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 15 May & 16 May 2025

This meeting was held in person and via Microsoft Teams

1. Present:

PTAC members:
Rhiannon Braund (Acting Chair)
Bruce King
Helen Evans
James Le Fevre
John Mottershead
Liza Lack
Matthew Dawes
Matthew Strother
Robyn Manuel
Stephen Munn

Apologies:
Brian Anderson
Elizabeth Dennett
Paul Vroegop

Observers:
Lucy Elwood (Pharmac Board Member) – Part of the meeting

Dr Margaret Wilsher (Pharmac Board Member) – Part of the meeting

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
9.3	Foslevodopa / foscarbidopa (branded as Vyalev) for people with advanced Parkinson's disease, subject to Special Authority criteria	Medium Priority
10.3	Etonogestrel subdermal implant (branded as Implanon NXT) for contraception	Cost Neutral to levonorgestrel implants (Jadelle)
11.3	Vanzacaftor, tezacaftor, deutivacaftor (VNZ, TEZ, D-IVA; 'VNZ') for the treatment of cystic fibrosis in people aged six years and older with a non-F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene responsive only to vanzacaftor, tezacaftor, deutivacaftor (non-F/VNZ-responsive), subject to Special Authority criteria	High Priority
11.4	Vanzacaftor, tezacaftor, deutivacaftor (VNZ, TEZ, D-IVA; 'VNZ') for the treatment of cystic fibrosis in people aged six years and over with F508del mutation(s) or another mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene responsive to Trikafta (elexacaftor, tezacaftor, ivacaftor (non-F/ETI-responsive), subject to Special Authority criteria.	Cost Neutral to currently funded Trikafta
12.3	Secukinumab (branded as Cosentyx) as a first line biologic for moderate to severe hidradenitis suppurativa	Declined

12.4	Secukinumab as a second line biologic for moderate to severe hidradenitis suppurativa, subject to Special Authority criteria	High Priority
13.3	Sacituzumab govitecan for triple negative, locally advanced or metastatic breast cancer, subject to Special Authority criteria	High Priority
14.4	Durvalumab (branded as Imfinzi) for the treatment of extensive-stage small cell lung cancer, subject to Special Authority criteria	High Priority

4. Record of PTAC meeting held 14 November & 15 November 2024

4.1. The Committee reviewed the record of the PTAC meeting held on 14 November & 15 November 2024.

4.2. The Committee accepted the record.

5. Action Points

5.1. 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 kaimahi and noted ongoing leadership and strategic changes occurring, within a changing health sector environment.

6.3. The Committee was informed that a five-year organisational reset is underway in response to multiple reviews and external reports. More information will be shared with PTAC as this work evolves.

6.4. The Committee spent some time discussing the following areas:

6.4.1. external reviews and sharing perspectives

6.4.2. future of advisory mechanisms and governance

6.4.3. benefits of improving connection between PTAC, the Board and new Chief Executive to inform organisation direction.

6.5. The Committee discussed the ongoing review of Special Authority criteria, aiming to align with the health sector principles. The Committee noted the work underway to support this review and recognised that changing criteria may introduce risks, particularly where data is limited, and could result in budget and access implications that may unintentionally disadvantage high-need groups.

Advisory Committee Records and Processes

6.6. The Committee discussed the timeliness and burden of current record-keeping practices and welcomed efforts to streamline advisory processes.

6.7. Proposed improvements include:

6.7.1. Reducing the length of committee records

6.7.2. Trialling the release of interim or proactive recommendations, with an opt-out option

for applicants

6.7.3. Removing one full committee round of review, retaining the Discussion Lead review and a single full committee review.

6.8. The Committee noted that recommendations rarely change after multiple reviews, supporting efforts to reduce redundancy with minimal risk.

6.9. It was acknowledged that increased transparency may not directly improve funding timelines. Clear communication will be required to support external expectations.

Societal Perspectives Pilot

6.10. The Committee was informed of the Societal Perspectives Pilot, which explores the potential application of a societal perspective in health assessments. The pilot involves collaboration with local and international experts and considers broader impacts—such as return to work and welfare benefits—that are not currently included in standard assessments.

7. Specialist Advisory Committee Record

October 2024 Cancer Treatments Specialist Advisory Committee Record

7.1. PTAC reviewed the records of the Cancer Treatments Specialist Advisory Committee meeting held on the 10th and 11th October 2024.

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

8. Update about proposal to fund emergency medicines used by PRIME and ambulances

8.1. Pharmac Staff presented an update on the PRIME (Primary Response in Medical Emergencies) medicines proposal to support the PRIME written material provided by Pharmac. The presentation outlined work to align medicine funding with the realities of trauma and emergency care delivery in the community, addressing gaps where not all PRIME medicines are currently funded for use outside hospital settings.

8.2. The Committee was asked to consider risks and mitigation strategies associated with the proposal.

8.3. The Committee noted that the PRIME medicines list comprises established trauma and emergency medicines appropriate for treating trauma and medical emergencies in the community. [redacted]

8.4. The Committee was informed that the proposal responds to requests from PRIME providers over a number of years.

8.5. The Committee discussed future additions to the PRIME list, noting feedback from Health NZ and Hato Hone St John regarding intravenous (IV) hydrocortisone. Members also discussed the risk of incremental medicine requests and the need for clear processes to manage these. Staff confirmed that the medicines used in trauma and medical emergencies in the community generally includes older, cost-effective medicines.

8.6. The Committee reviewed two additional community-funded indications for proposed medicines outside of PRIME scope:

8.6.1. IV tranexamic acid for postpartum haemorrhage, including for home births.

8.6.2. [redacted]

8.7. [redacted]

8.8. The Committee noted renewed interest from Health New Zealand in Pharmac being more closely connected to the funding of medicines for ambulance services. A paper is planned to be taken to Pharmac Board with a more fulsome briefing.

8.9. A map of PRIME sites will be shared with members post-meeting.

9. Foslevodopa / foscarbidopa for advanced Parkinson's Disease with severe motor fluctuations despite optimised alternative pharmacological treatment

Application

9.1. The Committee reviewed the application for foslevodopa / foscarbidopa (fosLD/fosCD) in the treatment of advanced Parkinson's Disease (aPD) with severe motor fluctuations despite optimised alternative pharmacological treatment (subsequently referred to as poorly managed aPD).

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 foslevodopa / foscarbidopa be funded for people with poorly managed aPD with a **medium priority**, subject to the following Special Authority criteria:

> **Initial application -** Advanced Parkinson's Disease
> Applications from any relevant practitioner. Approvals valid for 6 months meeting the following criteria:
> Both:
> 1. Patient has advanced Parkinson's disease with severe motor fluctuations despite optimised alternative pharmacological treatment; and
> 2. Apomorphine is unsuitable or patient is not responding to treatment with apomorphine.
>
> **Renewal** – Advanced Parkinson's disease
> Applications from any relevant practitioner**.** Approvals valid without further renewal for applications meeting the following criterion:
> 1. The patient is benefiting from treatment and treatment remains appropriate.

9.4. In making this recommendation, the Committee considered

9.4.1. The high health need of people with poorly managed aPD, who experience significant disability due to the impairment associated with motor fluctuations, dyskinesia during the ON-state, unpredictable OFF-states, acute akinesia, and dystonia.

9.4.2. The available evidence indicates fosLD/fosCD provides a meaningful health benefit that is sustained throughout the duration of treatment.

9.4.3. That fosLD/fosCD has an optimised pharmacokinetic profile compared to oral levodopa/carbidopa, delivering stable and continuous drug exposure which may reduce motor fluctuations.

9.4.4. FosLD/fosCD reduces the pill burden for patients on oral therapy and offers an alternative for individuals who do not respond to apomorphine or for whom apomorphine is unsuitable (e.g., contraindicated).

9.4.5. The significant proportion of people with aPD who discontinue apomorphine treatment (due to loss of efficacy, increased frailty, or the loss of a caregiver required to support administration) and thus have an unmet health need.

Discussion

Māori impact

9.5. The Committee discussed the impact of funding fosLD/fosCD for the treatment of poorly managed aPD on Māori health areas of focus and Māori health outcomes. The Committee noted the findings of Pitcher et al. Movement Disorders. 2018;33:1440-8, which report a lower prevalence of Parkinson's Disease among Māori compared to people of European or Asian descent. However, the Committee noted that this observation may be influenced by several important confounding factors, including under-diagnosis due to inequitable access to healthcare, differential treatment within the healthcare system, variations in the prevalence of protective and risk-related lifestyle factors, the presence of co-morbidities, and potential genetic differences (Alamri et al. Neurodegener Dis Manag. 2020;2:e000033).

9.6. The Committee also considered that there is a significant lack of research into the clinical presentation and progression of Parkinson's disease in Māori populations, resulting in uncertainty around specific impacts of the condition on Māori health outcomes.

Populations with high health needs

9.7. The Committee considered the high health need(s) of those with aPD 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 fosLD/fosCD on people who have been underserved by the health system.

9.7.1. The Committee did not identify any group with known inequitable health outcomes associated with aPD but noted that the lack of available evidence did not exclude the possible presence of these inequities.

9.7.2. The Committee noted that fosLD/fosCD requires access to specialist services and ongoing support from trained healthcare professionals. Members considered that this requirement may present additional barriers for priority populations, particularly those with reduced access to healthcare resources. This concern was noted to be especially relevant in rural communities.

Background

9.8. The Committee noted having previously reviewed an application for a levodopa / carbidopa intestinal gel (LCIG) for advanced Parkinson disease in February 2017.

9.9. The Committee was made aware that the supplier of LCIG had included LCIG in the economic modelling of their fosLD/fosCD funding application. The Committee noted a key assumption in that modelling was that fosLD/fosCD was similarly efficacious as LCIG.

Health need

9.10. The Committee noted that as Parkinson's disease progresses, individuals experience debilitating motor fluctuations: alternating periods of good motor control ("ON" time) and poor motor control ("OFF" time), which significantly impacts mobility and quality of life. The committee considered the health needs of those with aPD to be well documented in the previous consideration of LCIG (PTAC February 2017).

9.11. The Committee noted the target population, as with LCIG, was adults with aPD who experience severe motor fluctuations despite optimised pharmacological treatment. This includes individuals receiving combinations of oral therapies (e.g. levodopa, carbidopa, entacapone, pramipexole, or ropinirole) and, where appropriate, continuous subcutaneous apomorphine. The Committee considered that treatment approaches vary considerably

between clinicians, with some initiating dopamine agonists early to delay levodopa use, while others may use different sequences or omit certain agents altogether.

9.12. The Committee noted the majority of people with aPD and their carers are older adults. The Committee considered that the carer impact of Parkinson's disease was substantial, and many of those in the advanced stages of disease require around the clock care in residential settings.

9.13. The Committee considered a significant proportion of people discontinue apomorphine with reasons including loss of efficacy, adverse events (commonly hallucinations, skin reactions, confusions), increased frailty, and loss of a caregiver who would otherwise facilitate treatment. The Committee was made aware of a study that reported that 53% of participants discontinued apomorphine after a mean treatment time of 22 months (Camgrand et al. Parkinsonism Relat Disord. 2023;116:105859). However, the Committee noted that a significant proportion of those who discontinued in the study were using the therapy as a bridge to deep brain stimulation therapy, and approximated that around only 40% stopped because of adverse events or lack of efficacy. The Committee noted that apomorphine discontinuation rates were reported to be variable in Camgrand et al. 2023, and expressed caution and uncertainty in applying these estimates to the New Zealand context.

9.14. Overall, the Committee considered the limited alternative treatment options available for individuals with severe motor fluctuations despite optimised pharmacological treatment and identified an unmet health need for those with aPD who discontinue or are contraindicated to apomorphine.

Health benefit

9.15. The Committee noted that Australia (PBAC), Canada (CADTH), England/Wales (NICE), and Scotland (SME) recommended fosLD/fosCD for people with disabling motor fluctuations when available treatments did not provide satisfactory benefit.

9.16. The Committee noted that fosLD/CD is approved by Medsafe for advanced idiopathic Parkinson's disease with severe motor fluctuations despite optimised alternative pharmacological treatment (Medsafe Datasheet).

9.17. The Committee noted that continuous subcutaneous infusion with fosLD/fosCD provides an optimised pharmacokinetic profile compared to oral levodopa/carbidopa, delivering stable and continuous drug exposure (Rosebraugh et al. J Parkinsons Dis. 2021;11:1695-1702). The Committee noted that stable levodopa/carbidopa exposure may reduce motor fluctuations and prevent painful episodes of dystonia associated with the variable timing and pharmacokinetics of oral levodopa/carbidopa.

9.18. The Committee noted the phase three, double-blind, double-dummy, randomised controlled trial that provides primary evidence for the health benefits of fosLD/FosCD for aPD (Soileau et al. Lancet Neurol. 2022;21:1099-109). Participants received 12 weeks of treatment with either fosLD/fosCD (n=74) or oral levodopa/carbidopa (LD/CD) (n=67). Members noted that the study population had an average age of 66 years and experienced a mean daily OFF time of 6 hours.

9.18.1. The Committee noted that, compared with oral LD/CD, participants in the fosLD/fosCD arm had a significantly greater increase in daily ON time (mean change from baseline [SE] 2.72 [0.52] hours fosLD/CD vs 0.97 [0.50] hours oral LD/CD; p=0.0083) and a significantly greater reduction in OFF time (mean change from baseline [SE] -2.75 [0.50] hours fosLD/CD vs -0.96 [0.49] hours oral LD/CD; p=0.0054). The committee noted that the descriptive analysis was conducted in the intention to treat population.

9.18.2. The Committee noted that study discontinuations (fosLD/fosCD vs oral LD/CD: 22%

vs 1%, respectively) were mainly due to injection site reactions. The Committee also considered the occurrence of serious adverse events to be similar between arms and noted an increased incidence of hallucination in the fosLD/fosCD arm vs the oral LD/CD Arm (15% vs 3%, respectively).

9.18.3. The Committee noted that the trial publication did not report the proportion of participants who experienced treatment failure on apomorphine prior to study entry. The Committee considered that treatment failure with apomorphine was unlikely to be an effect modifier with respect to the treatment benefit of fosLD/fosCD.

9.18.4. Overall, the Committee considered this evidence to be of good quality, and the trial population was considered to be comparable to the New Zealand setting.

9.19. The Committee noted an additional phase 3, open-label, single-arm trial that provided key evidence for the health benefits of fosLD/fosCD in aPD over a longer trial period (Aldred et al. Neurol Ther. 2023;12:1937-58), where participants received fosLD/CD for 12 months (n=244).

9.19.1. The Committee considered the patient population to be comparable to the Soileau et al. 2022 phase 3 trial detailed above.

9.19.2. The Committee considered that for those who remained on treatment (n=137 completed treatment), fosLD/fosCD provided a treatment benefit with an increase in daily ON time (mean change from baseline [SD] 3.8 [3.3] hours) and decrease in daily OFF time (mean change from baseline -3.5 [3.1] hours) for the duration of the treatment period. Quality of life (QoL) outcomes (including sleep quality) were also noted to be improved from baseline. However, the Committee noted that it was unclear whether the final statistical analysis was conducted on an intention to treat basis, although members felt it appeared this was not the case. Given this, the Committee considered the potential influence of survivorship bias on the study outcomes and that the observed health benefits may only pertain to those who remained on treatment for the duration of the study.

9.19.3. The Committee noted that most adverse events were nonserious, and most commonly injection site reactions. The most common adverse events that led to study discontinuations were hallucination (4.1%), infusion site erythema (3.7%), infusion site cellulitis (3.7%), infusion site nodule (2.0%), and dyskinesia (2.0%).

9.19.4. Overall, the Committee considered that the trial population was comparable to the New Zealand population with aPD. However, the Committee noted concerns over the generalisability of the outcomes, specifically noting the risk of influence from survivorship bias.

9.20. The Committee was made aware of a publication reporting that the minimal clinically important difference (MCID) in OFF time in aPD is 1.3 hours (Hauser et al. Parkinsons Dis. 2014;1:467131). The Committee considered this estimate to be reasonable but noted the publication was specific to pramipexole, and there were several limitations in the MCID calculations.

9.21. The Committee considered that the evidence provided for fosLD/fosCD suggested similar efficacy to apomorphine and LCIG. Members considered that it was difficult to compare treatment persistence between these therapies without larger direct comparisons.

9.22. The Committee considered it likely that patients would experience a deterioration when discontinuing fosLD/fosCD, as the underlying condition will have progressed despite receiving the treatment.

Suitability

9.23. The Committee noted that fosLD/fosCD is administered via a portable pump as a continuous subcutaneous infusion, which can be initiated and discontinued in an

outpatient setting. The Committee noted that individualised dosing is required, similar to that used for continuous apomorphine, with healthcare professionals responsible for initiating therapy and calculating levodopa equivalent doses.

9.24. The Committee considered that a caregiver is often needed to manage the infusion, particularly for individuals with insufficient dexterity to self-administer. The Committee considered that, as with apomorphine, treatment persistence would likely depend on the ability and willingness of caregivers to administer treatment over time.

9.25. The Committee noted that fosLD/fosCD offers a reduced pill burden compared to oral therapies, which can be a significant challenge for people with Parkinson's disease. The Committee also noted fosLD/fosCD does not require a successful jejunostomy, as would be required for treatment with LCIG intestinal gel (although this medicine is not currently a funded treatment option).

Cost and savings

9.26. The Committee noted that funding fosLD/fosCD would lead to a requirement for additional specialist nurse time, as well as increased input from neurologists and geriatricians. The Committee considered this would present a challenge, noting the need for more specialist nurses in general, and difficulties maintaining skill certification and clinical competency for specialist nurses working in rural settings with lower patient volumes and potentially limited access to ongoing training.

9.27. The Committee noted that the supplier offered to provide support to people on treatment and training for initiating health care professionals but noted the uncertainty around the extent and duration of the resources provided. The Committee noted that nurse specialists in New Zealand receive support from the supplier of apomorphine to assist in managing patients receiving this treatment. However, members considered that such resources remain challenging to provide consistently, particularly in rural settings, regardless of supplier involvement.

9.28. The Committee considered that the vast majority of people initiating fosLD/fodCD would be people who had discontinued apomorphine due to intolerance or insufficient treatment benefit. The Committee considered that there was unlikely to be a large group of individuals currently receiving apomorphine, and experiencing a treatment benefit, who would switch immediately to receiving fosLD/fosCD if it were to be funded.

9.29. The Committee considered that there would be a small group of people (about 5% requiring an alternative to oral levodopa/carbidopa) who were contraindicated to apomorphine but not contraindicated to fosLD/fosCD. The Committee noted that shared contraindications for apomorphine and fosLD/fosCD included renal insufficiency, liver disease, unstable coronary heart disease, respiratory depression, central nervous system depression and certain psychiatric disorders. The Committee also noted that cerebrovascular disease and ischaemic heart disease were more severe contraindications for apomorphine than for fosLD/fosCD.

Funding criteria

9.30. The Committee considered that allowing any relevant practitioner to prescribe fosLD/fosCD may reduce barriers to accessing the treatment.

9.31. The Committee also noted that some people, such as those with contraindications to apomorphine, may benefit from earlier access to fosLD/fosCD, and therefore should be permitted access to treatment under the proposed Special Authority criteria.

Summary for assessment

9.32. The Committee considered that the table below summarises its interpretation of the most appropriate PICO table (population, intervention, comparator, outcomes) information for foslevodopa / foscarbidopa if it were to be funded in New Zealand for poorly managed aPD. 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 advanced Parkinson disease with severe motor fluctuations despite optimised alternative pharmacological treatment AND apomorphine injections are an unsuitable or inappropriate treatment option.
Intervention	Foslevodopa with foscarbidopa • Mean daily dose of foslevodopa of 2,347mg (equivalent of 1,666.6 mg levodopa) [M15-736] • This corresponds to 98.0% of people using 1 vial per day and 2.0% using 2 vials per day. An average of 1.02 vials consumed per day. • Treatment duration indefinite provided it is well-tolerated and the individual is benefitting from treatment. Foslevodopa with foscarbidopa is used as an adjunct to oral medications.
Comparator(s) (NZ context)	Oral medications for Parkinson disease (levodopa, carbidopa, catechol-O-methyl transferase[COMT] inhibitors)
Outcome(s)	Improved motor and non-motor symptom control • Reduced duration of 'off time' and improving performance as measured by Hoehn and Yahn scores. Improved symptom control is associated with improved health-related quality of life
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.	

10. Etonogestrel subdermal implant (Implanon NXT) for contraception

Application

10.1. The Committee reviewed the application for etonogestrel subdermal implant (Implanon NXT) for contraception.

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

Recommendation

10.3. The Committee **recommended** that etonogestrel subdermal implant (Implanon NXT) for contraception be listed if **cost neutral** to levonorgestrel implants (Jadelle).

10.4. In making this recommendation, the Committee:

10.4.1. Considered there to be a need for a range of contraceptive product options in New Zealand

10.4.2. Considered that the etonogestrel subdermal implant has a comparable efficacy to currently funded implant options and may have an increased suitability in some settings

10.4.3. Noted that the etonogestrel subdermal implant may be associated with higher rates of bleeding irregularities than currently funded implant options

10.4.4. Noted that the etonogestrel implant has a shorter duration of efficacy than currently funded hormone releasing long-acting reversible contraceptive options (three years compared to five years).

Discussion

Māori impact

10.5. The Committee discussed the impact of funding etonogestrel subdermal implants for contraception on Māori health areas of focus and Māori health outcomes. The Committee noted that Māori women have disproportionately reduced access, and poorer health outcomes, in the context of abortion care. Māori women also have higher odds of accessing less effective contraception compared to their NZ European counterparts (Parackal et al. Womens Health (Lond). 2023;19:17455057231161479). Members also considered that in the context of pregnancy, 'family planning' is a Western construct and many Māori families view pregnancy through a te ao Māori worldview, such as the concept of wairua.

Populations with high health needs

10.6. The Committee discussed the health need(s) of contraception 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 etonogestrel subdermal implants and considered:

10.6.1. Women living in rural areas of New Zealand experience reduced access to primary care (and subsequently contraception) and abortion care

10.6.2. Māori and Pacific women have higher odds of accessing less effective contraception compared to NZ European women (Parackal et al. 2023).

Background

10.7. The Committee noted that there are currently three hormone releasing long-acting reversible contraceptives (LARCs) funded in New Zealand, along with copper intra-uterine devices (IUDs) and six combined oral contraceptives (COCs). The hormonal LARCs funded include two IUDs (Jaydess and Mirena) and one subdermal implant (Jadelle).

10.8. The Committee noted that New Zealand has a maternal mortality rate of 7 deaths per 100,000 live births, and that the leading cause of maternal death is suicide (Elder et al. PHCC, 2024). The Committee noted that, although maternal death is relatively rare, there are significant risks associated with pregnancy.

10.9. The Committee noted that there has been an increase in the abortion rate in the last two years; however, this is considered to be due to service access improvements (Ministry of Health. 2024). Moreover, marked inequities of access to abortion care are still prominent for Māori women and women living in rural New Zealand communities (Ministry of Health. 2024).

10.10. The Committee noted the Whitley et al. J Womens Health (Larchmt). 2020;29:21-8 study of LARC use in New Zealand that reported a statistically significant association between increased LARC use and the decline in abortion rates.

10.11. The Committee noted a letter received from Sexual Wellbeing Aotearoa supporting the funding of etonogestrel subdermal implants in New Zealand.

Health need

10.12. The Committee considered that there is minimal unmet health need for contraceptive implants as the levonorgestrel implant is already funded.

10.13. The Committee considered that Māori, Pacific people and those in rural areas are less likely to be able to access primary care to receive treatment.

10.14. The Committee considered that there is a lack of data to suggest that the etonogestrel subdermal implant meets health needs where levonorgestrel implants were not tolerated, as side effects were likely to be the same with both implants.

Health benefit

10.15. The Committee noted that the etonogestrel subdermal implant consists of a single rod containing 68 mg of etonogestrel which has efficacy for up to three years. The Committee noted that this differs from currently funded levonorgestrel implant that consist of two rods containing levonorgestrel and has efficacy for up to five years.

10.16. The Committee noted the Funk et al. Contraception. 2005;71:319-26 single-arm clinical trial (n= 330) that investigated the safety and efficacy of etonogestrel subdermal implants. The trial reported no pregnancies. The Committee noted that 161 participants did not complete the two-year study duration. The most common reasons for discontinuation were bleeding pattern changes (n = 43; 13%) and other adverse events such as emotional lability (6.1%), weight increase (3.3%), depression (2.4%), and acne (1.5%). The Committee noted that the implant insertion time and removal time were 0.5 minutes (range 0.05-15 minutes) and 3.5 minutes (0.2-60 minutes), respectively. The Committee considered that the wide range in the insertion and removal times indicate that it is operator-dependent, and it is likely that those more experienced practitioners will be more efficient. The Committee noted that the return to normal menstrual cycles (in 88% of subjects) and to fertility (as indicated by post-treatment pregnancies) following removal of the implant was rapid which suggests that the chemical doesn't accumulate in the body.

10.17. The Committee noted the Monteiro-Dantas Reprod Health. 2007;4:11 randomised control trial (n = 111) that compared bone density over three years in people aged 19 to 43 receiving etonogestrel subdermal implants compared with those receiving levonorgestrel implants. The trial reported no difference in bone mineral density (BMD) between cohorts at 18 and 36 months. A reduction in BMD was observed at the distal radius in both groups, but no change in ultra-distal radius BMD in either group.

10.18. The Committee noted the Ali et al. Hum Reprod. 2016;31:2491-98 open-label randomised trial (n=1328) that compared etonogestrel-releasing subdermal implant with levonorgestrel-releasing subdermal implants over 3 years, with an extension to 5 years for some women using etonogestrel implants. The study reported no pregnancies between 3 to 5 years, however in either group, women using etonogestrel implants experienced higher rates of subjectively heavy bleeding with a risk ratio of 1.32 (95%CI 1.01, 1.73). The median removal time for etonogestrel implants was 60 seconds (95%CI 30.5, 117.5), 64 seconds less than for the levonorgestrel implants, which reported a median removal time of 124 seconds (77.0, 180.0).

10.19. The Committee noted the Bahamondes et al. Contraception. 2018;98:181-7 randomised trial (n=2,963) that compared etonogestrel-releasing subdermal implant and levonorgestrel-releasing subdermal implants with nonrandomised copper intrauterine device controls, to assess the effect on weight variations up to 3 years after placement. The Committee noted that at 36 months of use, etonogestrel and levonorgestrel implant users had similar significant mean weight increases of 3.0 kg (95% CI 2.5-3.5) and 2.9 kg (95% CI 2.4-3.4), respectively (p<.0001).

10.20. The Committee noted the Darney et al. Fertil Steril. 2009;91:1646-53 integrated analysis of 11 international non-comparative longitudinal observational studies of ENG (n = 942 people) reporting efficacy, safety and bleeding profile data. There were no pregnancies reported while the rod was in place, but six pregnancies occurred within the first 14 days after implant removal. Including these pregnancies, the 3-year cumulative reported pearl index (PI) measure of the contraceptive effectiveness was 0.38 in the 833 women aged up to 35 years at entry (equivalent to 38 in 10,000 women using the same contraceptive for one year becoming pregnant). The Committee noted that of the 330 women who discontinued from the study, 128 discontinued due to adverse events, and 105 discontinued due to bleeding irregularities. The Committee noted the limitations to the study including the use of small comparative studies.

10.21. The Committee noted the Bahamondes et al. Hum Reprod.2015;3:2527-38 multicentre randomised controlled trial of etonogestrel (n = 995) and levonorgestrel (n = 997) implants compared to a non-randomised cohort of matched copper-intrauterine device (n = 971) controls. The trial reported a three-year cumulative PI of 0.4 (95%CI 0.1, 1.4) for both

hormonal implants. A reported weight of over 70kg was considered unrelated to pregnancy risk.

10.22. The Committee noted the Blumental et al. Eur J Contracept Reprod Health Care. 2008;13 Suppl 1:29-36 integrated safety analysis of the same 11 international observational studies (n = 942 people) as Darney et al. 2009, which reported aggregated tolerability and clinical safety of the etonogestrel subdermal implant. The study reported an overall discontinuation rate of 32.7%, primarily attributed to adverse events (13.9%), bleeding irregularities (10.4%). There were 77 serious adverse events reported, of which 10 were considered to be either possibly, probably, or definitely drug-related. Insertion and removal times were reported as short, with few complications, none of which were major.

10.23. The Committee noted the Graesslin et al. Eur J Contracept Reprod Health Care. 2008;13 Suppl 1:4-12 integrated efficacy analysis of the 11 international clinical studies (n=923 people analysed) reporting contraceptive efficacy of etonogestrel subdermal implants. The study reported no in-treatment or pretreatment pregnancies; 50 posttreatment pregnancies (six occurring within 14 days of removal). The pregnancy rate over the nine-year marketing period was 0.049 (PI) and body weight was observed as non-influential to contraceptive efficacy.

10.24. The Committee also noted:

- Belgotti et al. Int J Gynaecol. Obstet. 2012;119:S531-S867 (not in public domain)
- Bhatia et al. Obstet Gynaecol India. 2011;61:422-5
- Mansour et al. Eur J Contracept Reprod Health Care. 2008;13 Suppl 1:13-28
- Meirik et al. Contraception. 2013;87:113-20

10.25. The Committee considered that the clinical evidence indicates that etonogestrel implants are effective at preventing pregnancies and that they are relatively safe, although they may cause more bleeding disturbances than levonorgestrel implants. The Committee considered that etonogestrel implants and levonorgestrel implants are associated with similar weight gain.

10.26. The Committee considered that evidence for a reduction in insertion and removal times in all noted studies was non-specific to clinician experience in the procedure. The Committee noted that there were small, non-significant differences in reported insertion and removal time in the studies between the etonogestrel subdermal implant and the levonorgestrel implant. The Committee considered that there are unlikely to be meaningful differences in insertion and removal times in clinical practice as the bulk of the variation in insertion and removal times tends to be operator-dependent.

10.27. The Committee considered that there is a need for a range of contraceptive product options in New Zealand.

10.28. The Committee considered that there are no clinically significant risks associated with etonogestrel subdermal implant use compared with currently funded implant options, and members anecdotally noted their clinical experience of a greater continuation rates for etonogestrel subdermal implants compared with currently funded implant options.

10.29. The Committee considered that the reduced active period (three years) of the etonogestrel implant may provide a better option for women who weigh more than 70kg, although noting the increased risk of venous thrombosis (VT) associated with users over 70kg. The Committee considered that the currently funded levonorgestrel implant is replaced every five years but is recommended to be replaced every four years in women who weigh more than 60kg to ensure continued efficacy.

10.30. Members were made aware of the Roke et al. J Prim Health Care. 2016;8:13-9 observational study that investigated women's experience of the Jadelle contraceptive implant (n =252). The study reported that 18% of women had their implant removed within the first year, with more than half of those citing bleeding pattern issues (usually prolonged bleeding) as the primary reason for removal. Aside from the 18% of women

who opted to remove the implant, the majority of women were satisfied with the contraceptive.

10.31. The Committee noted that there is no evidence on the effectiveness of etonogestrel implants in women where levonorgestrel implants are not tolerated. The Committee considered that etonogestrel and levonorgestrel implants have a similar side-effect profile, therefore women may experience similar side-effects with both of the implants.

10.32. The Committee considered that there is insufficient evidence to indicate that a single-rod implant reduces the rate of insertion and removal complications or time of the procedure. The Committee considered that women who experience rod removal complications are likely to receive a scan and be referred to a more experienced provider.

Suitability

10.33. The Committee noted the Sandle & Tuohy. N Z Med J. 2017;130(1454):40-6 qualitative study of the experiences and attitudes of service provides regarding the use of the levonorgestrel implant. The feedback reported was that the contraceptive was viewed as a good option due to its effectiveness, discreetness, and user independence. The Committee considered that the etonogestrel subdermal implant would be similarly favourable for service providers.

10.34. The Committee considered that most breakages of etonogestrel subdermal implants can be likely be resolved with a general practice clinic setting. The Committee noted that the etonogestrel subdermal implant is supplied in antiseptic packaging and requires less administrative equipment for insertion and removal, which may provide a suitability benefit – particularly for mobile clinics.

Cost and savings

10.35. The Committee considered that the uptake of etonogestrel implants may be high, and that it would not be limited to people who discontinue levonorgestrel implants for clinical reasons. The Committee considered that levonorgestrel implants would still be used due to the comparatively better side-effect profile.

10.36. The Committee noted that the etonogestrel subdermal implant needs to be replaced more frequently than the levonorgestrel implant, due to its reduced active period (three years), and that this needs to be factored into any budget impact and cost-utility analyses.

10.37. The Committee also considered that it is unlikely there would be a reduction in displacement and medical imaging requirements with use of the etonogestrel subdermal implant compared to currently funded implants, and that this would be primarily operator-dependent.

10.38. The Committee considered that if etonogestrel subdermal implants were offered alongside currently funded implant options, the market split would be observed as: current users of alternate implant options would continue that method, some women who could not use currently funded implant options would likely try the etonogestrel subdermal implant, and some practitioners may encourage the use of etonogestrel subdermal implants due to a perceived reduction in insertion and removal complication risk.

Summary for assessment

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

Population	Females of child-bearing potential who are looking for an alternative to a daily combined oral contraceptive pill, who may also be looking for a progestogen-only option and wish to avoid regular visits to a health care provider for renewal
Intervention	IMPLANON NXT etonogestrel 68mg subcutaneous implant, inserted subdermally, lasts up to three years.
Comparator(s) (NZ context)	Jadelle implant, levonorgestrel-releasing implant 75 mg x 2, which lasts up to 5 years
Outcome(s)	• Non-inferior efficacy • Discontinuation due to bleeding irregularity

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. Vanzacaftor, tezacaftor, deutivacaftor (VNZ, TEZ, D-IVA) for cystic fibrosis [aged six years and older], with F508del mutation(s) or another responsive mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene

Application

11.1. The Committee reviewed the application for Vanzacaftor, tezacaftor, deutivacaftor (VNZ, TEZ, D-IVA or VNZ) in the treatment of Cystic Fibrosis (CF) in people aged six years and over with F508del mutation(s) or another responsive mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. The Committee considered that the application related to people aged six years and older living with CF, and specifically addressed an unmet need for those who have a mutation that is unresponsive to ivacaftor or Trikafta (ELX, TEZ, IVA or ETI).

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 application for VNZ be listed with a **high priority** for the treatment of CF in people aged six years and older with a non-F508del mutation in the CFTR gene responsive to VNZ only (Non-F/VNZ-responsive) subject to the following Special Authority criteria:

Initial application

Applications only from a respiratory specialist or paediatrician. Approvals valid without further renewal unless notified.

All of the following:

1. Patient has been diagnosed with cystic fibrosis; and
2. Patient is 6 years of age or older; and
3. Either:
   - 3.1. Patient has two cystic fibrosis-causing mutations in the cystic fibrosis transmembrane regulator (CFTR) gene (one from each parental allele); or
   - 3.2. Patient has a sweat chloride value of at least 60mmol/L by quantitative pilocarpine iontophoresis or by Macroduct sweat collection system; * and
4. Either:
   - 4.1. Patient has a heterozygous or homozygous *F508del* mutation; or
   - 4.2. Patient has a mutation responsive to vanzacaftor/tezacaftor/deutivacaftor; and
5. The treatment is the sole funded cystic fibrosis transmembrane regulatory (CFTR) modulator therapy for this condition; and

6. Treatment with vanzacaftor/elexacaftor/deutivacaftor to be given concomitantly with standard therapy for this condition.

11.4. The Committee **recommended** that the application for VNZ for the treatment of CF in people aged six years and over with F508del mutation(s) (F/any) or another mutation in the CFTR gene responsive to ETI (non-F/ETI-responsive) be listed if **cost neutral** to ETI.

11.5. In making these recommendations, the Committee considered that:

11.5.1. There was greater health need for people with CF aged six years and over with a mutation in the CFTR gene responsive to VNZ only, as these people with CF were not currently receiving any CFTR genetic modulator treatment.

11.5.2. The Committee considered that significant interest would be expected from families of and patient support groups for people living with CF who are currently ineligible for CFTR gene modulator therapies.

11.5.3. The Committee noted that a Medsafe registration application had been lodged by the supplier with approval anticipated July 2025.

11.5.4. The Committee noted that the evidence provided as part of the application, including key clinical trials involving VNZ, were initiated by the supplier. The Committee however considered that each trial was of good quality and power with adequate sample size.

Discussion

Māori health impact

11.6. This application relates to respiratory health | romaha ora, which is a Pharmac Hauora Arotahi | Māori Health Area of Focus. The Committee noted that 10% of people with CF are Māori or Pacific (approx. 55 patients) and that Māori health needs and response to treatment is known. The Committee noted that the health needs of Māori are likely higher than NZ European/Other ethnic groups. The Committee considered that there are multiple studies being undertaken at the time of discussion and that Starship Children's Hospital patients are enrolled in clinical trials, with Māori being well represented in the study population.

Populations with high health needs

11.7. The Committee noted that 10% of people with CF in NZ are Māori or Pacific peoples (approx. 55 patients). The Committee considered that it was uncertain as to whether Māori and Pacific peoples were more or less likely to have CFTR mutations not amenable to treatment with ETI or ivacaftor. The Committee considered that the health needs of Māori and Pacific peoples are likely higher than NZ European/Other ethnic groups.

11.8. The Committee considered the Government Policy Statement on Health 2024-27 and noted that among the priority populations identified, people with CF living rurally may have an additional burden of both inpatient admissions and outpatient visits to manage their condition.

11.9. The Committee noted that ethnicity and socioeconomic status were not included as variables in the evidence used to inform the application.

Background

11.10. ETI (Trikafta) has been funded for people aged six years and above with CF, subject to eligibility criteria, from 1 April 2023 (Notification letter here).

11.11. A consumer-led application to expand the Pharmaceutical Schedule listing for ivacaftor (Kalydeco), to include patients with at least one mutation that has demonstrated responsiveness to ivacaftor is currently under assessment (Pharmac application P-001730).

11.12. A submission to expand the Pharmaceutical Schedule listing for ETI, to include patients

aged 2 to 5 years is currently under assessment (Pharmac application P-002024).

Health Need

11.13. The health need of people living with CF has been documented in previous advisory committee records (Respiratory Advisory Committee April 2022 and PTAC November 2021) and remains high. CF is a multisystem disease with shortened life expectancy if left untreated. The key feature of CF is an inherited (from both parents) defect in the CFTR protein, leading to production and retention of thick secretions, impacting the multiple organ systems, including the respiratory system, as people become colonised with microorganisms and frequently present to hospital with pulmonary exacerbations of their condition.

11.14. The Committee noted three relevant groups of patients with CF who will have mutations in the CFTR gene responsive to VNZ:

11.14.1. Group 1: People with CF aged six years and over with at least one F508del mutation in the CFTR gene (F/any – ETI responsive).

11.14.2. Group 2: People with CF aged six years and over with a non-F508del mutation in the CFTR gene responsive to ETI (Non-F/ETI-responsive).

11.14.3. Group 3: People with CF aged six years and over with a non-F508del mutation in the CFTR gene responsive to VNZ only (Non-F/VNZ-responsive only).

11.15. The Committee considered that people with mutations responsive to VNZ only (Group 3) have different health needs and treatment benefits compared with populations with mutations responsive to ETI (Groups 1 and 2). The Committee noted that without treatment of any kind, the life expectancy of people living with CF, with a mutation in the CFTR gene not responsive to ETI, is significantly reduced.

11.15.1. The Committee noted that the supplier's application projected an anticipated improvement in life expectancy with VNZ over ETI of 1.7 years, and the supplier stated an overall gain of 33.6 life years, when compared with best supportive care for Group 3 in the application.

11.16. The Committee considered that the applicant's estimate of between 1 to 2 patients per year having mutations in the CFTR gene responsive to VNZ only was uncertain, as CFTR genetic mutations are unknown in people who have not been genotyped. The Committee noted that genotyping in newly diagnosed patients is routine, thus some patients with responsive mutations may be older children or adults who have been living with CF for some time and may be more likely to have a mild, subclinical form of the condition due to phenotypic variation. The Committee considered that there was uncertainty in how many of these rare cases would respond to VNZ. The Committee also noted that the current Special Authority Criteria for ETI tracked FDA data that continues to be updated with novel mutations for the CFTR gene, and therefore there is potential for further mutations to become eligible in future, especially if using the same Special Authority criteria for VNZ.

11.17. The Committee noted the Respiratory Advisory Committee Meeting records from 27 April 2022, which identified that proposed strict access criteria would reduce the risk of access being extended less appropriately to (1.) people with a milder clinical phenotype of CF and (2.) those who may not benefit. PTAC understood this to be where the likelihood of response to treatment is determined by whether the genotype has been shown *in vivo*, *or in* vitro, to respond to ETI, with a risk of administering VNZ and assuming benefit for a patient group that is phenotypically responsive to VNZ but whose genotype has not yet been shown as responsive to other CF treatments.

11.18. The Committee considered the following publications detailing the health needs of people with CF and impacts on family, whānau and wider society:

- Daly et al. Ther Adv Respir Dis. 2022;24:16
- Suthoff et al. J. Pediatr. 2019;215:164-71
- Chudleigh et al. J. Pediatr. 2019;210:112-7

- Wojtaszczyk et al. Palliat Support Care. 2017;16:732-40
- Chevreul et al. Eur J Health Econ. 2016;17:7-18
- Chevreul et al. J Cyst Fibros. 2015;14:384-91.

Health benefit

11.19. The Committee considered the Zemanick et al. Cys Fib. 2025;24(2):246-54 pooled analysis of phase 3 CFTR modulator studies, which evaluated the relationship between attained values of sweat chloride and improvements in lung function, body mass index (BMI), patient reported outcomes, pulmonary exacerbations, and lung function change over time. CFTR modulator treatment was associated with reductions in sweat chloride concentration level (SwCl in mmol/L), and the Committee noted that a SwCl level of 60mmol/L or more is needed to diagnose CF. The analysis reported that FEV1 was improved if SwCl <30mmol/L; BMI increased, being a marker of improved general wellbeing, in CF patients with SwCl < 30mmol/L; and FEV1 deteriorated if SwCl >60 mmol/L. The authors identified that in phase 3 clinical trials of CFTR modulators, SwCl values of <30 mmol/L and ≥30 to <60 mmol/L in people with CF following CFTR modulator treatment were associated with better clinical outcomes than SwCl ≥60 to <80 mmol/L and ≥80 mmol/L.

11.20. The Committee considered the RIDGELINE Trial, a phase 3, single arm, international, multicentre study of VNZ in children with CF aged 6 to 11 years with at least one ETI-responsive mutation in the CFTR gene (Hoppe et al. Lancet Resp Med. 2025;13:3:244-55). The authors reported that treatment with VNZ led to further decreases in mean SwCl and an increase in the proportion of participants with SwCl below 60mmol/L and 30mmol/L, compared with baseline established on ETI.

11.20.1. Committee members noted that Figure 2A, showing absolute change in least squares mean FEV1 % predicted (percentage points), showed no statistically significant difference between groups at 24 weeks follow up, and considered that conclusions from this data were difficult to draw.

11.20.2. The Committee noted Figures 2B and 2C showed that the absolute change in least squares mean SwCl to week 24 was -8.6mmol/L (95% CI, -11.0, -6.3), with 94.9% (95% CI, 87.4 to 98.6) of participants having SwCl below 60mmol/L and 52.6% (40.9 to 64.0) having SwCl below 30mmol/L through week 24, compared with 84.4% and 39.0%, respectively, at baseline. The Committee considered that there was a significant reduction in SwCl over the course of the trial in patients taking VNZ compared with those taking ETI, but extrapolation of meaningful clinical benefit using SwCl only beyond 24 weeks could not be inferred.

11.21. The Committee noted the following unpublished conference poster presentations included in the application as supporting the previous point:

- Poster 122 from Hoppe et al. (2025) on the safety and efficacy of Vanzacaftor/Tezacaftor/Deutivacaftor (VNZ/TEZ/D-IVA) in Children 6 Through 11 Years of Age with Cystic Fibrosis.

11.22. The Committee considered the reporting of SKYLINE Trials: VX20-121–102 and VX20-121-103 (Keating et al. Lancet Resp Med. 2025;13:3:256-71). These were two phase 3, randomised, double-blind, active-controlled, parallel-group, international multicentre studies in people with CF aged 12 years and over. The studies differed by participant mutations, being either (1) heterozygous for F508del with a minimal function mutation (F/MF) (Study 102, n = 398) or (2) homozygous for F508del, heterozygous for F508del with a gating (F/G) or residual function (F/RF) mutation or at least 1 other ETI-responsive CFTR mutation and no F508del mutation (non F/ETI-responsive) (Study 103, n = 573). Members noted participants in Study 102 had a clinically worse phenotype. VNZ was reportedly non inferior to ETI for absolute change in ppFEV1 (percentage predicted) from baseline. SwCl reductions were observed in patients receiving VNZ compared with ETI and in patients with minimal functional mutations. Members noted the graph (Figure 2 in Keating et al. 2025) indicated SwCl reducing more with VNZ but this effect was greater in

Study 103 with the ETI-responsive group. Members considered the studies as applicable to the New Zealand context, noting that patients from Auckland had been enrolled and participated in the studies.

11.23. The Committee considered the health benefits of VNZ compared to ETI in people eligible for ETI treatment. The Committee considered that while VNZ was associated with greater reduction in SwCl, evidence linking this to clinically meaningful outcomes is limited, and there is a lack of long-term data to support definitive conclusions. Overall, the Committee considered that repeated SwCl measurements following diagnosis were not routine in clinical practice and protocols used to guide CF care in NZ. The Committee noted the Respiratory Advisory Committee in April 2022 considered that sweat chloride testing accessibility is variable, and some patients may have to travel distances to access testing. PTAC considered that there is a lack of data collection and analysis in NZ that correlates SwCl with disease progression and outcomes and that this data is unlikely to be collected and inform clinical practice in the foreseeable future. Therefore, the Committee considered it is difficult to apply SwCl measurements to CF outcomes in NZ.

11.24. The Committee noted there is likely to be wider health benefits to the patients if pulmonary exacerbations of CF were reduced. The Committee noted that hospitalisations for pulmonary exacerbations typically require two or more weeks of inpatient management with intravenous antibiotic therapy.

11.25. The Committee considered that the treatment effect would be meaningful for patients but also for caregivers, whānau, families and communities, particularly for people with CF who cannot take funded genetic modulator treatments. The Committee considered the care burden from providing best supportive cares to this patient group to be substantial, and that the benefit from reducing supportive cares would have significant positive impacts for whānau, caregivers, parents, and families.

11.26. The Committee considered there was no evidence documenting treatment benefit in the two- to five 5-year-old age group for VNZ compared to ETI.

11.26.1. The Committee was made aware of emerging evidence in the zero-to-two-year age group of slowed disease progression and considered there is rapidly evolving evidence of the effect from neonate onwards.

11.26.2. The Committee also noted that one of the studies in the application included children aged 6 to 11 years (Hoppe et al., 2025).

11.26.3. However, the Committee considered that initiating treatment earlier may reduce the risk of developing bronchiectasis and other complications associated with cystic fibrosis, including respiratory tract colonisation by common pathogens.

11.26.4. The Committee identified the Crestline study (currently in progress), which investigates commencing CFTR modulator treatment as early as possible to improve health outcomes and prevent progression of disease.

11.27. The Committee considered that the adverse effect profile of VNZ was similar to ETI.

11.27.1. The Committee noted Uluer et al. Lancet. Resp Med. 2023;11:6:550-62 (Study 101), which examined the safety of VNZ in adults. The study, which used multiple arms with different dosing of VNZ and no comparator arm that had ETI, did not identify increased safety concerns. The Committee considered that there were no additional concerns about drug safety.

Suitability

11.28. The Committee noted that current CFTR modulators are administered orally twice daily with food, whereas VNZ is taken orally once daily with food.

11.29. The Committee considered that the treatment appeared to be acceptable to patients, with for instance Hoppe et al. 2025 *(unpublished data)* reporting [redacted] of 6 to 11 year old participants indicating they liked the treatment very much as assessed by the Modified Facial Hedonic Scale.

11.30. The Committee noted that individuals with CF are accustomed to taking multiple tablets from a very young age, particularly from best supportive treatments, for example pancreatic enzymes. There is additional polypharmacy from best supportive cares such as nebulised treatments and supplemental feeds. The Committee noted that VNZ has weight-based dosing of 2 to 3 tablets daily with a cut off weight of 40Kg. As such, CFTR gene modulator treatments such as ETI tablets contribute a small proportion to their overall daily tablet burden. Therefore, the Committee considered the reduced dosing frequency of VNZ compared to ETI may not represent a significant advantage for this population.

11.31. The Committee noted that adolescents and young adults may prefer the once daily dosing regimen of VNZ, and people in this age group are more likely to be non-adherent. Members noted that the concept of 'relative forgiveness' (Assawasuwannakit et al. CPT Pharmacometrics Syst Pharmacol. 2015;4:3:e00004) may be used to describe adherence in this context, where 'forgiveness' refers to how sensitive or robust therapeutic outcomes are to common patterns of imperfect adherence.

11.32. The Committee noted the Poster 120 'Vanzacaftor/Tezacaftor/Deutivacaftor in Adolescents and Adults with Cystic Fibrosis: Results from Two Randomized, Active-Controlled Phase 3 Trials' unpublished conference poster presentation by Keating et al. (2025) included in the application. The Committee considered that this poster did not list any concerns about non-adherence.

11.33. The Committee noted the reduced shelf life of VNZ of 24 months from the date of manufacture when stored at controlled room temperature (FDA. NDA Approval record. 2024), compared to ETI with a shelf life of 36 months (see Medsafe Data Sheet for further information). However, members considered this reduced shelf life may change as the drug development process progresses.

11.34. The Committee discussed the importance of patient choice, particularly in giving people an additional treatment option if they experienced medication related adverse effects with VNZ. The Committee noted the analysis by Keating et al. 2025 reported no specific concerns about treatment non-adherence. While Members acknowledged that patients value having options, they also emphasised the influential role of clinical guidance in treatment decisions. The Committee considered that, given the widespread positive reception among patients to ETI, patients would likely require significant reassurance that VNZ would offer them additional benefit or be at least non-inferior compared with ETI before considering a switch in treatment.

11.35. The Committee considered that it would have been preferable for Pharmac to have sought patient perspectives on the suitability of VNZ in comparison to ETI prior to the PTAC meeting, perhaps as part of the CF Registry data set requested by the applicant.

Costs and savings

11.36. The Committee considered that the patient numbers estimate provided by the supplier was reasonable. It included projections for both the incident and prevalent populations.

11.37. The Committee noted the supplier's assumption that 95% of people currently receiving ETI would likely switch to VNZ, while those on ivacaftor would not. However, the Committee considered it unlikely that patients on ETI or ivacaftor would switch unless VNZ demonstrated a clinically significant treatment benefit. The Committee noted that the 33 patients currently receiving VNZ as part of a clinical trial would be likely to transfer to funded treatment, if VNZ became funded, at a rate of around 11 patients per year. The Committee considered that the most likely incentive for current patients on ETI to change therapy would be once daily dosing with VNZ, but this was not expected to be a major factor influencing patient behaviour.

11.38. The Committee considered that the direct treatment costs of VNZ would be more expensive to fund than ETI, but other health-sector related expenditure, such as hospitalisations and other medications, would remain the same for those who switched from ETI to VNZ.

11.39. Members considered that any health system savings (eg. due to reduced hospitalisations) estimated by the supplier would apply mainly to newly eligible patients, assuming the projections were accurate.

11.40. The Committee considered that patients with comparable ppFEV1 outcomes would likely experience similar health-related quality of life, regardless of the treatment option they receive.

General discussion points

11.41. The Committee noted that internationally:

11.41.1. the Pharmaceutical Benefits Advisory Committee (PBAC) in Australia would be considering VNZ at its upcoming July 2025 meeting (Agenda link here)

11.41.2. the National Institute of Health and Care Excellence (NICE) in England/Wales had selected VNZ for assessment through its Technical Appraisal programme, with an expected date of publication of 21 August 2025 (NICE. Vanzacaftor–tezacaftor–deutivacaftor for treating cystic fibrosis with 1 or more F508del mutations in the CFTR gene in people aged 6 years and over [ID6372]. Last accessed 30 May 2025)

11.41.3. Canada's Drug Agency (CDA-AMC) had not yet assessed VNZ

11.41.4. the Scottish Medicines Consortium (SMC) had not yet been reported as assessing VNZ for CF.

11.42. Regarding any potential open listing for VNZ, the Committee noted that the diagnostic workup for CF is well documented in New Zealand (NZ) guidelines and is procedurally consistent. The Committee also noted that the CF population has a stable incidence in NZ. The Committee considered that open listing would be perceived differently by people, and that there were significantly different implications for those patients not able to currently access treatment, compared to those switching treatment regimens from ETI or ivacaftor to VNZ. However, the Committee considered that there was no strong reason not to consider an open listing for VNZ in people with CF aged six years or older who have a mutation that is not responsive to ETI.

Summary for assessment

11.43. The Committee considered that the PICO table below reflected the intended population, intervention, comparator, and outcomes) for the application. 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 may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	**Group 1:** People with CF aged six years and over with at least one F508del mutation in the CFTR gene (F/any) *90% of eligible population (CF aged ≥six years, 380 patients)*	**Group 2:** People with CF aged six years and over with a non-F508del mutation in the CFTR gene but is responsive to ELX/TEZ/IVA (Non-F/ETI-responsive and VNZ-responsive) *9.7% of eligible population (41 patients)*	**Group 3:** People with CF aged six years and over with a non-F508del mutation in the CFTR gene responsive to VNZ/TEZ/D-IVA only (Non-F/VNZ-responsive) 0.3% of *eligible population (1-2 patients)*
	Safety and efficacy of ELX/TEZ/IVA in children aged less than six years has not been established.		
Intervention	VNZ/TEZ/D-IVA co-administered with best supportive care^ - Once daily dose provided as tablets taken with fat-containing meals - Dose based on weight, with two fixed-dose combinations available for people aged		

<table>
<tr><td></td><td colspan="2">six years and older:
○ Weight < 40kg:
Three tablets once daily, each containing 4 mg vanzacaftor, 20 mg tezacaftor and 50 mg deutivacaftor
Each pack contains 84 tablets, constituting a 4-week supply.
○ Weight ≥ 40kg:
Two tablets once daily, each containing 10 mg vanzacaftor, 50 mg tezacaftor and 125 mg deutivacaftor.
Each pack contains 56 tablets, constituting a 4-week supply.
- Continue treatment for the lifetime of the patient or until clinical decision made to reduce dose or stop treatment.
- High adherence rate assumed by supplier (95%)</td></tr>
<tr><td>Comparator(s)
(NZ context)</td><td>ELX/TEZ/IVA plus best supportive care^ (Group 1 and 2 patients are eligible for at least one funded CFTR modulator)
A small subset of these populations who have a gating genotype will also be eligible for ivacaftor treatment; however, it is assumed that ELX/TEX/IVA will be the preferred treatment choice.</td><td>Best supportive care^
(Group 3 patients are not eligible for any funded CFTR modulators)</td></tr>
<tr><td>Outcome(s)</td><td colspan="2">The key therapeutic intent of VNZ/TEZ/D-IVA is to improve overall survival and quality of life by stopping disease progression.
Therefore, the most relevant clinical outcomes for this assessment are:
• health-related quality of life
• overall survival
• adverse effects of treatment.
The outcomes measured in the trials provided by the supplier include:
• change in sweat chloride (SwCl)
• change in percent predicted forced expiratory volume (ppFEV1)
• change in lung function (measured as $LCI_{2.5}$)
• frequency of pulmonary exacerbations (PEx) and CF-related hospitalisations
• change in Cystic Fibrosis Questionnaire-Revised (CFQ-R) score (Child's version)
• change in body mass index (BMI), weight, height, and related z-scores.
It is unclear to what extent which of the outcomes measured in the VNZ/TEZ/D-IVA trials correspond to long-term clinical outcomes.</td></tr>
<tr><td colspan="3">^ Best supportive care includes treatments that manage the symptoms and complications of CF: mucolytics, osmotic agents, antibiotics, bronchodilators, enzyme and vitamin replacements and supplements, and chest physiotherapy (Respiratory Advisory Committee, August 2021

<u>Table definitions:</u>
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.</td></tr>
</table>

12. Secukinumab for moderate to severe hidradenitis suppurativa, first-line biologic treatment and second-line biologic treatment

Application

12.1. The Committee reviewed the application for secukinumab in the treatment of moderate to

severe hidradenitis suppurativa (acne inversa), in the first-line or second-line biologic setting.

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 secukinumab in the first line biologic setting for hidradenitis suppurativa be **declined**.

12.3.1. In making its recommendation, the Committee considered that secukinumab has inferior efficacy compared to other treatments currently funded in the first line biologic setting of hidradenitis suppurativa.

12.4. The Committee **recommended** that secukinumab in the second line biologic setting for hidradenitis suppurativa be funded with a **high priority** subject to the following Special Authority criteria:

> **Initial application — (Hidradenitis suppurativa)** from any relevant practitioner on the recommendation of a dermatologist. Approvals valid for 4 months for applications meeting the following criteria:
>
> All of the following:
> 1. Patient has hidradenitis suppurativa Hurley Stage II or Hurley Stage III lesions in distinct anatomic areas; and
> 2. Patient has 3 or more active lesions; and
> 3. Either:
>   3.1. Patient has tried, but experienced an inadequate response to at least a 90-day trial of systemic antibiotics; or
>   3.2. Patient has experienced intolerable side effects with or has contraindications to relevant systemic antibiotic treatments; and
> 4. Either:
>   4.1. Patient has received an inadequate response or loss of response to treatment with adalimumab; or
>
>   4.2. Patient has experienced intolerable side effects with or has contraindications to adalimumab; and
> 5. The patient has a Dermatology Life Quality Index (DLQI) score of 10 or more and the assessment is no more than 1 month old at time of application.
>
> **Renewal — (Hidradenitis suppurativa**) from any relevant practitioner. Approvals valid for 2 years for applications meeting the following criteria:
> Both:
> 1. The patient has experienced a reduction in active lesions (eg inflammatory nodules, abscesses, draining fistulae) of 25% or more from baseline; and
> 2. The patient has experienced a DLQI improvement of 4 or more from baseline.

12.5. In making its recommendation, the Committee:

12.5.1. Noted the high unmet need for individuals for whom adalimumab is ineffective and acknowledged the need for additional treatment options for hidradenitis suppurativa (HS) in the second-line biologic setting.

12.5.2. Considered that the pivotal trials were of high quality and presented a low risk of bias, but that evidence supporting two-weekly (Q2W) treatment compared to four-weekly (Q4W) treatment was weak.

12.5.3. Considered that secukinumab is less effective than adalimumab in first-line biologic treatment, but is more effective than placebo (ie. best supportive care in the absence of other specific treatment) in the second-line biologic setting.

12.6. The Committee considered that the access criteria in the Special Authority for adalimumab for hidradenitis suppurativa should be updated to reflect the proposed special authority criteria for secukinumab in terms of authorised prescribers, ie adalimumab should be available from any relevant practitioner on the recommendation of a dermatologist, with renewals by any relevant practitioner.

Discussion

Māori impact

12.7. The Committee discussed the impact of funding secukinumab for the treatment of HS on Māori health areas of focus and Māori health outcomes. The Committee noted that while HS prevalence in Māori is unknown, there may be an increased prevalence due to several factors. Comorbidities of HS often including obesity and diabetes (Del Duca et al. Int J Mol Sci. 2020;21:8436; Malvaso et al. Pharmaceutics. 2023;15:2450; Peterson et al. Dermatology. 2020;236:413-20), likewise with the correlation between smoking and the pathophysiology of HS, where smoking rates are higher in Māori than other ethnicities (Ministry of Health, 2015).

Populations with high health needs

12.8. The Committee discussed the health need(s) of HS 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, and also discussed for people in these populations the potential impact of any funding of secukinumab for HS:

12.9. The Committee was made aware of a cross-sectional study of 65,766 dermatology patients in California, U.S.A, that examined the relationship between socioeconomic status (SES) and the odds of being newly diagnosed with HS, reporting increased age/sex/race/ethnicity-adjusted odds ratios for lower-SES neighbourhood compared with higher-SES neighbourhoods (Chang et al. JAMA Dermatol. 20254:e251190).

Background

12.10. The Committee noted that adalimumab is funded in New Zealand for people with HS, and provides effective treatment in the first-line setting in terms of improvements in health-related quality of life (HRQoL) and clinical symptoms (measured by proportions of people who experienced a Hidradenitis Suppurativa Clinical Response (HiSCR), ie a ≥50% reduction in abscess and inflammatory nodule count, with no increase in abscess and draining fistula counts relative to baseline) (Hafner et al. J Eur Dermatol Venerol. 2021;35:2277-84).

12.11. The Committee noted that secukinumab is a fully human IG1/kappa monoclonal antibody directed against IL-17.

Health need

12.12. The Committee noted that although there is a lack of New Zealand-specific data for HS prevalence, Australia has a prevalence of 0.67%, compared to a 1% worldwide prevalence (Maarouf et al. J Dermatolog Treat. 2018;29:441-49).

12.13. The Committee noted the current treatment landscape for HS patients in New Zealand, where adalimumab is the first-line treatment and the second-line treatment is best supportive care, including topical antiseptics, oral antibiotics and surgery when required. The Committee considered that approximately 60% of individuals receive HiSCR within 12 months of using adalimumab, indicating an insufficient effect in approximately 40% of individuals (Khosravi et al. J Am Acad Dermatol. 2021 May;84(5):1406-09). Among those with an early response to adalimumab (12 weeks), the average duration of adalimumab use is approximately four years, after which the Committee understood the effectiveness of adalimumab wanes appreciably for many individuals. The Committee recognised the unmet need among HS patients for whom adalimumab is ineffective.

12.14. The Committee noted HS is a chronic disease characterised by initial inflammation of hair follicles in the apocrine gland-bearing regions (underarms, under the breasts, inner thighs, groin and buttocks), which subsequently develop into painful nodules or subcutaneous boils. The disease is categorised into three severity stages, known as Hurley stages I, II, and III. The Committee understood that after reaching Hurley stage II, patients take on average two years to progress to Hurley stage III.

12.15. The Committee noted that most individuals with HS are relatively young, with pivotal

clinical trials having 60% of participants under 40 years of age. Individuals with HS also tend to have higher body mass indexes, are current or former smokers (67% in pivotal clinical trials), and approximately one third of disease burdened individuals have a family history of HS. The Committee noted that whilst being overweight is a risk factor for HS, reverse causality does not necessarily exist, and there is no evidence to support that weight loss reduces the severity of HS symptoms. The majority of people with HS receive antibiotic treatment, and approximately 40% of pivotal clinical trial participants required surgical intervention.

12.16. The Committee noted that HS is more frequently observed in women from western countries and in African Americans (Polaskey & Chovatiya. JEADV Clin Pract. 2024;3:945-61). However, this increased frequency has not been observed on the African continent.

12.17. The Committee noted the significant disutility associated with HS and noted a Danish study reporting individuals with HS having an average EQ-5D health utility of 0.705 compared to the population average of 0.887 (Riis et al. Acta Derm Venereol. 2016;96:222-6).

Health benefit

12.18. The Committee noted Kimball et al. Lancet. 2023;401:747-61, a phase-3, randomised, double-blind, placebo controlled, parallel group trial (n = 1084) investigating the efficacy of secukinumab compared to placebo in moderate-to-severe HS (Hurley stage II-III) among individuals who had either previously received a biologic or were treatment naïve. The two parallel trials included in the publication were SUNSHINE and SUNRISE.

12.18.1. The Committee noted that the randomised placebo-controlled segment of the trial arms ran for 16 weeks, after which the placebo group was switched to active treatment. The Committee considered that the 16 weeks duration was a relatively short time.

12.18.2. The primary outcome reported in both trials was the proportion of participants who experienced HiSCR (the ≥50% reduction in abscess and inflammatory nodule count and with no increase in abscess and draining fistula counts relative to baseline) at week 16. Secondary outcomes included changes from baseline in abscess and inflammatory nodule count (AN), HS flares, the proportion of participants with a 30% or greater reduction of two units or more from baseline using the Global Assessment of Skin Pain on a continuous numeric rating scale (NRS30), and health related quality of life (HRQoL) measured using the Dermatology Life Quality Index (DLQI) and EQ-5D visual analogue scale (VAS).

12.18.3. The Committee noted the following outcomes from the SUNSHINE and SUNRISE trials:

- HiSCR: At 16 weeks, the total mean change in HiSCR scores (ie difference between change experienced by secukinumab groups versus changes experienced by placebo groups) ranged from 8 to 14% over the four study/dose frequency couplets (SUNSHINE secukinumab Q2W vs. placebo, SUNRISE secukinumab Q2W vs. placebo, SUNSHINE secukinumab Q4W vs. placebo, SUNRISE secukinumab Q4W vs. placebo). These changes were statistically significant for all comparisons except the four-weekly dosing (Q4W) group in the SUNSHINE trial.
- AN: At 16 weeks, the total mean change in AN count ranged from 8 to 14%. These changes were statistically significant for all comparisons except the Q4W group in the SUNSHINE trial.
- Flares: At 16 weeks, the total mean change in proportion of individuals with flares ranged from 6 to 14%. These changes were statistically significant in the two-weekly dosing (Q2W) group in the SUNSHINE trial and the Q4W group in the SUNRISE trial, but non-significant in the Q2W SUNRISE and Q4W

SUNSHINE groups.

- NRS30: At 16 weeks, the total mean change in NRS30 ratings ranged from 10 to 14%. These changes were statistically significant in the Q2W groups in both trials, but not the Q4W groups.
- DLQI: At 16 weeks, all active treatment groups experienced marked improvement from baseline compared to the placebo groups. After the placebo group transferred to active treatment with secukinumab, improvements in DLQI response were observed.
- EQ-5D VAS: At 16 weeks, all active treatment groups experienced a slight improvement from baseline compared to the placebo groups.

12.18.4. The Committee noted that the EQ-5D VAS scale is not dermatology-specific, and considered the results from the DLQI to be of higher clinical relevance.

12.18.5. The Committee noted that the in pivotal trials, all participants were instructed to use topical antiseptics on affected areas. Additionally, the Committee noted that 10 to 14% of patients in both the secukinumab and placebo groups were receiving maintenance oral antibiotics.

12.18.6. The Committee noted that adverse event (AE) and serious adverse event (SAE) reporting across the two trials was similar between treatment and placebo groups. However, two cases of inflammatory bowel disease (IBD) were identified in the treatment arms.

12.19. The Committee noted the Zouboulis et al. Br J Dermatol. 2024;190:836-45 analysis of efficacy and safety in participants with previous biologic exposure from the SUNSHINE and SUNRISE trials. For second-line use, week-16 HiSCR scores of both the Q2W and Q4W groups were not significantly different from the placebo groups' (Q2W vs. placebo: OR 1.60 (95% CI 0.83, 3.08); p=0.19 calculable from data in the published paper; and Q4W vs. placebo: OR 1.67 (95% CI 0.86, 3.22); p=0.15 calculable from data in the published paper). However, the week-16 AN and NRS30 differences between placebo and active treatment groups were statistically significant, although differences for HS flares were not.

12.20. The Committee noted the Kimball et al. N Engl J Med 2016;375:422-34 phase 3, double-blinded, placebo-controlled, randomised clinical trials; PIONEER I and PIONEER 2. These trials investigated the use of adalimumab for HS, a pharmaceutical that is currently funded.

12.21. The Committee was made aware of the Calabrese et al. J Eur Acad Dermatol Venereol. 2025. Epub ahead of print meta-analysis of phase-3 clinical trials, investigating adalimumab, secukinumab, and bimekizumab in the treatment of HS. Acknowledging this evidence, the Committee considered that adalimumab would be the primary comparator to secukinumab in the New Zealand setting, and that adalimumab provided increased health benefits in terms of HiSCR at an earlier stage (12 weeks) and a superior safety profile.

12.22. The Committee was made aware of the prospective monocentric Martora et al. Clin Cosmet Investig Dermatol. 2024;17:159-66 observational study, which investigated the efficacy and safety of secukinumab in a real-world setting. The study reported that 8 out of 14 participants (57%) experienced the pre-determined endpoint of HiSCR, however the Committee noted that the reporting excluded three individuals whose disease was non-responsive or who experienced serious adverse effects. Including these three individuals, the adjusted HiSCR rate was 47%.

12.23. Members were also made aware of the Blanch et al, ISPOR Annual European Congress, Nov 2024, Poster EE29 poster presentation observational follow-up study of treatment with secukinumab as first line and adalimumab as second line, which signaled an HiSCR achievement rate of ~50%.

12.24. The Committee noted reports of secukinumab being associated with HS paradoxically developing in individuals who are already being treated for other autoimmune conditions

(Navarro-Triviño et al. Dermatol Ther. 2020;33:e13150).

12.25. The Committee noted that the severity of HS fluctuates over time for each individual, and this leads to intrinsic serial imprecision with the HiSCR measure (Frew et al. JAAD Int. 2020;1:208-21). The Committee considered this may explain the high HiSCR achievement rate in the placebo group at week-16 in the pivotal trials, ie the background fluctuation in disease severity makes it more difficult to detect a significant difference produced by the experimental drug.

12.26. The Committee considered overall that increases in HiSCR rates translated to clinically relevant improvements in quality of life, and that observed increases in HiSCR rates associated with secukinumab likewise meant improvements in quality of life with secukinumab that were clinically relevant.

12.27. The Committee considered however that, over time, individuals would no longer receive benefit or experience high HiSCR with secukinumab. The Committee anticipated a treatment duration of approximately 16 months.

12.28. Overall, the Committee considered that the evidence indicates that secukinumab is inferior to currently funded treatments in the first line biologic setting of treatment for HS. In the second line biologic setting of treatment for HS, the Committee considered however that secukinumab demonstrates increased efficacy in comparison to placebo and improves clinically meaningful outcomes for the previously treated population.

Suitability

12.29. The Committee considered that dosing schedules should begin with an induction of one dose per week for the first four weeks, followed by one dose every four weeks thereafter. Dose frequency can be increased to two-weekly as needed, based on clinician evaluation of disease severity and individual response. The Committee noted that in second-line use, the majority of individuals would likely start with two-weekly dosing after the induction period.

12.30. The Committee noted that the doses used in the pivotal trials in HS were 300 mg Q2W and 300 mg Q4W. However, only the 150 mg injection was submitted for consideration, so two subcutaneous injections would be needed per dose.

12.31. The Committee considered that if caregivers were needed to administer the biologic, it may be preferable to use an agent that requires less frequent administration. However, this must be balanced against comparative efficacy.

Cost and savings

12.32. The Committee considered that the SUNSHINE and SUNRISE trials included a higher proportion of individuals with Hurley stage II compared to Hurley stage III disease (58% compared to 39%). However, individuals who had previously undergone biologic treatment were more likely to present in Hurley stage III HS than Hurley stage II (52% compared to 48%). Consequently, in second-line treatment scenarios, the Committee anticipated that the cohort would have more severe disease. Members noted that on average, the progression from Hurley stage II to Hurley stage III takes approximately two years (Vanlaerhoven et al. Dermatology. 2018;234:232-233).

12.33. The Committee noted that the initial response expected from the use of secukinumab in a second-line setting is 40% experiencing HiSCR by 16 weeks, with an improvement to 60% by 52 weeks (Zouboulis et al. 2024). The anticipated treatment duration would be 16 months.

12.34. The Committee noted that several disease-specific HRQoL tools have been developed, although they have not yet been utilised in pivotal trials of biologics for HS. These tools include HIDRAdisk, HSIA, HiSQOL, and HSQoL-24. These tools may offer improved assessments of post-treatment outcomes in HS patients (Chernyshov et al. Int J Environ Res Public Health. 2021;18:6131).

12.35. The Committee considered that New Zealand's health sector expenditure will be similar to that of adalimumab treatment but will increase overall due to the extended duration of biological therapies. While there is no evidence to suggest that secukinumab reduces the need for surgeries, it may have a delaying effect if the disease treated earlier.

Funding criteria

12.36. Members noted that the current Special Authority criteria for adalimumab for HS limited prescribing to dermatologists only. Members considered this led to significant inequities in accessing this treatment, as accessing a dermatologist is very difficult. Members considered that, if funded, secukinumab should be available from any relevant practitioner on the recommendation of a dermatologist.

12.37. At the same time, although not directly the subject of the Committee's deliberations, the Committee considered that, as with that recommended for secukinumab as second-line, the Special Authority for adalimumab for HS should be amended. Specifically, this amendment would be so that adalimumab too could be initiated by any relevant practitioner on the recommendation of a dermatologist and could be renewed by any relevant practitioner.

Summary for assessment

12.38. The Committee considered that adalimumab is very likely to be more effective than secukinumab in the first-line biologic treatment of HS. However, an estimated 40% of HS cases will experience a loss of disease control, be contraindicated to, or unable to tolerate adalimumab and will then use secukinumab. The Committee considered that these people will have tried adalimumab prior to secukinumab, so use will still be in the second-line for this population.

12.39. The Committee considered that the best guide for uptake of secukinumab would be the number of people starting adalimumab per annum, assuming that most of those people will eventually try secukinumab after no longer receiving benefit from adalimumab.

12.40. The Committee considered that in addition to DLQI and HiSCR measures, the outcomes reported upon in the SUNSHINE and SUNRISE trials should be considered in economic modelling, including the frequency of flares, NRS30 measures, and EQ-5D VAS.

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

	Second Line Biologic
Population	Adults with moderate-to-severe hidradenitis suppurativa (Hurley scale II or III) who experience an inadequate response to conventional systemic hidradenitis suppurativa therapy and to adalimumab (including adalimumab being unable to be tolerated/contraindicated or people on adalimumab experiencing a loss of disease control after receiving an initial response).
Intervention	Secukinumab 300 mg* administered as a subcutaneous injection with: • initial dosing weekly for 4 weeks, followed by a maintenance dose of 300mg either every 4 weeks or every 2 weeks. (majority using every 2 weeks initially) *Each dose is 2 injections of 150 mg pre-filled syringe.

Comparators (NZ context)	Adalimumab maintained at a dose of 40 mg per week	Best supportive care
Outcomes	Uncertainty in the magnitude of benefit from a second-line biologic (vs its use in 1L).	
	Response includes a reduction in active lesions, abscesses, and inflammatory nodules (as summarised by HiSCR rates). Improvement may be measured using the Dermatology Life Quality Index (DLQI). Other outcomes including the NRS30 pain scale, EQ5D health-related quality of life measure, and frequency of HS flares.	
Table definitions: **P**opulation: The target population for the pharmaceutical, including any population defining characteristics (eg line of therapy, disease subgroup) **I**ntervention: Details of the intervention pharmaceutical (dose, frequency, treatment duration/conditions for treatment cessation). **C**omparator: Details the therapy(s) that the patient population would receive currently (status quo – including best supportive care; dose, frequency, treatment duration/conditions for treatment cessation). **O**utcomes: Details the key therapeutic outcome(s), including therapeutic intent, outcome definitions, timeframes to achieve outcome(s), and source of outcome data.		

13. Sacituzumab govitecan for triple negative, locally advanced or metastatic breast cancer

Application

13.1. The Committee reviewed the application for sacituzumab govitecan (SG) in the treatment for triple negative, locally advanced or metastatic breast cancer (mTNBC).

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 sacituzumab govitecan (SG) for triple negative, locally advanced or metastatic breast cancer (mTNBC) be listed with a **high priority**, subject to the following Special Authority criteria:

> **Initial application** (**locally advanced or metastatic breast cancer**) – from any relevant practitioner. Approvals valid for 6 months if the following criteria are met:
> All of the following:
> 1. Patient has triple negative metastatic or inoperable locally advanced breast cancer; and
> 2. Patient has progressive disease following two or more prior systemic therapies, at least one of them in the locally advanced or metastatic setting; and
> 3. Patient has performance status ECOG 0-2; and
> 4. Patient has not received prior sacituzumab govitecan treatment; and
> 5. Baseline measurement of overall tumour burden is documented clinically and radiologically; and
> 6. Treatment to be discontinued at disease progression.
>
> **Renewal application (locally advanced or metastatic breast cancer)** – from any relevant practitioner. Approvals valid for 6 months if the following criteria are met:
> Both:
> 1. The cancer has not progressed at any time during the previous approval period whilst on sacituzumab govitecan; and
> 2. Treatment to be discontinued at disease progression.

13.4. In making this recommendation, the Committee:

13.4.1. noted that mTNBC is a phenotypically different form of breast cancer, being more aggressive and less responsive to treatment than non-mTNBC.

13.4.2. considered that the impacts of this condition were more likely to affect younger women and people living with breast cancer in paid and unpaid work, which may involve caring for children.

13.4.3. considered that people with mTNBC had fewer treatment options and shorter survival from diagnosis compared with people with non-mTNBC.

13.4.4. noted that SG provides progression free survival and overall survival benefits compared to physician's choice of treatment.

Discussion

Māori impact

13.5. Breast cancer | mate pukupuku is one of Pharmac's Hauora Arotahi | Māori Health Areas of Focus. The Committee considered there was no evidence of increased incidence of mTNBC in Māori, but it was uncertain if further testing and diagnosis in people with mBC would lead to higher reported incidence rates. The Committee noted that the population age structure of Māori was younger than the New Zealand (NZ) European/Other population. The Committee noted that Māori were not included in the ASCENT trial population (Bardia et al. J Clin Oncol. 2024;42(15)).

Populations with high health needs

13.6. The Committee discussed the health need(s) of people living with mTNBC among Pacific peoples, disabled peoples including tāngata whaikaha Māori, and other priority populations identified by the Government Policy Statement on Health 2024-2027 (GPS, 2024-27) to have high health needs.

13.7. The Committee reviewed the Breast Cancer Foundation NZ's 30,000 voices: informing a better future for breast cancer in Aotearoa New Zealand. Te Rēhita Mate Ūtaetae: Breast Cancer Foundation National Register Report 2003-2020. Auckland: Breast Cancer Foundation NZ, 2022, which showed that TNBC (both metastatic and non-metastatic forms) accounted for 6.5% of all breast cancers in Pacific peoples, 7.5% in Māori, 10% in Asian and 10.3% in NZ European/Other.

13.8. The Committee considered that:

13.8.1. there was a lack of evidence of increased incidence of mTNBC among Pacific peoples.

13.8.2. there were additional considerations for people living in rural settings, particularly people also living in deprivation, in regard to accessing infusion centres for treatment with sacituzumab govitecan which is given as an intravenous infusion. The Committee noted that this may lead to reduced rural patient preference for SG.

Background

13.9. The Committee noted research describing the intrinsic molecular subtypes of breast cancer (Zagami & Carey. NPJ Breast Cancer. 2022;8(1):95). The Committee noted that triple negative breast cancer, ER+ breast cancer and HER2+ breast cancers are broader categories of breast cancer, with TNBC comprising 10-20% of all breast cancers. The Committee considered that recent definitions of HER2 low and HER2 ultralow breast cancers may alter the proportion of these different categories, particularly for TNBC as a proportion of these patients are redefined and re-categorised, which may increase the eligible population size.

13.10. The Committee noted that SG is a first in class, antibody-drug conjugate composed of an anti-trophoblast cell-surface antigen 2 (Trop-2) IgG1 kappa antibody coupled to SN-38, the active metabolite of irinotecan and a topoisomerase I inhibitor, through a propriety hydrolysable linker. The Committee noted that the efficacy of any antibody drug conjugate depends on the antibody target as well as linkers and payload (Dumontet et al. Nature Rev Drug Disc. 2023;22:641-61).

13.11. The Committee noted that SG utilises TROP2 expression, where SG targets TROP2, a transmembrane glycoprotein that is involved in intracellular calcium signalling; TROP2 is over-expressed in cancerous tissues relative to non-cancerous tissues, it is not unique to cancerous tissue; and based on this differential expression in cancer cells, SG is able to target cancerous tissue with higher TROP2 expression (Stepan et al. J Histochem Cytochem. 2011;59(7):701-10). The Committee discussed whether therefore to include an exclusion criterion within access criteria to restrict access to those tumours in the 2nd quartile and above for TROP2 expression.

13.11.1. Members considered that 50% of patients had a TROP2 expression of 0, and 60-65% of patients were in the first quartile. Testing for TROP2 expression would be done with IHC with formaldehyde fixed or fresh tissue samples.

13.11.2. The Committee considered that there was not enough data to support a treatment threshold, despite the existence of a correlation between higher TROP2 expression and greater clinical benefit in the study population. The Committee considered that although there may be grounds for limiting access to SG based on TROP2 status, this would be a first-in-kind approach that would require further discussion and consideration, including consideration by CTAC and wider consultation with patients and patient support groups.

13.12. The Committee considered data on single agent therapy for metastatic breast cancer with irinotecan (Perez et al. J Clin Oncol. 2004;22(14):2849-55). Irinotecan is a prodrug which metabolises into SN-38. The Committee considered that people with the homozygous genotype of UGT1A1*28 were predisposed towards experiencing adverse treatment effects from SN-38. Therefore, toxicity from SG could be reduced if people were screened genotypically before commencing treatment, although this is not current practice. Irinotecan has cycle dependent toxicity with some schedule dependence when trialled at different schedules, where weekly cycles demonstrated less toxicity than individuals on three weekly cycles. The Committee noted that this pharmaceutical has similar properties to SG but has not been studied further beyond Perez et al. 2004.

13.13. The Committee noted there are evolving areas of research with SG. In particular, genotype testing for UGT1A1*28 homozygotes correlates with increased toxicity from SN-38 and may need to be a part of pre-treatment clinical evaluation though this was not formally recommended (Wong et al. Cancer Med. 2024;13(16):e70096).

13.14. The Committee noted that additional ADC pharmaceutical treatments for TNBC are in clinical trials in the USA (Bianchini et al. Nature Rev Clin Oncol. 2021;19(2):91-113). Members also considered that multiple TROP2 targeted agents are in late phase development that could be considered for treating TNBC in the future.

13.15. At the time of the application to Pharmac the pharmaceutical had not been approved by Medsafe, but registration had been lodged by the supplier for the requested indication. Medsafe had acknowledged the New Medicine Application on 26 July 2024 and current registration was pending (link to Medsafe Product Detail of the application).

Health need

13.16. The Committee noted the European Society of Medical Oncology Clinical Practice Guideline for metastatic breast cancer including mTNBC (Gennari et al. Annal Oncol. 2021;32(12):1475-95), identified that not only is the clinical phenotype of mTNBC more aggressive, but clinicians no longer have hormone and HER2 targets as markers of treatment efficacy.

13.17. The Committee considered New Zealand Breast Cancer Register | Te Rēhita Mate Ūtaetae data on the prevalence of TNBC in New Zealand from 30,000 voices: informing a better future for breast cancer in Aotearoa New Zealand (Te Rēhita Mate Ūtaetae: Breast Cancer Foundation National Register Report 2003-2020. Auckland: Breast Cancer Foundation NZ, 2022). The Committee considered that the majority of patients with TNBC were diagnosed without metastatic disease, with 46.9% of women diagnosed with any form of invasive breast cancer at stage 1 of disease, 35.2% at stage 2, 12.7% at stage 3 and 5.2% at stage 4 (Figure 5.2-12, p. 90).

13.18. The Committee reviewed the New Zealand Breast Cancer Foundation (Breast Cancer Foundation NZ. "I'm still here" Insights into living – and dying – with Advanced Breast Cancer in New Zealand. Auckland: Breast Cancer Foundation NZ, 2018), which cited the median overall survival for people with mTNBC being 6.6 months.

13.19. The Committee reviewed the Breast Cancer Foundation NZ's National Register Report (2022), which reported that 9.7% of all breast cancers were Triple Negative Breast Cancer (TNBC), and 14.4% of breast cancers in people aged under 45 years were TNBC, showing that this subtype affects younger people.

13.20. The Committee noted Kesireddy et al. (Cancers. 2024;16(10):1791), a US based cohort study that reported median overall survival (OS) of 13.6 months (95% CI, 12.8, 14.7 months) for people living with mTNBC. The authors compared first-line chemotherapy with immunotherapy in patients with mTNBC and reported that while these treatments improve OS, neither confer good prognosis relative to non-TNBC.

13.21. The Committee noted alternative treatments for breast cancer funded in New Zealand or waiting for a funding decision:

13.21.1. Capecitabine was considered and approved for locally advanced or metastatic breast cancer after failure of two prior chemotherapeutic regimes in November 2002. The status on the application tracker is here.

13.21.2. Nab-paclitaxel was considered by CTAC in April 2023 with a high priority recommendation for funding. The application has been ranked on the Options for Investment List. The status on the application tracker is here.

13.21.3. Gemcitabine hydrochloride was funded without restriction for metastatic breast cancer in November 2012.

13.21.4. An application for trastuzumab deruxtecan from AstraZeneca Limited is currently seeking clinical advice for the indication of breast cancer, unresectable or metastatic, HER2 low (IHC 1+ or IHC 2+ or ISH negative). The status on the application tracker is here.

13.21.5. The Committee summarised that there was an unmet health need for treatment options for mTNBC that are available in other jurisdictions.

Health benefit

13.22. The Committee noted the key clinical trial of SG for mTNBC, was the ASCENT trial (Bardia et al. J Clin Oncol. 2024;42(15).

13.22.1. Trial participants had progressive disease following two or more prior systemic therapies, at least one of them in the locally advanced or metastatic setting. Participants were randomised to either SG at 10mg/Kg intravenously on day one and day eight of a twenty-one-day cycle, or treatment of Physicians' choice (TPC). Eribulin was the main treatment used in TPC, with approximately 50% of the comparator group on this treatment.

13.22.1.1. Members noted that eribulin is not available in NZ, therefore, there would be some uncertainty about extrapolating the magnitude of benefit in the comparator arm of ASCENT to the NZ context. Members considered that eribulin may have a similar impact on PFS compared with capecitabine (Zhao et al. BMC Cancer. 2021;21(1):758), although noting that as a network meta-analysis the underlying data was an indirect comparison of cohorts of RCTs across different treatment-comparator settings, with inherent risks of bias relating to transitivity, therefore equivalence could not be readily assumed. As capecitabine is available in New Zealand, Members suggested it may be reasonable to assume that the PFS outcomes observed in ASCENT would be likely to reflect what can be expected in the New Zealand context, in relation to the mix of available comparators.

13.22.2. The primary endpoint of ASCENT was PFS (radiographic progression or death) in

the mTNBC population without brain metastases. The secondary endpoints were OS, objective response rate, investigator PFS, and safety. Median follow up times were 11.2 months and 6.3 months for SG and TPC respectively.

13.22.3. In ASCENT, PFS among patients without brain metastasis for SG was 5.6 months (95% CI, 4.3, 6.3) and 1.7 months (95% CI, 1.5, 2.6) for TPC, with a hazard ratio (HR) for disease progression or death of 0.41 (95% CI, 0.32, 0.52, P<0.001). The Committee noted the OS of SG was 12.1 months (95% CI, 10.7, 14.0) and 6.7 months (95% CI, 5.8, 7.7) in TPC (Bardia et al. 2024).

13.22.4. The Committee noted in ASCENT that there were a number of patients that were diagnosed as TNBC post prior treatment, indicating there is phenomena where patients who were initially ER or HER2 positive, convert to TNBC after a re-biopsy as they go through subsequent lines of therapy. The Committee considered that approximately 5-10% of conversion can be expected, however there is uncertainty around the occurrence of this in New Zealand as there is no driver to re-biopsy due to a lack specific treatments requiring this confirmation for TNBC and mTNBC.

13.22.5. The ASCENT trial used a combined no-crossover design and defined censorship at the last radiographic assessment (as Last Observation Carried Forward i.e. LOCF analysis). The Committee considered this design introduced an inherent risk of appreciable bias (Lachin JM. Clin Trials. 2016;13(2):161-8), but the impact on interpretation of final results in ASCENT was uncertain. It was noted that although censoring was higher in the comparator group, withdrawals and physician-initiated discontinuations were relatively balanced across treatment arms in the final analysis, and therefore the Committee considered that any bias introduced by censoring may have been limited.

13.22.6. The Committee considered the results from the ASCENT trial to be high-quality evidence, that the European Society of Medical Oncology (ESMO) Magnitude of Clinical Benefit System scored sacituzumab 4 out of 5, indicating substantial clinical benefit with 1 point deducted for toxicity and that this score was based on ASCENT data.

13.23. The Committee reviewed work by Yin et al. (Nat Med. 2025) where researchers used a different TROP2 inhibitor, sacituzumab tirumotecan. This was compared with chemotherapy in patients with locally recurrent or mTNBC who had received two or more prior therapies, including at least one for metastatic disease. The median PFS by blinded independent central review was 6.7 months (95% CI, 5.5, 8.0) with sacituzumab tirumotecan and 2.5 months (95% CI, 1.7, 2.7) with chemotherapy (HR 0.32; 95% CI, 0.24, 0.44; $P < 0.00001$). The Committee considered the clinical benefit to be comparable with SG versus chemotherapy agents in Bardia et al. (2024).

13.23.1. The Committee considered that the median PFS gain between the SG group and TPC group in Bardia et al. 2024 was reasonable and broadly applicable to the NZ population. The Committee considered that, based on the trial inclusion criteria, in New Zealand most patients with mTNBC would be likely to receive SG as a second line treatment for mTNBC, since many would receive one line of chemotherapy in the (neo)adjuvant setting.

13.24. The Committee noted an observational study of SG in mTNBC in the UK (Hanna et al. Br J Cancer. 2024;130:1916-20) reporting similar PFS outcomes to ASCENT and similar toxicity, although noting known issues of accuracy with adverse events being recorded retrospectively. The observed OS was slightly lower, which Members surmised may have been due to Hanna et al. (2024) having a less selective study participant population than clinical trials such as ASCENT thus greater baseline morbidity and decreased survival.

13.25. The Committee noted the post-hoc analysis of ASCENT (O'Shaughnessy et al. Breast Cancer Res Treat. 2022;195(2):127-39) reported 30% (70/235) and 33% (76/233) of patients who received SG and TPC, respectively, did not have TNBC at initial diagnosis. Clinical benefit with SG versus TPC was observed in this subset. Median PFS was 4.6 months versus 2.3 months (HR 0.48; 95% CI 0.32, 0.72), median OS was 12.4 months

versus 6.7 months (HR 0.44; 95% CI 0.30, 0.64), and objective response rate (ORR) was 31% versus 4%; those who also received prior CDK4/6 inhibitors had ORRs of 21% versus 5%.

Suitability

13.26. The Committee noted that oral treatments, particularly capecitabine, are preferred in the first-line setting, as they help reduce demand on infusion centres. Vinorelbine is generally used in later lines of therapy but may be used first-line in older patients. However, since TNBC is more common in younger individuals, first-line use of vinorelbine is expected to be limited. Given the therapeutic equivalence between oral and intravenous vinorelbine, oral administration is expected to be preferred whenever feasible.

13.27. The Committee considered research by Géraud et al. (Cancer Treatment Reviews. 2025;135:102922) which identified a short half-life for antibody drug conjugates (ADCs) such as SG. This is not unique for SG compared with other chemotherapeutics. The Committee identified that SN-38 (the active metabolite from SG chemical reactions in the body) exposure predicts drug toxicity from ADCs, and that if the patients' weight was >110Kg there would be increased systemic exposure to SN-38 and potential for drug related toxicity from SG. The Committee considered this would support weight-based dosing of SG. The Committee was not aware of any defined relationships of exposure for ADC to outcome, either OS or progression free survival (PFS), other than the average concentration (C in µg/mL) of SG in the blood.

13.28. The Committee considered that compared with physician's choice of chemotherapy agent (eg. capecitabine, eribulin, vinorelbine or gemcitabine), SG was inferior regarding changes from baseline for nausea/vomiting and diarrhoea. However, median time to first clinically meaningful worsening endpoint was longer for SG than physicians' choice for physical functioning (22.1 vs. 12.1 weeks, P<0.001), role functioning (11.4 weeks vs. 7.1 weeks, P<0.001), fatigue (7.7 weeks vs. 6.0 weeks, P<0.05), and pain (21.6 weeks vs. 9.9 weeks, P<0.001), indicating superiority compared with other available chemotherapy agents, where impacts on a person's life are material (Loibl et al. Eur J Cancer 2023;178:23-33).

13.29. The Committee noted Dacoregio et al. (Breast. 2024;79) had reported treatment with SG did not predispose to greater risk of grade 3 and 4 toxicity events compared with other chemotherapeutics in the treatment setting of metastatic breast cancer.

13.30. The Committee considered that adverse events from SG were related to TROP2 inhibition, which causes stomatitis, and SN-38 which has a toxicity profile that aligns with the most commonly experienced adverse events of neutropenia and diarrhoea. The Committee noted Table S7 of ASCENT (Bardia et al. 2024) summarising treatment-emergent adverse events of any grade (≥10% of patients) and by worst grade ≥3 (≥5% of patients), where neutropenia occurred in 64% (165 people) of patients on SG and 44% (98) of patients on TPC, with any grade of diarrhoea in 65% (168) of SG patients and 17% (38) of TPC patients.

13.31. The Committee considered that people with the homozygous genotype of UGT1A1*28 were predisposed towards experiencing adverse treatment effects from SN-38, as they have slower glucuronidation of SN38. Therefore, toxicity from SG could be reduced if people were screened genotypically before commencing treatment, however this would need to be considered further in context of testing and resources. The Committee noted that patients with Gilbert's disease were excluded from the study population in ASCENT (Bardia et al. 2024) due to impacts on the glucuronidation pathway, and that as SN-38 is metabolised entero-hepatically Members considered that this exclusion was appropriate. The Committee considered that UGT1A1*28 testing may be a non-clinical feature that would affect use in New Zealand, which was not considered in the information provided in the application.

Cost and savings

13.32. The Committee considered that 5-10% of HER2+ or ER+ patients initially diagnosed with non-mTNBC may develop mTNBC, due to selective pressures as the individual goes

through treatment lines. As a result, with SG being funded specifically for mTNBC, there may be an increase in biopsies in patients not originally diagnosed with TNBC to open new lines of therapy for some patients. This would have cost and resource implications for the NZ health care sector as additional imaging, interventional radiology, and pathology services would be required. An increase in eligible TNBC patients due to re-biopsy, should be taken into account if using pembrolizumab mTNBC prescribing data to estimate the size of the patient population.

13.33. The Committee considered that the estimates for second- and third-line use of SG would likely evolve over time. Initially, a significant proportion of SG use might be anticipated in the third-line treatment setting due to the existing prevalent population. Over time, as this prevalent population decreases, the relative proportion of second-line use could be anticipated to rise, with third-line use becoming limited to a small subset of patients with mTNBC diagnosed with de novo metastatic disease.

13.34. The Committee considered, based on the observational data for SG for people with mTNBC in the UK (Hanna et al. 2024), that ECOG performance status would have a meaningful impact on clinical outcomes, particularly OS and PFS, and would therefore be a reasonable Special Authority access criterion. However, the Committee noted that as ECOG status is based on the prescribing clinician's subjective assessment, estimates of the proportion of patients meeting specific ECOG criteria in published literature may not fully reflect what is observed in clinical practice.

13.35. The Committee noted that line of therapy appears to have a relatively small influence on SG clinical outcomes (Hanna et al. 2024).

Funding criteria

13.36. The Committee considered that the Special Authority criteria were accurate and aligned with the PICO (population, intervention, comparator, outcomes).

General

13.37. The Committee noted the international Health Technology Assessments for SG for unresectable locally advanced or mTNBC had made a variety of recommendations:

13.37.1. The Pharmaceutical Benefits Advisory Committee (PBAC) in Australia had recommended funding in March 2022.

13.37.2. The National Institute for Health and Care Excellence (NICE) in England/Wales had recommended funding for treatment of unresectable triple-negative locally advanced or metastatic breast cancer in adults after two or more systemic therapies, at least one of which was for advanced disease, under a commercial arrangement.

13.37.3. The Scottish Medicines Consortium (SMC) had recommended funding, taking into account a confidential discount offered by the pharmaceutical company. The SMC had noted SG would be used for what is a rare condition (TNBC) and where patients taking current treatments are likely to live less than three years.

13.37.4. The Canadian Agency for Drugs and Technologies in Health (CADTH) had recommended SG be reimbursed by public drug plans for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior therapies, at least one of them for metastatic disease if certain conditions are met.

13.38. The Committee noted that all international approvals were in the context of two prior lines of treatment, but only one prior treatment line had to be in the metastatic setting.

Summary for assessment

13.39. The Committee noted that, if funded, SG would primarily be used as a second-line treatment for mTNBC. Only a small subset of patients, specifically those diagnosed with de novo metastatic disease, would receive SG as a third-line option for mTNBC.

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

Population	Treatment of adults with unresectable, locally advanced or metastatic triple negative breast cancer (mTNBC) who have received two or more standard chemotherapy regimens, at least one of which was for metastatic disease.
Intervention	Sacituzumab govitecan (SG): 10mg/kg administered as an IV infusion once weekly on days one and eight of 21-day treatment cycles until disease progression or unacceptable toxicity. In the ASCENT trial, patients had a median treatment duration of seven cycles on sacituzumab govitecan (Bardia et al. Supp App. J Clin Oncol. 2024;42(15)p.13)
Comparator(s) (NZ context)	Current funded systemic chemotherapy treatment options in New Zealand include gemcitabine, capecitabine and vinorelbine. Best supportive care is unlikely to be a comparator as it is assumed that there is not a large group of people currently going without any treatment, who would take up sacituzumab govitecan.
Outcome(s)	Treatment outcomes for sacituzumab govitecan compared to a treatment of physician's choice – ASCENT trial (Bardia et al. J Clin Oncol. 2024;42(15)): • Increased median progression free survival (PFS) (4.8 vs 1.7 months; hazard ratio (HR), 0.41 [95% confidence interval (CI), 0.33 to 0.52]). • Improved overall survival (OS) (11.8 vs 6.9 months; HR, 0.51 [95% CI, 0.42 to 0.63]) • Manageable safety profile, with ≤5% of treatment-related discontinuations because of adverse events and no treatment-related deaths. • Greater improvements and delayed worsening of health-related quality of life (HRQoL) (Loibl et al. Eur J Cancer. 2023).
Table definitions: **P**opulation: The target population for the pharmaceutical, including any population defining characteristics (eg line of therapy, disease subgroup) **I**ntervention: Details of the intervention pharmaceutical (dose, frequency, treatment duration/conditions for treatment cessation). **C**omparator: Details the therapy(s) that the patient population would receive currently (status quo – including best supportive care; dose, frequency, treatment duration/conditions for treatment cessation). **O**utcomes: Details the key therapeutic outcome(s), including therapeutic intent, outcome definitions, timeframes to achieve outcome(s), and source of outcome data.	

14. Durvalumab in combination with etoposide and either carboplatin or cisplatin for the first-line treatment of patients with extensive-stage small cell lung cancer (ES-SCLC)

Application

14.1. The Committee reviewed an application from AstraZeneca Ltd for the use of durvalumab (Imfinzi) for the first-line treatment of extensive-stage small cell lung cancer (ES-SCLC).

14.2. The Committee noted that Pharmac staff sought to understand the potential health benefits of durvalumab (a PD-L1 inhibitor) for ES-SCLC relative to those of two other PD-L1/PD-1 inhibitors: atezolizumab, which Pharmac has previously assessed for this indication, and pembrolizumab, given that there is a published phase III clinical trial investigating pembrolizumab for ES-SCLC although Pharmac has not received an application for this.

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

Recommendation

14.4. The Committee **recommended** the listing of durvalumab be widened to include the treatment of ES-SCLC with a **high priority**, subject to the following Special Authority criteria:

Initial approval – (extensive-stage small cell lung cancer) only from a medical oncologist or medical practitioner on the recommendation of a medical oncologist. Approvals valid for 4 months.
Both
1. Patient has extensive-stage small cell lung cancer; and
2. Either:
    - 2.1. The patient has ECOG performance status 0-1 before chemotherapy commences for previously untreated disease; or
    - 2.2. The patient has received one cycle of chemotherapy and has experienced ECOG performance status 0-1 prior to the initiation of chemotherapy cycle 2.

Renewal only from a medical oncologist or medical practitioner on the recommendation of a medical oncologist. Approvals valid for 4 months for applications where there has been no evidence of disease progression.

14.5. In making this recommendation, the Committee considered the following:

14.5.1. High health need of people with ES-SCLC, especially in terms of Quality of Life (QoL) impact from the disease on the individual and their family, whānau, partners, caregivers and loved ones.

14.5.2. That durvalumab would provide an overall survival (OS) benefit and likely an improvement in PFS (although not significant in the key clinical trial) for ES-SCLC.

14.5.3. Durvalumab's safety profile was as expected in this setting.

14.5.4. There is a class effect of atezolizumab and durvalumab in ES-SCLC.

Discussion

Background

14.6. The Committee noted that durvalumab (brand name Imfinzi) has been funded from August 2022 for the treatment of people with locally advanced (Stage III), unresectable non-small cell lung cancer (NSCLC).

14.7. The Committee noted that an application for atezolizumab for the first-line (1L) treatment of ES-SCLC was considered by the Cancer Treatments Advisory Committee (CTAC) in April 2022, which recommended it be funded with a high priority. At that time, in making the high priority recommendation for atezolizumab for 1L treatment of ES-SCLC, the Committee considered:

14.7.1. the high clinical need of people with ES-SCLC due to the burden of this rapidly progressive disease which is associated with a poor prognosis, high hospitalisation rates and a high symptom burden

14.7.2. the unmet need for improvements in treatment given that chemotherapy does not provide durable long-term responses for people with ES-SCLC

14.7.3. the high impact on Māori who are disproportionately affected by SCLC and are more likely to die from lung cancer than non-Māori.

Māori impact

14.8. The Committee discussed the impact of funding durvalumab for the treatment of ES-SCLC on Māori health areas of focus | Hauora Arotahi and Māori health outcomes, noting that Respiratory Health | Romaha Ora is a Māori health area of focus. The Committee noted that relevant considerations about the high impact of ES-SCLC on Māori had been detailed previously regarding atezolizumab for ES-SCLC.

Populations with high health needs

14.9. The Committee discussed the health need(s) of people with ES-SCLC among Māori, Pacific peoples, disabled peoples including tāngata whaikaha Māori, and other populations identified by the Government Policy Statement on Health 2024-27 to have high health needs. The Committee noted that CTAC had previously noted that there is limited data for the impact of ES-SCLC on Pacific peoples and on other groups experiencing health disparities relative to the wider New Zealand population.

Health need

14.10. The Committee was made aware of evidence that the QoL of individuals with lung cancer declines over time and that their caregivers experience a proportionate QoL decrease irrespective of the patient's stage of disease (Borges et al. J Bras Pneumol. 2017;43:18-23). The Committee considered that the health needs of those with ES-SCLC, the impact of ES-SCLC on priority populations and the current treatment paradigm were well documented in the previous consideration of atezolizumab (Pharmac Application link).

Health benefit

14.11. The Committee noted that durvalumab and atezolizumab are both approved by Medsafe and are indicated for use in combination with etoposide and carboplatin (or cisplatin) for the first-line treatment of patients with ES-SCLC, among other indications. The Committee noted that pembrolizumab has many Medsafe approved indications, although ES-SCLC is not among them.

14.12. The Committee noted that international health technology assessment agencies in Australia (PBAC), Canada (CDA-AMC), England/Wales (NICE) and Scotland (SMC) have recommended atezolizumab and durvalumab, respectively, for the treatment of ES-SCLC. The Committee noted that in England/Wales, appraisal by NICE was discontinued in November 2022 due to the supplier company no longer pursuing an EMA application for pembrolizumab for ES-SCLC, following the results of the KEYNOTE-604 trial. Members noted that an application to the United States Federal Drug Agency (FDA) for pembrolizumab for ES-SCLC was also withdrawn.

Durvalumab

14.13. The Committee noted that the key evidence for durvalumab comes from the phase III CASPIAN trial: a randomised (1:1:1), open-label, multicentre, phase III trial in 537 adults with untreated ES-SCLC, WHO performance status (PS) of 0 or 1 and measurable disease per RECIST v1.1 (Paz-Ares et al. Lancet. 2019;394:1929-39). The Committee noted that in the relevant treatment arms, the median age of participants was ~63 years, that most (>90%) participants had stage IV disease and that two thirds had PS of 1. In the relevant two treatment arms, participants received either durvalumab + platinum-etoposide (EP; up to four cycles) every three weeks, then maintenance durvalumab every four weeks or EP alone (up to six cycles) every three weeks, plus prophylactic cranial irradiation (at investigator's discretion).

14.13.1. The Committee noted that the primary endpoint was OS in the intention-to-treat population, OS was median 13.0 months (95% CI 11.5, 14.8) with durvalumab + EP versus 10.3 months (9.3, 11.2) with EP alone (hazard ratio [HR] 0.73 (95% CI 0.59, 0.91; *P*=0.0047]). Members considered that the Kaplan-Meier curve for OS did not follow a typical pattern where the two curves converged and instead the treatment group had a long tail which could suggest longer survival for a small proportion.

14.13.2. The Committee noted that progression-free survival (PFS) could not be tested for significance because of the study design, but an HR of 0.78 (95% CI 0.65, 0.94) for the comparison was recorded. The median PFS was 5.1 months (95% CI 4.7, 6.2) with durvalumab + EP vs 5.4 months (4.8, 6.2) with EP alone (with 12-month PFS of 18% and 5%, respectively). Members considered that this outcome could have been significant if the mean was used rather than the median for this outcome.

14.13.3. The Committee noted that there were statistically non-significant differences in adverse events (AEs) and serious AEs in the durvalumab + EP and EP alone groups, including events leading to treatment discontinuation. The Committee noted that immune mediated AEs occurred in 52/265 (20%) of those receiving durvalumab + EP with the most common being hypothyroid events which were all grade 1 or 2. The Committee considered that the safety profile was as expected given the EP chemotherapy backbone in both arms.

14.14. The Committee noted two publications reporting CASPIAN follow-up OS data at two and three years, respectively (Goldman et al. Lancet Oncol. 2021;22:51-65 and Paz-Ares et al. JW. ESMO Open. 2022;7:100408). Members considered this also indicated a long tail for OS in the Kaplan-Meier curve, which appeared similar to that seen in other immune checkpoint inhibitor (ICI) trials in other cancer indications such as malignant melanoma where there is evidence of a significant difference in OS out to three years.

14.15. The Committee noted a publication of patient-reported outcomes from CASPIAN which reports that patients receiving durvalumab + EP experienced similar or better improvements in symptom burden and time to deterioration vs those who received EP alone (Goldman et al. Lung Cancer. 2020;149:46-52).

14.16. The Committee considered that the CASPIAN trial was of high quality and while it was not blinded, the lack of blinding was deemed non-significant, given the study provided similar outcomes to those seen in other evidence, for other ICIs in this disease and other cancers.

14.17. The Committee were made aware of a conference abstract presenting data from an open-label, single-arm, multicentre phase II study of 57 people with poor PS (PS of 2–3) receiving durvalumab for ES-SCLC in Japan (Saida et al. J Clin Oncol. 2024; 42:Suppl_16). Members noted that durvalumab was well tolerated and provided good response rates in this population, despite these rates being of lesser magnitude than those received in people with PS 0-1 in CASPIAN. The Committee considered this evidence supported the intention of the funding criteria to allow durvalumab treatment for those with improved PS from cycle two onwards, as previously recommended for atezolizumab based on evidence with that treatment.

Pembrolizumab

14.18. The Committee noted evidence from the Keynote-604 trial: a randomised (1:1), double-blind, placebo-controlled, multicentre phase III trial of 453 adults with untreated ES-SCLC, PS 0 or 1 and measurable disease per RECIST v1.1 (Rudin et al. J Clin Oncol. 2020;38:2369-79; Kim et al. JTO Clin Res Rep. 2023;4:100572). Members considered that there was an imbalance between arms in terms of the proportion of participants with brain metastases which may have had some influence on the reported survival outcomes. The Committee noted that OS in the intention to treat population was not significant at the time of the initial report but was significant at a later timepoint, and again noted the voluntary withdrawals of both EMA and FDA applications for pembrolizumab for this indication.

Atezolizumab

14.19. The Committee noted previously reviewed evidence for atezolizumab came from the IMpower133 trial (Horn et al. N Engl J Med. 2018;379:2220-9). The Committee considered that the OS benefit for atezolizumab in ES-SCLC showed a traditional converging median pattern rather than having a long tail.

General

14.20. The Committee also noted the following evidence regarding durvalumab, atezolizumab, and treatment of ES-SCLC with ICIs:

- Xie et al. Mol Cancer. 2024;23:115
- Paz-Ares et al. Clin Cancer Res. 2024;30:824-35

- Shibaki et al. Lung Cancer. 2024;196:107958
- Liu et al. J Clin Oncol. 2021;39:619-30
- Reck et al. J Thorac Oncol. 2022;17:1122-9
- Bria et al. Oncologist. 2024;29:e690-8
- Korde et al. Curr Med Res Opin. 2022 Aug;38(8):1361-1368
- Ando et al. Curr Oncol. 2021;28:1094-113
- Wang et al. Lung Cancer. 2023:178:47-56
- Roisman et al. Clin Lung Cancer. 2025:S1525-7304(25)00027-0
- Landre et al. Ther Adv Med Oncol. 2020:12:1758835920977137
- Yu et al. Cancer Immunol Immunother. 2022;71:637-44
- Kang et al. Front Oncol. 2022:11:740091
- Arriola et al. Oncol Ther. 2022;10:167-84

14.21. Members considered that the treatment effect in CASPIAN and Impower133 was particularly sensitive to the presence of brain metastases, which were present at baseline in about 10% of participants in each of these trials, and that subgroup analyses reported a smaller benefit from ICI + chemotherapy in these individuals than in those without brain metastases. The Committee further noted that participants with brain metastases were excluded from the primary analysis population in CASPIAN.

14.22. Overall, the Committee considered that the available evidence (including a high-quality non-sponsored meta-analysis by Wang et al. Lung Cancer. 2023:178:47-56) consistently supported a class effect of durvalumab and atezolizumab in terms of median OS, QoL, and AEs. The Committee noted that the CASPIAN trial was not blinded, however, IMpower133 was. Members were made aware of a meta-analysis regarding blinding in clinical trials (Moustgaard et al. BMJ. 2020:368:l6802) and based on this, considered that the impact of non-blinding was unlikely to be influential on the reported outcomes noting the similar odds ratios between these trials and consistency with the benefits seen with these and other ICIs in other cancers.

14.23. Members considered that atezolizumab and durvalumab would be likely to provide the same or similar health benefits (relative to chemotherapy) on safety, PFS and OS in this population, such that either could be funded for this indication. Members considered that the available evidence was weaker for pembrolizumab for this indication, and that pembrolizumab was likely to be considered the less preferred immune checkpoint inhibitor in ES-SCLC.

14.24. The Committee considered that at this time, there was no conclusive information about any biomarkers that may help to differentiate those who would benefit most from ICIs for ES-SCLC.

14.25. The Committee considered that there is clinical interest in the use of ICIs for limited stage SCLC (LS-SCLC) and would welcome a funding application for this indication.

Cost and savings

14.26. The Committee considered that there was limited evidence for ICI use as monotherapy in ES-SCLC and that it was reasonable to expect all funded use would be in combination with chemotherapy.

Funding criteria

14.27. The Committee considered it appropriate for the funding criteria to allow treatment for those whose ECOG PS improved to 0 or 1, following a first cycle of chemotherapy, as has previously been recommended for atezolizumab for ES-SCLC. The Committee noted the evidence reported by Saida et al. (J Clin Oncol. 2024; 42:Suppl_16) supported PS

improvement in this setting.

Summary for assessment

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

Population	People requiring first-line treatment for extensive-stage small cell lung cancer (ES-SCLC) who either: • Have ECOG performance status (PS) 0-1 before chemotherapy commences for previously untreated disease or • Received one cycle of chemotherapy and has achieved an ECOG PS 0-1 prior to the initiation of chemotherapy cycle 2.
Intervention	All of the below: • durvalumab 1500mg 3 weekly until disease progression. • carboplatin 5AUC on day 1 of the first of the four 21-day cycles. etoposide 100mg/m2 on days 1-3 of the first four 21-day cycles.
Comparator(s)	All of the below: • carboplatin 5AUC on day 1 of the first four 21-day cycles. • etoposide 100mg/m2 on days 1-3 of the first four 21-day cycles. Cycle 1-4 administration time 2.5 hours subsequent
Outcome(s)	*Compared to chemotherapy alone:* Improved overall survival (OS) - CASPIAN reported durvalumab was associated with a median OS of 13 months, compared to 10.3 months with platinum-etoposide (HR=0.73; 95% CI 0.5, -0.91; *P*=0.0047). *Compared to atezolizumab:* Likely to offer similar benefits for PFS and OS compared to atezolizumab. Wang et al. Lung Cancer. 2023:178:47-56
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.	