) with bevacizumab for severe HHT, however, this risk was variable in the study reports.

11.20. The Committee noted that there is limited evidence available on the link between Hb and QOL, although considered there is some research in the context of cancer where a 1mg increase was associated with improved QOL however this was dependent on baseline Hb and QOL and was affected by transfusions (no specific reference reviewed at this time). Members considered that there is the potential for reduced mortality with bevacizumab for severe HHT and that treatment of severe HHT is expected to improve QOL (Faughnan et al. Ann Intern Med. 2020;173:989-1001).

11.21. The Committee noted that there are no large prospective randomised trials for IV bevacizumab in HHT. The Committee considered that InHIBIT-Bleed is a good quality retrospective study which appropriately used participants as controls. The Committee noted that the treatment effect was big and given that the natural history of HHT is well known, outcomes were considered very credible.

11.22. The Committee considered that outcomes from bevacizumab for New Zealand individuals with severe HHT would be similar to those in InHIBIT-Bleed and that the study was broadly comparable, however, the Committee acknowledged differences in the treatment pathway (eg due to overseas availability of alternative biologic treatment which individuals

could switched to or from, and different access criteria to iron products). The Committee considered that approximately the same magnitude of benefit would be expected, although this would depend on whether the individual was treated for epistaxis, anaemia or both, or if HOCF is present.

Suitability

11.23. The Committee noted that widening access to bevacizumab for HHT would lead to increased long-term use of clinical resource for IV treatment administration.

Cost and savings

11.24. The Committee considered it reasonable to assume that:

11.24.1 Approximately 10% might require dose escalation to 7.5 mg/kg based on 92% of those in INHIBIT receiving 5 mg/kg after six to 12 months on bevacizumab treatment.

11.24.2 Uptake of bevacizumab for severe HHT would be 100% of those eligible to access it (if funded) given the high health need in this disease

11.24.3 Approximately 90% of those receiving bevacizumab for severe HHT would continue to use it long-term as continuous maintenance (duration as per INHIBIT), with most receiving four-weekly dosing. The Committee noted the European Reference Network for Rare Vascular Diseases (VASCERN) article (Dupuis-Girod et al. Eur J Med Genet. 2022;65:104575) described relapse after bevacizumab withdrawal being almost universal by one year.

11.24.4 Based on INHIBIT, widening access to bevacizumab for severe HHT would be associated with significant reductions in the frequency of the following outcomes:

- Iron transfusions from median eight to two, per six months
- RBC transfusions from median nine to zero units per six months
- Emergency Department visits reduced by 68%
- Hospitalisations reduced by 62%.

11.25. The Committee considered that there might be a reduction in carer burden and increase in employment for the individual as reported by Wang et al (Blood Adv. 2024;8:2835-45) if access to bevacizumab were widened to include severe HHT.

11.26. Members noted anecdotal reports of individuals with HHT being considered for liver transplant due to advanced liver AVMs and/or HOCF; these rare individual cases received benefit from bevacizumab treatment, experienced improved QOL and no longer required a liver transplant. While this indicated there were other, clinically meaningful benefits from bevacizumab in this setting, members considered that transplant avoidance was too rare an event to incorporate into economic modelling.

Funding criteria

11.27. The Committee considered that the applicant-provided criteria was reasonable to target population who would benefit most. The Committee noted that although only 10% of those with HHT are diagnosed it is likely that highly affected individuals (eg those with severe epistaxis or GI bleeding) would be among the diagnosed cases and thus be targeted by funding.

11.28. The Committee considered that the elemental iron requirement criterion would be affected by any future funding of ferric derisomaltose, which would mean that more people would be likely to fulfil this criterion for bevacizumab.

11.29. The Committee considered that Pharmac staff could consider applying renewal criteria to bevacizumab for HHT if appropriate based on further advice or information. This could be

similar to renewal criteria used for those receiving bevacizumab for severe HHT via the Named Patient Pharmaceutical Assessment (NPPA) pathway, or based on additional advice from relevant specialists and/or Specialist Advisory Committees (eg haematologists, gastroenterologists, ear nose and throat [ENT] specialists.

Summary for assessment

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

Population	People with severe HHT defined as any of the following: • Epistaxis severity score >=7 or NOSE HHT score >=2 • Greater than 2000 mg IV elemental iron/year to maintain normal or near-normal Hb • Hepatic or cardiopulmonary complications from liver AVMs
Intervention	Induction: 5 mg/kg every 2 weeks for 4-6 doses Maintenance: to prevent recurrent bleeding every 4 to 12 weeks (ongoing long-term treatment in ~ 90% with most receiving four-weekly dosing) Duration of treatment is unclear.
Comparator(s)	Best supportive care including: • Iron infusions • RBC transfusions

Outcome(s)	• Improvement in haemoglobin levels. With benefits including a reduction in (Al-Samkari et al Haematologica 2021;106;2162):
	  ○ Median RBC transfusions from nine to zero
	  ○ Median iron transfusions from eight to two
	  ○ Hospitalisation by 62%
	  ○ Emergency department visits by 68%
	• Improved quality of life associated with improved haemoglobin levels.

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. Subcutaneous pembrolizumab for all currently funded indications

Application

12.1. The Committee reviewed the application regarding subcutaneous (SC) pembrolizumab for all currently funded indications.

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

Recommendation

12.3. The Committee **recommended** that subcutaneous pembrolizumab for the treatment of all currently funded intravenous pembrolizumab indications be funded only if **cost neutral** to intravenous pembrolizumab, subject to the existing Special Authority criteria relevant to each indication.

12.4. In making this recommendation, the Committee considered:

12.4.1 The available evidence indicates a non-inferior treatment effect between subcutaneous and intravenous formulations of pembrolizumab

12.4.2 The meaningful suitability benefit for the individual and their family, specifically reducing the duration of a treatment visit.

12.4.3 The potential resource savings to the health sector, including a time-saving route of administration that may ease demand on overburdened infusion centres across New Zealand.

12.4.4 There to be uncertainty regarding Medsafe approval status and whether any such approval, if granted, would extend to all currently licensed IV indications (including classical Hodgkin lymphoma).

12.4.5 The likely longer duration of patent protection for subcutaneous pembrolizumab, and that the potential suitability and resource sparing benefits associated with subcutaneous administration should be considered against the potential cost savings that could be realised if intravenous pembrolizumab biosimilars became available.

Discussion

Māori impact

12.5. The Committee discussed whether funding pembrolizumab SC would have specific impacts on Māori health outcomes, and noted that pembrolizumab is indicated for the treatment of lung and breast cancer, one of the five Hauora Arotahi | Pharmac Māori Health Areas of Focus.

Impact on Pacific peoples, disabled people, tāngata whaikaha Māori, and other people who have been underserved by the health system

12.6. The Committee discussed the health need(s) associated with conditions pembrolizumab is currently indicated for among Māori, Pacific peoples, disabled peoples including tāngata whaikaha Māori, and other groups identified to have high health needs by the Government Policy Statement on Health 2024-2027. The Committee considered people from these populations would not be expected to derive additional benefit compared to the general population from pembrolizumab SC given current infusion centre resourcing. The Committee considered that if administration was enabled closer to home (eg community

administration) there may be some additional benefit for those who live far from an infusion centre.

Background

12.7. The Committee noted that at the time of consideration, intravenous (IV) pembrolizumab was funded for 12 indications on the hospital medicines list including:

12.7.1 1L MSI-H/dMMR advanced colorectal cancer

12.7.2 2L MSI-H/dMMR advanced colorectal cancer

12.7.3 Metastatic Urothelial Carcinoma

12.7.4 Advanced Triple Negative Breast cancer

12.7.5 Recurrent or metastatic Head and neck squamous cell carcinoma (HNSCC) monotherapy

12.7.6 Recurrent or metastatic HNSCC combination therapy

12.7.7 Metastatic NSCLC monotherapy

12.7.8 Metastatic non-squamous NSCLC combination therapy

12.7.9 Squamous NSCLC combination therapy

12.7.10 Relapsed/refractory classical Hodgkin lymphoma

12.7.11 Neo/adjuvant stage III or IV resectable melanoma

12.7.12 Unresectable or metastatic melanoma

12.8. The Committee noted that the supplier application requested pembrolizumab SC for all currently funded pembrolizumab IV indications, as well as any pembrolizumab IV proposals that receive funding in the future. The Committee considered that it would not be appropriate to make recommendations for undefined populations, as recommending future indications prior to regulatory consideration does not represent best practice and may introduce unnecessary risk, particularly given the unclear value of doing so. The Committee further noted that future applications for new indications would be expected to detail all available formulations.

12.9. The Committee noted that the United States Food and Drug Administration (FDA) has approved pembrolizumab SC (Keytruda Qlex) for indications involving solid tumours, but not for lymphomas, noting that the supplier's FDA submission did not include lymphoma among their requested indications. The Committee noted one of the currently funded indications for pembrolizumab IV in New Zealand is relapsed/refractory classical Hodgkin lymphoma and this submission proposes that funding for this indication be extended to the SC formulation. The Committee acknowledged that Medsafe's approval for the subcutaneous formulation remains pending and considered there to be uncertainty whether such approval (if granted) would extend to all currently approved intravenous indications.

Health need

12.10. The Committee considered pembrolizumab is used to treat a variety of malignancies, many of which are associated with poor prognosis and limited treatment options. The Committee noted information regarding indication-specific health need is well documented in previous records of Committee considerations, which may be accessed through Pharmac's Application Tracker.

12.11. The Committee noted that pembrolizumab IV is widely used, with an estimated [redacted] New Zealanders receiving infusions each month according to the supplier's application.

Health benefit

12.12. The Committee noted the MK-3475A-D77 trial as key evidence, a phase III, global, open-label study that investigated platinum-doublet chemotherapy with either pembrolizumab SC (n=251) or pembrolizumab IV (n=126) in people with newly diagnosed metastatic non-small cell lung cancer (mNSCLC) (Felip et al. Ann Oncol. 2025;36:775-785).

12.12.1 The Committee noted the investigation met pre-specified pharmacokinetic outcomes demonstrating that drug exposure and trough concentrations observed from pembrolizumab SC were non-inferior to those observed from pembrolizumab IV. The Committee noted pembrolizumab SC exhibited a lower maximum plasma concentration, a comparable area under the curve, and higher plasma trough concentrations. Members did not consider the pharmacokinetic differences likely to have a significant impact on the efficacy or risk of toxicity of pembrolizumab, given that pembrolizumab has a flat exposure-response relationship across the large exposure span associated with currently used dosing regimens. The Committee noted that the pharmacokinetic findings from pembrolizumab SC in the MK-3475A-D77 study were consistent with those reported in the phase I investigation of pembrolizumab SC (Cohen et al. Euro J Cancer. 2025;270:115709).

12.12.2 The Committee noted the investigations endpoints related to drug efficacy (progression-free survival, overall survival, objective response rate, duration of response) were comparable between SC and IV arms.

12.12.3 The Committee considered that the safety profiles were similar, with ≥1 treatment-related adverse event (any grade) reported in approximately 90% of participants in the SC arm and 96% in the IV arm. Severe treatment-related adverse events (grade 3–5) occurred in 47.0% of the SC arm and 47.6% of the IV arm. The Committee noted the reported immunogenicity of pembrolizumab and of berahyaluronidase alfa, a component of the SC formulation, and considered that there appeared to be no clinically significant immunogenic risk associated with the SC formulation.

12.12.4 Overall, the Committee considered the available evidence indicates that pembrolizumab SC was non-inferior to pembrolizumab IV with respect to efficacy, safety, and exposure, and members were not aware of any clinically meaningful differences in treatment effect between formulations.

12.12.5 The Committee considered the MK-3475A-D77 investigation to be well conducted and of good quality. The Committee considered the findings of the MK-3475A-D77 trial to be generalisable to the New Zealand context. The Committee considered the evidence using the GRADE framework and noted no serious concerns regarding risk of bias, inconsistency, imprecision, or publication bias. However, the Committee identified concerns regarding indirectness, specifically the ability to generalise the findings—predominantly observed in the mNSCLC setting—to other indications. While the evidence supporting comparable efficacy for pembrolizumab SC compared with IV in mNSCLC was considered high certainty, the Committee downgraded the certainty for other indications to moderate due to these concerns. Overall, the Committee discussed the clinical claim that pembrolizumab SC was non-inferior to pembrolizumab IV across the indications being assessed and considered this was not unreasonable. However, as most of the evidence originated from a single indication, the Committee noted there remains some level of risk associated with this claim, given that other subcutaneous biologics have demonstrated clinically important disease-specific immunogenicity.

12.13. The Committee noted having reviewed the findings of Song et al. Eur J Cancer. 2025;230:115711, which reported pharmacokinetic modelling supporting the dose-selection for pembrolizumab SC.

Suitability

12.14. The Committee noted the findings of George et al. Cancer Treat Rev. 2025;139:102974, a systematic literature review comparing subcutaneous formulations of 19 intravenous oncology therapies (not including pembrolizumab SC). Across 46 studies, SC and IV formulations showed comparable efficacy, pharmacokinetics/pharmacodynamics, and tolerability, while SC administration was associated with cost and time savings. The review reported that patients and healthcare providers generally preferred subcutaneous administration due to shorter visits and preparation time, greater convenience, comfort and reduced IV access burden. The difference in health-related quality of life outcomes were not significant. The Committee noted the supplementary data regarding chair time and healthcare worker time per dose, which altogether suggested a 50-75% reduction in chair time for people receiving treatment, and 30-60% less active healthcare worker time.

12.15. The Committee noted the findings of De Cock et al. J Thorac Oncol. 2025;20:S32, a time-and-motion study conducted alongside MK-3475A-D77. The study reported that 46% reduction in active healthcare worker time and a 50% reduction in chair time when pembrolizumab was administered subcutaneously compared with intravenously. The Committee noted these findings did not include the time associated with chemotherapy administration. The Committee noted these findings were communicated via a conference abstract, without the level of detail required to comment on the quality of the evidence. The Committee noted these results were consistent with the findings reported in George et al. 2025, and therefore considered the time and resource savings reported in De Cock et al. 2025 to be reasonable and applicable to the New Zealand context for certain indications.

12.16. The Committee considered there were likely to be a small group of individuals for whom pembrolizumab SC was not suitable, including but not limited to people with hypersensitivity reactions, those with anatomical abnormalities interfering with subcutaneous injection, and individuals requiring a desensitisation regimen for pembrolizumab.

12.17. The Committee considered that although community administration of subcutaneous oncology therapies may be feasible in international settings, administration of pembrolizumab SC in New Zealand would remain in infusion centres in the short term. The Committee considered that significant changes to health service delivery would be required to enable community administration.

12.18. The Committee considered that if a patient is already receiving an intravenous therapy, pembrolizumab IV may not significantly extend treatment time and IV administration may be preferred over SC for some individuals. The Committee reiterated the findings of George et al. (2025), noting that most patients would prefer SC over IV. The Committee considered that a reasonable estimate of preference for pembrolizumab SC would be approximately 80% among those receiving monotherapy.

Cost and savings

12.19. The Committee acknowledged the high demand and limited capacity of infusion centres across New Zealand and considered that funding pembrolizumab SC provides a time- and resource-sparing route of administration for pembrolizumab compared with IV.

12.20. The Committee considered that the suitability benefit offered by pembrolizumab SC would vary between indications in relation to time and resource savings. Members noted there would be less opportunity to realise this benefit when concurrent medicines are

administered intravenously, and that the greatest savings would likely occur in monotherapy settings.

12.21. The Committee noted that pembrolizumab IV biosimilars are expected to become available [redacted], which could substantially reduce treatment costs. The Committee considered that if pembrolizumab SC were funded, it may be challenging to transition to an IV biosimilar. The Committee considered the potential cost savings from intravenous biosimilars should be weighed against the potential benefits of subcutaneous administration when making funding decisions.

12.22. The Committee considered that the resource requirement and costs likely to be incurred if pembrolizumab SC were administered in community settings would be considerable. These include, but are not limited to, competency training and skill maintenance, staff upskilling to manage cytotoxic medicines, development of standard operating protocols, clinical governance, audit and quality assurance processes, and monitoring during observation periods.

12.23. The Committee considered uptake of pembrolizumab SC would occur rapidly.

Funding criteria

12.24. The Committee noted the existing pembrolizumab IV special authority criteria for each indication would be used to access pembrolizumab SC

Summary for assessment

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

Population	All populations currently eligible for publicly funded IV pembrolizumab, and for whom the SC formulation has received Medsafe approval. Populations with funded access to pembrolizumab in New Zealand: 1. 1L MSI-H/dMMR advanced colorectal cancer 2. 2L MSI-H/dMMR advanced colorectal cancer 3. Metastatic Urothelial carcinoma (UC) 4. Advanced Triple Negative Breast cancer (mTNBC) 5. Recurrent or metastatic Head and neck squamous cell carcinoma (HNSCC) monotherapy 6. Recurrent or metastatic HNSCC combination therapy 7. Metastatic Non-small cell lung cancer (NSCLC) monotherapy 8. Metastatic non-squamous NSCLC combination therapy 9. Squamous NSCLC combination therapy 10. Relapsed/refractory classical Hodgkin lymphoma (cHL) 11. Neo/adjuvant stage III or IV resectable melanoma 12. Unresectable or metastatic melanoma
Intervention	Pembrolizumab SC in adults: • 790 mg pembrolizumab and 9,600 units of berahyaluronidase alfa-pmph every 6 weeks, administered into the thigh or abdomen over 2 minutes, OR • 395 mg pembrolizumab and 4,800 units of berahyaluronidase alfa-pmph every 3 weeks, administered into the thigh or abdomen over 1 minute Paediatric dosing guidance is currently unclear. Treatment continued until disease progression or unacceptable toxicity, or as described in the prescribing information (will differ by indication).

Comparator(s)	Pembrolizumab IV in adults: - 400 mg every 6 weeks, administered over 30 minutes OR - 200 mg every 3 weeks, administered over 30 minutes Pembrolizumab IV in children (if relevant, pending Medsafe approval): - 2 mg/kg (up to a maximum of 200 mg) every 3 weeks Treatment continued until disease progression or unacceptable toxicity, or as described in the prescribing information (will differ by indication).
Outcome(s)	Clinical claim: Pembrolizumab SC is noninferior to pembrolizumab IV in terms of efficacy and safety Outcomes Domain Assessed in 3475A-D77 Trial (Felip et al. Ann Oncol. 2025;36:775-785): - Pharmacokinetic exposure measures: o Cycle 1 area under the curve ($AUC_{0\text{-}6wks}$) o Steady-state trough concentration (Cycle 3 C_{trough}) - Efficacy endpoints o Objective Response Rate (ORR) o Progression-Free Survival (PFS) o Overall Survival (OS) o Duration of Response (DOR) o Health-related quality of life (HRQoL) o Safety profile
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.	

13. Vedolizumab subcutaneous formulation for ulcerative colitis and Crohn's disease

Application

13.1. The Committee reviewed the application for subcutaneous vedolizumab for ulcerative colitis and Crohn's disease.

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

Recommendation

13.3. The Committee **recommended** that subcutaneous vedolizumab be funded for the treatment of ulcerative colitis and Crohn's disease only if cost-neutral to intravenous vedolizumab, subject to Special Authority criteria

13.4. In making this recommendation, the Committee considered:

13.4.1. The convenience of self-administering vedolizumab at home and the flexibility of providing individuals with an alternative formulation provides a meaningful suitability benefit.

13.4.2. The available evidence supports the clinical claim of non-inferior efficacy and safety between subcutaneous and intravenous formulations of vedolizumab.

13.4.3. The high demand for infusion resources across New Zealand, which can delay individuals initiating intravenous treatments

Discussion

Māori impact

13.5. The Committee discussed the impact of funding subcutaneous (SC) vedolizumab for the treatment of ulcerative colitis (UC) and Crohn's disease (CD) on Māori health outcomes. The Committee noted that while ulcerative colitis and Crohn's disease are more common among New Zealanders of European decent, the reported incidence is increasing among Māori (Qiu et al. NZMJ. 2022;135).

13.6. The Committee noted that the treatment of inflammatory bowel diseases (IBD), including both UC and CD, is not among the five Hauora Arotahi | Pharmac Māori Health Areas of Focus.

Impact on Pacific peoples, disabled people, tāngata whaikaha Māori, and other people who have been underserved by the health system

13.7. The Committee discussed the health need regarding IBD among Māori, Pacific peoples, disabled peoples including tāngata whaikaha Māori, and other groups identified to have high health needs by the Government Policy Statement on Health 2024-2027. The Committee noted that individuals who live rurally or far from infusion centres may face an additional burden while adhering to intravenous vedolizumab

Background

13.8. The Committee noted the target population requested by the supplier application was adults with UC or CD who are currently eligible for funded maintenance therapy with vedolizumab, and who have responded to induction treatment on vedolizumab IV.

13.9. The Committee noted its most recent consideration of vedolizumab in February 2024, where the Committee made a high priority recommendation for vedolizumab's Special Authority criteria to be amended to allow for maintenance dose frequency escalation in individuals with secondary loss of response. The Committee noted that this proposal is currently under assessment.

Health need

13.10. The Committee noted that the health need for vedolizumab in the treatment of IBD was previously reviewed by PTAC in November 2020 and by the Gastrointestinal Advisory Committee in March 2017. The Committee agreed with the previous advice provided to Pharmac regarding the health need and reiterated that IBD is a chronic, progressive, and disabling condition with substantial impacts on health-related quality of life. These impacts include effects on employment, disability, education, whānau and caregivers, and mental health.

13.10.1. The Committee noted that ulcerative colitis predominantly affects the large bowel and typically presents with diarrhoea, bloody bowel movements, abdominal pain, urgency, tenesmus, incontinence, and potential extraintestinal manifestations.

13.10.2. The Committee noted that Crohn's disease is characterised by transmural inflammation of the gastrointestinal tract, which can occur from the mouth to the perianal area, most commonly in the small intestine or colon. People with Crohn's disease commonly experience abdominal pain, faecal urgency and incontinence, bloody or mucous diarrhoea, and systemic features such as weight loss, fever, anaemia, and fatigue, alongside extraintestinal manifestations.

13.10.3. The Committee noted that New Zealand has one of the highest reported incidence rates of IBD worldwide (Qiu et al. NZMJ. 2022;135).

13.10.4. The Committee noted an estimate provided by Pharmac that 1298 individuals accessed vedolizumab IV between 2022-2025.

13.11. The Committee discussed the currently funded biologic treatment options for people with moderate-to-severe IBD and noted that ustekinumab and adalimumab are available as subcutaneous formulations, whereas vedolizumab and infliximab are administered intravenously in New Zealand, subcutaneous presentations may be available but are unfunded.

Health benefit

13.12. The Committee discussed the Special Authority criteria used to access vedolizumab IV.

13.13. The Committee noted the various disease activity scoring tools used for Crohn's disease and ulcerative colitis, including the Crohn's Disease Activity Index (CDAI) and the Paediatric Crohn's Disease Activity Index (PCDAI), the Simple Clinical Colitis Activity Index (SCCAI) and the Paediatric Ulcerative Colitis Activity Index (PUCAI), as well as endoscopic assessments of mucosal healing and biochemical assays such as faecal calprotectin and C-reactive protein (CRP).

13.14. The Committee noted the VISIBLE 1 study as key evidence (Sandborn et al. Gastroent. 2020;258:62-72), an industry-sponsored, phase III, multicentre, randomised, double-blind, placebo-controlled trial assessing the efficacy and safety of subcutaneous vedolizumab in people with UC who had responded at six weeks to induction therapy with vedolizumab IV (300 mg). The study featured three arms receiving maintenance treatment: vedolizumab SC (n=106), placebo SC (n=56), and vedolizumab IV (n=54).

13.14.1. The Committee noted that the primary outcome was the proportion of individuals who achieved clinical remission at week 52, which was reported as 46.2% in the vedolizumab SC arm, 42.6% in the vedolizumab IV arm, and 14.3% in the placebo arm. Members noted that the proportion was significantly greater in both vedolizumab arms compared with the placebo arm ($p<0.001$ for both comparisons). The Committee considered the evidence indicates that vedolizumab SC exhibits non-inferior efficacy in UC compared to the IV formulation.

13.14.2. The Committee noted that no statistically significant differences were reported in the post-hoc comparison of the vedolizumab SC and IV arms for the proportion of individuals who experienced any adverse event, a drug-related adverse event, or discontinued treatment due to adverse events. The Committee noted that the proportion of individuals with anti-vedolizumab antibodies, indicating immunogenicity of the preparation, was reported to be 6% in both arms. The Committee considered the safety profile to be similar between SC and IV formulations.

13.14.3. The Committee discussed the evidence in relation to the GRADE system and considered the findings from VISIBLE 1 to be of moderate to high certainty. Members noted that the comparison between the vedolizumab SC and IV arms was based on an indirect, post hoc analysis and considered that the study featured low to moderate heterogeneity. The Committee considered the risk of bias to be low.

13.15. The Committee noted the VISIBLE 2 study as key evidence (Veremeire et al. J Crohns Colitis. 2022;16:27-38), an industry sponsored, phase III, multicentre, randomised, double-blind, placebo-controlled trial directly comparing vedolizumab SC (n=275) and placebo SC (n=134) in individuals with moderate to severe CD who clinically responded at six weeks to induction therapy with vedolizumab IV (300mg).

13.15.1. The Committee noted that the primary outcome was the proportion of individuals who achieved clinical remission at week 52, which was reported as 48.0% in the vedolizumab SC arm and 34.3% in the placebo arm (relative difference 14%; p=0.008).

13.16. The Committee noted the GEMINI 2 study as key evidence (Sandborn et al. N Engl J Med 2013; 369:711-21), an industry sponsored, phase III, double-blind, placebo-controlled trial directly comparing vedolizumab IV and placebo IV in individuals with moderate to severe CD who clinically responded at six weeks to induction therapy with vedolizumab IV (300 mg).

13.16.1. The Committee noted that the primary outcome was the proportion of individuals who achieved clinical remission at week 52, which was reported as 39.0% in the vedolizumab IV arm, 21.6% in the placebo arm (relative difference 17%; p=0.0007).

13.17. The Committee reviewed an indirect treatment comparison between VISIBLE 2 and GEMINI 2 provided in the supplier's application. The Committee discussed the quality of both studies and considered them to be of moderate to high quality, with a low risk of bias and low to moderate heterogeneity. The Committee acknowledged the limitations of indirect comparisons, as well as differences between the studies, including varying placebo response rates, changes in the standard of care available at the time each study was conducted, and differing monitoring schedules. Overall, the Committee considered the indirect comparison between these key studies to be appropriate and of reasonable quality.

13.17.1. The Committee discussed the indirect comparison of safety and noted that no statistically significant differences were reported between vedolizumab formulations in the occurrence of treatment-emergent adverse events, serious adverse events, or discontinuations due to adverse events. The Committee considered that administering vedolizumab subcutaneously did not significantly alter the safety profile.

13.17.2. The Committee considered the available evidence to suggest non-inferior efficacy between SC and IV formulations of vedolizumab for people with CD.

13.18. The Committee discussed the pharmacokinetics of the subcutaneous formulation and noted that the median trough vedolizumab concentrations reported in VISIBLE 1 were significantly higher in the vedolizumab SC arm compared to the Vedolizumab IV arm. The Committee considered these differences were not likely to be clinically meaningful.

13.19. The Committee Considered all three key studies (VISIBLE 1, VISIBLE 2, and GEMINI 2) to be generalisable to the New Zealand context.

13.20. The Committee reviewed the findings of the following meta-analyses, which generally reported no significant differences in efficacy and no increased safety risk when vedolizumab was administered subcutaneously compared with intravenously for maintenance therapy:

13.20.1. Hui et al. Cochrane database Syst Rev. 2023;7: CD013611

13.20.2. Hu et al. Therap Adv Gasterenterol. 2023;16

13.20.3. Elford et al. Eur J Gastroenterol Hepatol. 2025;37:47-54

13.21. The Committee noted the findings of Berggvist et al. Aliment Pharmacol Ther. 2022;55:1389-1401, which reported real-world data from people with IBD switching from vedolizumab IV to SC. Members noted that transient severe local injection reactions were experienced by 1.2% of people.

13.22. The Committee noted that in New Zealand, ustekinumab is commonly administered to people with CD while vedolizumab in commonly prescribed for those with UC.

Suitability

13.23. The Committee noted that vedolizumab SC is supplied as a pre-filled pen, administered biweekly, with a refrigerated shelf life of 24 months or 7 days at room temperature (in darkness). Members considered that this presentation offers people the convenience of self-administration in a setting of their choice. The Committee noted that funding vedolizumab SC could reduce the treatment burden by eliminating infusion time and potentially reducing travel required for care, both of which were expected to be meaningful for individuals and their whānau.

13.24. The Committee noted that access to infusion centres for IBD treatments is highly variable and considered this leads to regional inequities. The Committee considered people with IBD can experience delays in initiating treatment due to limited infusion capacity. The Committee noted the high demand for infusion centre resources within the health system, and considered that funding vedolizumab SC would reduce the current infusion resource required to administer the medicine.

13.25. The Committee considered that funding vedolizumab SC would allow for individuals to be involved in treatment decisions (eg choice in route of administration) which may improve treatment adherence. The Committee noted that long term adherence to biologics in IBD is low, and non-adherence is associated with increased morbidity, mortality, and healthcare costs (Khan et al. J Clin Pharm Ther. 2019;4:495-507).

13.26. The Committee considered that there may be an additional suitability benefit for adalimumab SC patients who would have otherwise progressed onto vedolizumab IV, as they would be able to progress to vedolizumab SC instead and therefore remain on an SC formulation.

Intentional Recommendations

13.27. The Committee noted recommendations made by HTA agencies from other countries. Members noted that vedolizumab SC was recommended for funding by the SMC (Scotland). The PBAC (Australia) and CADTH (Canada) recommended funding vedolizumab SC if it were offered at a price cost-neutral to vedolizumab IV.

Cost and savings

13.28. The Committee noted that the supplier intends to provide vedolizumab IV at a price that is cost-neutral to the health system relative to vedolizumab SC.

13.29. The Committee considered that people who have already received at least two doses of vedolizumab IV could switch without further induction.

Funding criteria

13.30. The Committee noted that vedolizumab SC would only be available as a maintenance therapy for individuals who responded to at least two doses of vedolizumab IV.

Summary for assessment

13.31. The Committee considered that the below summarises its interpretation of the most appropriate PICO table (population, intervention, comparator, outcomes) information for subcutaneous vedolizumab if it were to be funded in New Zealand for ulcerative colitis and Crohn's disease. This PICO table captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO table is based on the Advisory Committee's assessment at this time and may differ from that

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

Population	People with ulcerative colitis or Crohn's disease who are eligible for and have responded to at least two doses of vedolizumab IV.
Intervention	Vedolizumab, subcutaneous pre-filled pen, every two weeks (108 mg/0.68mL)
Comparator(s)	Vedolizumab, intravenous, every 8 weeks infusion (300 mg)
Outcome(s)	• Non-inferior efficacy to Vedolizumab IV • Similar safety and tolerability to Vedolizumab IV
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.	

14. Biosimilar – tocilizumab

Application

14.1. The Committee reviewed a request from Pharmac staff to provide advice regarding the potential for a future change from reference tocilizumab to biosimilar intravenous (IV) tocilizumab, and the potential introduction of a subcutaneous (SC) tocilizumab biosimilar, for currently funded indications.

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

Recommendation

14.3. The Committee **recommended** that it was clinically acceptable for Pharmac to progress a competitive procurement process for tocilizumab that could result in a biosimilar tocilizumab (IV, or IV and SC) being listed and being the only available tocilizumab product for all funded indications (Principal Supply Status), if the cost saving is worthwhile and supply is secured.In making this recommendation, the Committee:

14.3.1. Considered that the available evidence was of good quality with biosimilar tocilizumab demonstrating efficacy and safety equivalence to reference tocilizumab

14.3.2. Noted that the evidence included only rheumatoid indications, however, considered that this conclusion could be reasonably applied to all currently funded indications for tocilizumab and to both IV and SC tocilizumab biosimilar formulations

14.3.3. Noted the need for both consumer and primary health care professional education and implementation strategies to support a change.

14.3.4. Noted it would be worthwhile understanding what indications have been approved tocilizumab through Pharmac's exceptional circumstances process.

Discussion

Māori impact

14.5. The Committee discussed the impact of funding a subcutaneous tocilizumab 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.

14.5.1. The Committee considered that a SC formulation would be beneficial for people with high health needs as it would support greater ease of access compared to the current IV formulation, especially for those living in rural or remote areas.

14.5.2. Members considered that some people might have individual reasons to prefer to receive an IV formulation (eg physical disability or needle phobia).

Background

14.6. The Committee noted that tocilizumab (Actemra) concentrate for IV infusion is currently funded for a range of indications and that the health need of people with those conditions has been established. The Committee noted that PTAC and other Advisory Committees have provided advice to Pharmac regarding funding applications for tocilizumab for several indications, including tocilizumab SC formulation for giant cell arteritis (GCA) and rheumatoid arthritis (RA) (refer to Application Tracker for detail).

14.8. The Committee noted that Pharmac has received and approved Named Patient Pharmaceutical Assessment (NPPA) applications for tocilizumab for many different indications over the past two years, with the evidence supporting approved NPPA indications generally being from case reports.

14.9. Members discussed that from a regulatory perspective, biosimilars are compared to the reference biologic. The Committee noted that, similar to the variability between batches of a reference biological medicine, there may be small differences between biosimilars due to the molecules in these medicines being from living cells.

14.10. The Committee noted that several tocilizumab biosimilars have been approved in other jurisdictions including Australia, United Kingdom and Europe.

Health benefit

14.11. The Committee noted that Medsafe applications for IV and SC biosimilar tocilizumab (Avtozma; CT-P47) are under evaluation and that this biosimilar has been approved in Europe, the USA and Australia. The Committee noted that the evidence base included a range of tocilizumab biosimilars including CT-P47.

14.12. The Committee noted a phase III double blind equivalence study comparing the efficacy of reference tocilizumab to biosimilar tocilizumab (BAT1806/BIIB800) in individuals with moderate to severe rheumatoid arthritis (RA) (Leng et al. Arthritis Res Ther. 2024; 26(1):157). Individuals in the study received reference IV tocilizumab up to week 48, or reference tocilizumab up to week 24 followed by BAT1806/BIIB800 up to week 48 or BAT1806/BIIB800 up to week 48. The Committee noted that efficacy and safety were comparable between treatment groups including the proportion of ACR20 responses in the study groups at week 48 reported as 87.8%, 90.3%, and 90.4% respectively.

14.13. The Committee noted a subsequent double-blind, multicentre, phase III study comparing the efficacy of biosimilar tocilizumab (CT-P47) to reference tocilizumab for individuals with moderate to severe RA (Burmester et al. Clin Drug Investig. 2025; 45:551-563). The Committee noted that 225 participants received CT-P47, 109 received reference tocilizumab (r-TCZ) maintenance and 110 switched from r-TCZ to CT-P47. At week 52, the mean change from baseline in Disease Activity Score in 28 joints-erythrocyte sedimentation rate was − 4.279, − 4.231 and − 4.376 in the CT-P47 maintenance, r-TCZ maintenance and CT-P47 switched groups, respectively.

14.14. The Committee noted a single-arm, open-label, phase III study reviewing the usability, efficacy, and safety of candidate tocilizumab biosimilar CT-P47 self-administration via auto-injector and pre-filled syringe in 33 patients with RA (Burmester et al. Expert Rev Clin Immunol. 2025; 21:521-529). Efficacy was by assessed by Disease Activity Score in 28 joints and its components. Mean DAS28 (CRP) and DAS28 (ESR) scores decreased from baseline to Week 12, with mean (SD) changes from baseline of − 2.810 (0.9458) and − 3.659 (1.1341), respectively. The Committee considered this evidence also indicated the SC formulation was useable and acceptable to participants.

14.15. The Committee also noted the following evidence for tocilizumab biosimilars:

- Leng et al. Lancet Rheumatol. 2024; 6:e40-e50
- Zubrzycka-Sienkiewicz et al. RMD Open. 2024 5;10e003596
- Smolen et al. RMD Open. 2024 18;(4):e004514
- Schwabe et al. Expert Rev Clin Immunol. 2022; 18:533-543

14.16. The Committee considered that in summary there exists a strong evidence base for transitioning to a biosimilar tocilizumab (IV and SC) with efficacy and safety post-switch being equivalent to reference tocilizumab across a range of outcome measures and in participants who had received disease-modifying drugs previously.

14.17. The Committee noted that the evidence was predominately in the rheumatoid arthritis (RA) indication and appropriately represented the disease by including a large proportion of women, however considered that due to the nature of international regulatory approval for biosimilars, other indications were unlikely to be subject to similar clinical trials. The Committee considered that tocilizumab biosimilar equivalence could be reasonably applied to all currently funded indications for tocilizumab and could reasonably be assumed with both IV and SC biosimilar tocilizumab formulations.

14.18. The Committee noted the potential to realise cost savings from Pharmac running a competitive process that may lead to the introduction of a biosimilar tocilizumab.

14.19. The Committee was supportive of a potential competitive process that could result in the introduction a biosimilar tocilizumab (IV, or IV and SC) into the New Zealand market.

Suitability, clinical service and implementation considerations

14.20. The Committee considered that it would be important for education (e.g. tutorial video, demonstration devices, information on Healthify and Healthpathways) to be provided to support patients, prescribers and other primary care health professionals involved in treatment management regarding any future change from reference to biosimilar tocilizumab, especially if the SC formulation were introduced.

14.21. The Committee noted that if a SC formulation were introduced some people might have individual reasons to prefer to receive the IV formulation (eg those with physical disability or a phobia of needles) and it would therefore be beneficial to fund IV alongside SC rather than SC alone.

14.22. The Committee noted there may be an impact on primary care healthcare resource especially if the SC formulation were introduced and individual patients already receiving tocilizumab were to change from an IV to SC formulation, which should be considered as part of any competitive process.

14.23. The Committee considered that although equivalent efficacy has been demonstrated, a nocebo effect may occur for some people. However, the Committee considered that as a

SC formulation of the reference tocilizumab is not currently funded in New Zealand, this impact may be small.

15. Tezepelumab for chronic rhinosinusitis

Application

15.1. The Committee reviewed the application from AstraZeneca for the use of tezepelumab (TEZSPIRE) for the treatment of chronic rhinosinusitis with nasal polyps (CRSwNP). The application targeted people with uncontrolled CRSwNP symptoms despite persistent use of intranasal corticosteroids (INCS) and at least one prior nasal polyp surgery.

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

Recommendation

15.3. The Committee **recommended** that tezepelumab be listed for the treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) with a **high priority**, subject to the following Special Authority criteria:

Initial application — Severe chronic rhinosinusitis with nasal polyps
Applications only from a respiratory physician, clinical immunologist, ear nose and throat specialist (ENT), or relevant practitioner. Approvals valid for 12 months for applications meeting the following criteria:
All of the following:

1. Diagnosis of chronic rhinosinusitis with nasal polyps (CRSwNP); and
2. No other clear indication for surgery or medical imaging; and
3. Either:
   - 3.1 Both:
     - 3.1.1 Patient has had at least one comprehensive sinus operation (which includes frontal sinus drill-out) plus a course of oral corticosteroids for the treatment of nasal polyps (see Note 1); and
     - 3.1.2 Recurrence has occurred within one year of the most recent comprehensive surgery; or
   - 3.2 Patient is not a candidate for comprehensive sinus surgery due to comorbidities or contraindications to the surgery; and
4. Patient has severe CRSwNP defined as having at least two of the following:
   - 4.1 Bilateral endoscopic nasal polyp score of at least five (out of a maximum score of eight, with a minimum score of two in each nasal cavity); or
   - 4.2 Disease symptoms have a severe impact on individual's quality of life (eg due to loss of smell, nasal congestion, rhinorrhoea); or
   - 4.3 High symptom burden (score ≥40) on sinonasal outcome test (SNOT-22) questionnaire (see Note 2); and
5. Disease inadequately controlled with optimised nasal polyps' therapy (see Note 3).

Note 1: Comprehensive sinus operations include comprehensive functional endoscopic sinus surgery (FESS) with frontal sinus drill-out. Standard FESS alone is not considered comprehensive in this context.
Note 2: SNOT-22 questionnaire available as Supplementary Material to Kennedy et al. Ann Allergy Asthma Immunol. 2013;111:246-251.e2.
Note 3: Optimised nasal polyps therapy defined as: (a) adherence to intranasal corticosteroid therapy for at least three months prior, unless contraindicated or not tolerated, and (b) nasal irrigation with saline, unless not tolerated or not clinically required, and (c) short-course oral corticosteroids, if required.

Renewal from any relevant practitioner. Approvals valid for 12 months where the treatment remains appropriate, and the patient is benefitting from treatment (see Note)
Note: Treatment benefit based on either:

1. Any of the following features: reduced nasal polyp size, reduced need for systemic corticosteroids, improved quality of life, improved sense of smell, reduced impact of co-morbidities (eg asthma); or
2. Improvement in the SNOT-22 score of at least nine (Chowdry et al. Int Forum Allergy Rhinol. 2017;7:1149-55).

15.4. In making this recommendation, the Committee considered:

15.4.1. The high health needs of those with CRSwNP, being previously described as on a par with (or greater than) the needs of those with other chronic health conditions

15.4.2. That the evidence from one key clinical trial (WAYPOINT) indicates that tezepelumab is an effective treatment providing meaningful benefits for CRSwNP (ie increased quality of life, reduction in surgery, reduction in corticosteroid use, and improvements in associated asthma).

15.5. The Committee considered that Pharmac staff could consider amending the post-surgery recurrence timeframe in the initial Special Authority criteria to 18 months (instead of 12 months), noting that it would be appropriate for the same timeframe to be applied to both tezepelumab and mepolizumab for CRSwNP.

Discussion

Māori impact

15.6. The Committee discussed the impact of funding tezepelumab for the treatment of CRSwNP on Māori health areas of focus and Māori health outcomes. The Committee noted that there is high incidence of respiratory illness in Māori and that there is a disproportionate impact of respiratory disease on Māori. However, it was unclear whether the incidence and impact of CRSwNP for Māori was similar or different to other groups.

Impact on Pacific peoples, disabled people, tāngata whaikaha Māori, and other people who have been underserved by the health system

15.7. The Committee noted that the impact of respiratory disease such as CRSwNP on groups that have been underserved by the health system is described in the record of the Respiratory Advisory Committee meeting and had no further comments at this time.

Background

15.8. The Committee noted that the Respiratory Advisory Committee previously considered dupilumab and mepolizumab for CRSwNP in August 2024 and that invited Ear, Nose and Throat (ENT) specialists joined the meeting for relevant discussion items including CRSwNP. The Committee noted that the Respiratory Advisory Committee had recommended mepolizumab for funding with a high priority (subject to Special Authority criteria) and did not make a formal recommendation for dupilumab as it had not been submitted to Medsafe at that time. In making their recommendation for mepolizumab for CRSwNP, the Respiratory Advisory Committee had considered:

15.8.1. The high symptom burden of CRSwNP and the substantial (and somewhat underappreciated) impact it has on quality of life (QOL) and health utility, which is on a par with several severe chronic health conditions.

15.8.2. The high unmet health need of people with CRSwNP that recurs despite good medical and surgical management, especially for people with comorbid asthma and NSAID sensitivity who require higher rates of revision surgery.

15.8.3. That mepolizumab reduces CRSwNP symptoms, polyp size and the need for repeat surgery, and substantially improves QOL including sense of smell.

15.8.4. That mepolizumab is a suitable treatment for this population.

15.9. The Committee noted that tezepelumab was previously considered by PTAC in November 2024 for the treatment of severe uncontrolled asthma and was recommended for funding with a high priority. In making their recommendation for tezepelumab for asthma, PTAC had considered:

15.9.1. Tezepelumab provides a health benefit for the group with non-eosinophilic, severe asthma phenotypes who have an unmet health need due to not being eligible for currently funded biologics.

15.9.2. Tezepelumab use would be associated with a reduction in hospitalisations due to reduced asthma exacerbations in this group, providing a benefit to the health system.

15.9.3. Funding tezepelumab would improve equity of access to biologics for people with asthma (for example access for those with non-allergic and non-eosinophilic phenotypes).

15.9.4. Tezepelumab has similar suitability to existing biologics for severe uncontrolled asthma.

Health need

15.10. The Committee noted that the health needs of those with CRSwNP had recently been described by the Respiratory Advisory Committee in August 2024.

15.11. The Committee noted the treatment paradigm for CRSwNP including sinus washouts, corticosteroid treatments (intranasal and systemic, with a low threshold to commence these options) and the role of repeat surgery. The Committee noted that some scores and scales used in CRSwNP assess nasal symptoms and polyps, and considered that the impact of treatment on both nasal and sinus symptoms was more important for providing improvement for patients.

15.12. Members noted that polyp regrowth after functional endoscopic sinus surgery (FESS) in CRSwNP is reported to be 20-40% within six to 18 months and reaches 79% at 12 years, although this is highly variable and is influenced by the presence of underlying comorbidities including NSAID sensitivity and asthma (Respiratory Advisory Committee, August 2024).

15.13. The Committee considered that it was unclear whether there was an equitable distribution of access to Ear, Nose and Throat specialists (ENTs), and further, whether the geographic distribution of CRSwNP in New Zealand was aligned with access to ENTs.

Health benefit

15.14. The Committee noted the mechanism of action of tezepelumab, including its interaction with upstream epithelial cytokines and action on TSLP-mediated type 2 inflammation, which differs to that of eosinophil-receptor targeting medicines. The Committee considered that even noting differences in mechanism of action, monoclonal antibodies including tezepelumab and mepolizumab would be expected to reduce CRSwNP symptoms but not offer a cure due to inflammatory processes driving CRSwNP and fibrotic or polyp structures which may remain even once inflammation is resolved.

15.15. The Committee noted evidence from WAYPOINT; a phase 3, multicentre, parallel-group, double-blind, randomised (1:1) controlled trial in 410 people aged at least 18 years with CRSwNP for at least 12 months, severity consistent with a need for surgery, total endoscopic nasal score of at least 5, and a minimum score of at least 2 for each nostril, total SNOT-22 score of at least 30 and nasal congestion score at least 2 (Lipworth et al. NEJM 2025;392:1178-88). Participants had treatment with systemic corticosteroids (SCS) in the previous 12 months or previous nasal-polyp surgery of any type (~70% previously had nasal surgery, median seven years prior). Members considered that this did not necessarily align exactly with the treatment paradigm that would be expected in New Zealand due to access to ENT surgeons (as described in *Health need*).

15.15.1. Tezepelumab 210 mg was administered subcutaneously (SC) at week 0 and every 4 weeks thereafter, with the final dose given at week 48, or placebo SC every four weeks for 52 weeks. The Committee noted that tezepelumab prefilled syringe was used in the trial, however, the funding application is for the prefilled pen.

15.16. The Committee noted that the co-primary endpoints of WAYPOINT were the change from baseline to week 52 in both the endoscopic nasal-polyp score (NPS) and the nasal congestion sore (NCS), and that a range of secondary endpoints were reported.

15.16.1. The least-squares (LS) mean change in NPS with tezepelumab was -2.46 compared with LS mean change -0.38 with placebo; LS mean difference vs placebo: -2.07 (95% CI -2.39, -1.74; P<0.001).

15.16.2. The LS mean change in NCS with tezepelumab was -1.74 compared with LS mean change of -0.70 with placebo; LS mean difference vs placebo: -1.039 (95%CI -1.21, -0.86; P<0.001).

15.16.3. The Committee also noted outcomes were improved with tezepelumab for loss-of-smell score (LS mean difference vs placebo: -1.00, 95%CI -1.18, -0.83), Sino-Nasal Outcome Test 22 Domain (SNOT-22; LS mean difference vs placebo: -27.26, 95%CI -32.32, -22.21), sinus opacification (Lund-Mackay; LS mean difference vs placebo: -5.72, 95%CI -6.39 -5.06), and total symptom score (LS mean difference vs placebo: −6.89; 95% CI, −8.02 to −5.76) with P<0.001 for all scores.

15.17. The Committee noted that 0.5% of people receiving tezepelumab in WAYPOINT required surgery for nasal polyps compared with 22.1% with placebo (HR: 0.02, 95% CI, 0.00, 0.09; P<0.001) and considered this a meaningful difference. The Committee considered it was unclear whether this reflected a reduction in the need for surgery (although likely for most) and/or an increased delay between required surgeries (eg if underlying process driven by TSLP-mediated type 2 inflammation), given that the one-year trial was relatively short in duration compared with the range of time to repeat surgery for CRSwNP (eg one to 10 years). The Committee considered that whether the reduction in nasal surgery observed if tezepelumab was listed would be lower than reported within the WAYPOINT trial was dependent on the access criteria applied to such a listing, but that this would be likely if a first comprehensive surgery was required before accessing tezepelumab.

15.18. The Committee noted that there was a lower requirement for SCS for nasal polyps in those receiving tezepelumab (5.2%) in WAYPOINT compared with placebo (18.3%; HR: 0.12, 95% CI: 0.04 to 0.27, P < 0.0001).

15.19. Members considered that the magnitude of reductions in need for surgery or systemic corticosteroids in WAYPOINT might not be seen in standard of care if tezepelumab were to be funded due to regional variation in surgical decision-making, access and corticosteroid-use thresholds.

15.20. The Committee noted safety data from WAYPOINT including a reduction in the rate of asthma exacerbations with tezepelumab (0.5%) compared with placebo (5.9%), and that FEV1 was similar between treatment groups although a meaningful change in FEV1 would not be expected to occur within one year. The Committee considered that there were no clinically significant risks when using tezepelumab compared with currently funded treatments or the other biologics previously considered for CRSwNP.

15.21. The Committee also noted the following evidence:

- Lipworth et al. JACI 2025;13:1943-51
- Jacobs et al. Adv Ther. 2025;42:510-22

- Supplier authored indirect comparison of tezepelumab with mepolizumab and dupilumab for CRSwNP

15.22. The Committee considered that evidence from WAYPOINT was generalisable and relevant to the New Zealand population, although asthma is more prevalent in New Zealand, but other comorbidities occurred in similar proportions of trial participants. The Committee considered that WAYPOINT provided good quality evidence of meaningful benefits for people with CRSwNP who had chronic conditions and received nasal polyp surgery a median of seven years prior. The Committee noted that some improvements were small, but these exceeded the relevant minimal difference to be meaningful for individuals with CRSwNP. The Committee considered that the magnitude of benefits might differ for those with milder disease or patients who have not yet had surgery or systemic corticosteroids and noted that long term data beyond 52 weeks is limited.

15.23. The Committee considered it was reasonable to assume a class effect exists between tezepelumab and mepolizumab (and dupilumab) in CRSwNP based on evidence reviewed to date. The Committee considered that while evidence had not been comprehensively reviewed at this time, there is likely a class effect including benralizumab in this context also.

15.24. The Committee noted that direct comparisons between tezepelumab and other biologics in CRSwNP are lacking, as is data on sequencing biologics in CRSwNP. The Committee considered that the choice of therapy, if multiple biologics were funded, would depend on individual patient phenotype, prior treatment responses, and comorbidities (eg asthma). The Committee considered Pharmac staff could seek advice on sequencing of biologic treatments for CRSWNP (if necessary) from Ear, Nose and Throat specialists.

Suitability

15.25. The Committee considered that the proposed place of tezepelumab for CRSwNP was appropriate in the treatment paradigm and that it was reasonable to assume that treatment with tezepelumab would be lifelong, although the need for long term treatment might depend on the presence of comorbidities.

15.26. The Committee considered that ENTs could view a reduction in repeat surgeries as helpful due to limited access to ENT surgeons, and that there could be a desire to access a funded biologic for CRSwNP such as tezepelumab where surgery is not accessible (eg locations where an ENT is not available such as small centres).

Cost and savings

15.27. The Committee considered that it was unclear to what extent waning of efficacy would be expected with tezepelumab for CRSwNP, especially post-surgery and washout, and therefore an appropriate rate of treatment discontinuation to use in economic modelling was not confirmed. However, the Committee considered that there was no reason to assume that the total number of patients, uptake or waning of efficacy would differ for tezepelumab compared to mepolizumab for CRSNP.

Funding criteria

15.28. The Committee considered it was reasonable to apply the same funding criteria to tezepelumab as has been recommended for mepolizumab, however, that Pharmac could consider changing the timeframe for “recurrence within one year of the most recent comprehensive surgery” to 18 months for biologic(s) for CRSwNP.

Summary for assessment

15.29. The Committee considered that the below summarises its interpretation of the most appropriate PICO table (population, intervention, comparator, outcomes) information for

tezepelumab if it were to be funded in New Zealand for the treatment of chronic rhinosinusitis with nasal polyps (CRSwNP). This PICO table captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO table is based on the Committee's assessment at this time and may differ from that requested by the applicant. The PICO table may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	Patients with chronic rhinosinusitis with nasal polyps (CRSwNP) with uncontrolled symptoms despite use of intranasal corticosteroids (INCS) AND either: ○ At least one prior comprehensive nasal polyp surgery with recurrence within either one year (potentially 18 months) of the most comprehensive surgery, OR ○ Contradictions or comorbidities that prevent sinus surgery
Intervention	Standard of care plus add-on therapy of tezepelumab administered as a subcutaneous injection every 4 weeks.
Comparator(s)	Standard of care includes: ○ Intranasal corticosteroids ○ Short courses of oral corticosteroids (OCS) ○ Saline rinses ○ Endoscopic Sinus Surgery (ESS) if necessary (likely all will require based on disease severity)
Outcome(s)	• Improvement in overall QOL ○ Mean differences of 27.26 points (95%CI -32.32, -22.21) in SNOT-22 score between the tezepelumab and placebo arm of the WAYPOINT trial (Lipworth et al. NEJM 2025;392:1178-88) • Improvement in sense of smell ○ Mean difference of 1.00 points (95%CI -1.18, -0.83) in Loss-of-Smell score between the tezepelumab and placebo arm of the WAYPOINT trial (Lipworth et al. NEJM 2025;392:1178-88) • Reduction the need for surgery ○ 0.5% experienced surgery within the tezepelumab group compared to 22.1% within the placebo group (WAYPOINT trial) (Lipworth et al. NEJM 2025;392:1178-88) • Reduction in the need for glucocorticoids ○ 5.2% required glucocorticoids within the tezepelumab group compared to 18.3% within the placebo group (WAYPOINT trial) (Lipworth et al. NEJM 2025;392:1178-88)
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.	