Record of the Dermatology Advisory Committee Meeting held on 9 June 2023

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

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

The Dermatology Advisory Committee may:

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

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

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

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

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

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

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

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1. Attendance

Present
Rhiannon Braund (Chair)
Marius Rademaker
Martin Denby
Paul Jarrett
Sharad Paul
Sarah McLean-Orsborn

Apologies
Diana Purvis
Lisa Stamp

2. Summary of recommendations

Pharmaceutical and Indication	Recommendation
• Alitretinoin for the treatment of severe chronic hand eczema in adults that is unresponsive to treatment with potent topical corticosteroids	High Priority
• Sirolimus in the treatment of facial angiofibromas associated with tuberous sclerosis complex	High Priority
• Guselkumab for the first-line treatment of moderate to severe plaque psoriasis	High Priority
• Guselkumab for the second-line treatment of moderate to severe plaque psoriasis	High Priority
• Ustekinumab for the first-line biologic treatment of chronic plaque psoriasis	High Priority
• Ustekinumab for the second-line biologic treatment of chronic plaque psoriasis	Medium Priority
• Adalimumab for Flexural or Genital Psoriasis	High Priority

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

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

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

3.3. The Dermatology Advisory Committee is a Specialist Advisory Committee of Pharmac. The Dermatology Advisory Committee and PTAC and other Specialist Advisory Committees have complementary roles, expertise, experience, and perspectives. The Dermatology Advisory Committee and other Specialist Advisory Committees may therefore, at times, make recommendations for treatments for

Dermatology that differ from PTAC's, including the priority assigned to recommendations, when considering the same evidence. Likewise, PTAC may, at times, make recommendations for treatments for Dermatology that differ from the Dermatology Advisory Committee's, or Specialist Advisory Committees may make recommendations that differ from other Specialist Advisory Committees'.

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

4. Record of advice for Upadacitinib for the treatment of atopic dermatitis (AD) held over Zoom, 26 July 2022.

4.1. The Advisory Committee reviewed the record of advice for Upadacitinib for the treatment of atopic dermatitis held over Zoom, 26 July 2022 and agreed that the record be accepted.

5. Previous action points/recommendations made

5.1. The Committee reviewed records of previous meetings of the Dermatology Committee including the November 2020 meeting and the July 2022 advice.

5.2. The Committee noted the record of the advice received in July 2022 regarding upadacitinib for Atopic Dermatitis (AD), noting that the advice recommended the following Special Authority criteria/hospital indication restriction for upadacitinib for atopic dermatitis:

> **Initial application – (atopic dermatitis)** only from a dermatologist.
> Approvals valid for 6 months for applications meeting the following criteria:
> All of the following:
> 1. Patient has moderate to severe atopic dermatitis, severity as defined by an Eczema Area and Severity Index (EASI) score of greater than or equal to 16 or a Dermatology Life Quality Index (DLQI) score of greater than or equal 10; and
> 2. Patient must be over the age of 12; and
> 3. Patient must have received insufficient benefit from topical therapies (including topical corticosteroids or topical calcineurin inhibitors) for a 28-day trial over a period within the last 6 months, unless contraindicated to all; and
> 4. Patient has trialled and received insufficient benefit from at least one systemic therapy for a minimum of three months (eg ciclosporin, azathioprine, methotrexate or mycophenolate mofetil), unless contraindicated to all; and
> 5. An EASI assessment or DLQI assessment has been completed for at least the most recent prior treatment course, preferably while still on treatment but no longer than 1 month following cessation of each prior treatment course; and
> 6. The most recent EASI or DQLI assessment is no more than 1 month old at the time of application.
>
> **Renewal – (atopic dermatitis)** only from a relevant specialist
> Approvals valid for 12 months for applications meeting the following criteria:
> Any of the following:
> 1. Patient has achieved a 75% or greater reduction in EASI score (EASI 75) as compared to baseline EASI prior to commencing upadacitinib; or
> 2. Patient has achieved a DLQI improvement of 4 or more as compared to baseline DLQI prior to commencing upadacitinib.

5.3. The Committee noted the previous recommendation of both PTAC and the Dermatology committee regarding the appropriate Special Authority for upadacitinib for AD. Specifically, members noted the restriction to Dermatologist initiation only for the medicine and that this had the potential to be inequitable because of limited

access to Dermatologists due to an ongoing shortage of Dermatologists in public healthcare.

5.4. Members noted that clinical evidence and physician experience with upadacitinib had continued to evolve since the previous meeting and considered that it generally supported the safety and efficacy of upadacitinib.

5.5. The Committee noted correspondence between Pharmac and primary care practitioner (PCP) members of Pharmac's advisory committees around the potential for non-dermatologist prescribing of upadacitinib for AD. The Committee noted that the feedback from PCP was generally supportive of allowing prescription of upadacitinib, or other new medicines for AD by PCP with the caveat of requiring proper training, support and resourcing of primary care to allow proper diagnosis and treatment of AD with immunosuppressant medicines.

5.6. The Committee noted previous concerns that there may be misdiagnosis of AD if specialist input is not sought. Members noted that while the concerns around misdiagnosis remained, many of the indications which could be misdiagnosed as AD were inflammatory conditions that would respond positively to treatment with upadacitinib, so the loss in efficacy via misdiagnosis was likely to be minimal. The Committee further noted that if there was a requirement for a trial of medicines such as methotrexate or ciclosporin before accessing upadacitinib and this further reduced the chance of inappropriate diagnosis. The Committee noted that some diseases such as rare types of lymphoma could present in a similar way to AD and that treatment with upadacitinib would not be appropriate in these cases. The Committee recommended that any training for PCP must include identification and differentiation of these indications from AD due to the potential for harm.

5.7. The Committee noted that there was substantial variation in the appearance of AD between lighter and darker skin tones which could be a complicating factor in diagnosis by practitioners who were less experienced in diagnosing AD. This may lead to inequity by underestimating the severity of eczema in patients with skin of colour. While telemedicine dermatology support for PCP would be able to assist in diagnosis the Committee considered that training and resources for diagnosis would be key to safely allowing PCP to prescribe upadacitinib for AD.

5.8. Members noted that other medicines like isotretinoin were available for PCP prescribing and that the Committee was not aware of any serious incidents arising from that availability. Members of the Committee with primary care experience noted that current wait times for Dermatologist referral made access to specialist treatment impractical for the majority of people.

5.9. The Committee noted that access under the currently proposed Special Authority was effectively a third-line treatment irrespective of prescriber type. People must first attempt therapy with potent topical therapies before progressing to systemic immunosuppressants such as methotrexate or ciclosporin before being able to meet the Special Authority criteria. Given the minimum four-month period of alternative treatments required by the currently proposed Special Authority this imposed significant barriers to access irrespective of the prescriber type due to the time required to progress through the required stages of treatment.

5.10. The Committee noted that these barriers to treatment access will be more prevalent for people from lower income backgrounds and Māori and Pacific peoples due to lower overall access to healthcare and the frequency of physician visits required for assessments, prescriptions, and maintenance of the required therapies. Health resources and information are also predominantly produced and made available in English which can be a barrier for those who do not speak English as a first

language. Due to this it was important that access be simplified to the greatest extent possible to support equitable access.

5.11. The Committee noted that due to the high relative cost of the medicine compared to the currently funded treatments it was important to target use to those most likely to benefit. The Committee considered that access to upadacitinib for Atopic Dermatitis would be appropriately targeted through the eligibility criteria rather than including specific prescriber types in the Special Authority.

5.12. The Committee noted that management of AD with topical treatments was very difficult for many people due to the time and complexity of a proper topical treatment regimen, noting that a full skin regimen for severe Atopic Dermatitis occupied at least 45 minutes in both the morning and evening making it difficult to maintain. Clinical practice often includes systemic immunosuppressant pulses to bring disease flares back under control, before returning to topical treatment.

5.13. The Committee considered the potential for upadacitinib as a second line treatment, occupying the position in the treatment paradigm currently occupied by systemic immunosuppressants (ciclosporin, azathioprine, methotrexate or mycophenolate mofetil). The Committee considered that while such an amendment to the treatment paradigm was possible that the preference would be for the second line position in treatment to be filled with superior topical treatments, specifically tacrolimus and topical JAK inhibitors. Members noted that often topical treatments were under-utilised. The Committee noted that the current systemic therapies available are well understood, effective for many individuals and that they are relatively inexpensive, so to pursue upadacitinib as a second line treatment was unlikely to be cost-effective at this time.

5.14. The Committee considered that if upadacitinib was made available as a second-line treatment (after topical corticosteroids) there was a potentially significant impact on the pharmaceutical budget due to the large number of people with Atopic Dermatitis. The Committee considered that while there were no notable safety signals that would prevent use as a second-line treatment but that upadacitinib was still a relatively new medicine with limited data on long term treatment. Due to this some physicians may be reluctant to prescribe upadacitinib as a second-line treatment due to unfamiliarity compared to the experience physicians have with existing systemic immunosuppressants. The Committee also noted the lack of paediatric approval for upadacitinib and the unknown potential for oncogenic risk in children.

5.15. The Committee noted that upadacitinib was currently funded for Rheumatoid arthritis (RA), and that if primary care access was allowed for AD that primary care access for RA should be considered alongside it. The Committee considered that advice should be sought from the Rheumatology Advisory Committee on any changes to the Special Authority for RA.

5.16. The Committee noted that if upadacitinib for AD was to be funded that there would be a clinical need to also fund a recombinant herpes zoster (shingles) vaccination for people receiving upadacitinib, as reactivation of herpes zoster was a known side effect of treatment with upadacitinib.

5.17. The Committee noted the potential for future Janus Kinase (JAK) inhibitor applications, for both systemic and topical formulations in treating inflammatory Dermatoses and considered that Pharmac should be aware of the potential for benefit from these medications as they become indicated for diseases for which there are limited or no funded treatments.

5.18. The Committee **recommended** the proposed Special Authority criteria for upadacitinib for Atopic Dermatitis be amended to the following:

Initial application – (atopic dermatitis) from any relevant specialist
Approvals valid for 6 months for applications meeting the following criteria:
All of the following:

1. Patient has moderate to severe atopic dermatitis, severity as defined by an Eczema Area and Severity Index (EASI) score of greater than or equal to 16 or a Dermatology Life Quality Index (DLQI) score of greater than or equal 10; and
2. Patient must be over the age of 12; and
3. Patient must have received insufficient benefit from topical therapy (including topical corticosteroids or topical calcineurin inhibitors) for a 28-day trial over a period within the last 6 months, unless contraindicated to all; and
4. Patient has trialled and received insufficient benefit from at least one systemic therapy for a minimum of three months (eg ciclosporin, azathioprine, methotrexate or mycophenolate mofetil), unless contraindicated to all; and
5. An EASI assessment or DLQI assessment has been completed for at least the most recent prior treatment course, preferably while still on treatment but no longer than 1 month following cessation of each prior treatment course; and
6. The most recent EASI or DQLI assessment is no more than 1 month old at the time of application.

Renewal – (atopic dermatitis) only from a relevant specialist
Approvals valid for 12 months for applications meeting the following criteria:
Any of the following:

1. Patient has achieved a 75% or greater reduction in EASI score (EASI 75) as compared to baseline EASI prior to commencing upadacitinib; or
2. Patient has achieved a DLQI improvement of 4 or more as compared to baseline DLQI prior to commencing upadacitinib.

6. Correspondence and Matters Arising

6.1. The Committee noted a recent FDA approval of a topical gene therapy for recessive dystrophic epidermolysis bullosa (RDEB), noting an approximate cost of $US 600,000. The Committee considered that the number of people in New Zealand with severe RDEB would be fewer than 10.

6.2. Members noted an ongoing international expansion for the indications for IL 17 and 23 inhibitors to include non-psoriasis disorders such as pityriasis rubra pilaris and ichthyoses.

6.3. The Committee noted correspondence from members of the New Zealand Dermatological Society (NZDS) regarding medicines for dermatological conditions.

6.3.1. The Committee noted a request for consideration of funding for topical policresulen (Albothyl). Members noted that topical policresulen was used as a haemostatic agent internationally and that policresulen has both an antiseptic effect and promotes the selective coagulation of necrotic and pathologically altered tissues while leaving healthy tissues intact.

6.3.2. The Committee noted a request for a funding of a Janus Kinase (JAK) inhibitor, specifically baricitinib or upadacitinib, for treatment of alopecia areata or severe vitiligo.

6.3.3. The Committee noted a request for funding of an anti-TNF biologic or secukinumab for generalised pustular psoriasis as a first- or second-line treatment.

6.3.4. The Committee noted correspondence regarding a number of dermatological products that dermatologists considered are currently over-prescribed including:

6.3.4.1. Clobetasol propionate in large quantities for long periods.

6.3.4.2. Promethazine tablets for all ages including in children and the elderly as a long-term, anti-itch, night-time sedative. Members noted Medsafe's

guidelines suggest limited duration use and do not recommend it for infants.

6.3.4.3. The combination of 1% Hydrocortisone, 1% Natamycin and 0.35% Neomycin cream as a general treatment for skin rashes.

6.3.4.4. Oral antibiotics for uninfected eczema.

6.3.4.5. Oral terbinafine for unconfirmed dermatophyte infections including nail dystrophy due to psoriasis or trauma.

7. Therapeutic Group and NPPA Review

7.1. The Committee noted the record of the Anti-infective Advisory Committee from September 2022 which sought input from the Dermatology Advisory Committee on the use of low dose oral antibiotics for the treatment of acne.

7.1.1. The Committee noted low dose doxycycline was a potential treatment for acne but that it was more effective for rosacea. The Committee considered that there was mixed evidence around the hypothesis that a low 40 mg daily dose of doxycycline did not induce antibiotic resistance, but that sub-clinical dosing always had the potential risk of resistance generation. The Committee noted correspondence from members of the New Zealand Dermatological Society (NZDS) supporting the listing of a low-dose doxycycline product.

7.1.2. The Committee noted that low-dose minocycline was already available via Special Authority as a rosacea treatment but that there were side effects associated with long term use.

7.1.3. The Committee noted that there was a relatively new narrow-spectrum low-dose alternative tetracycline in Sarecycline, which is thought to have a lower risk of antibiotic resistance, but that at present this is not Medsafe approved.

7.1.4. The Committee noted that from an anti-microbial resistance perspective while the preference was to cease use of antibiotics for both acne and rosacea, a suitable alternative would need to be available, such as simplified access to isotretinoin or benzoyl peroxide. The Committee noted that there were alternatives to pharmaceutical treatments for both indications in development, primarily around energy-based (e.g. laser) treatment of affected areas.

7.1.5. The Committee considered the funded topical antibiotics available and noted that they were supportive of the phase-out of these medicines for Dermatological indications noting the threat posed by anti-microbial resistance and the presence of alternatives.

7.2. The Committee considered the medicines associated with the highest expenditure in the Dermatology therapeutic group.

7.2.1. The Committee noted that there was significant expenditure associated with betamethasone dipropionate with calcipotriol, which is used for psoriasis, with a large proportion of the expenditure resulting from use of the foam spray formulation. The Committee considered that this was due to the suitability advantages and ease of use of the foam spray compared to the gel and ointment.

7.2.2. The Committee noted the high expenditure on hydrocortisone butyrate and the formulation of it as a lipid cream. The Committee considered that there was a potential for savings from switching to a non-lipo-cream formulation of hydrocortisone butyrate. The Committee noted that savings may be difficult to realise because of greater wastage for the non-lipid creams and ointments due to different consistency and the relative ease of application of lipo-creams.

Biologics for Dermatological conditions

7.3. The Committee reviewed the use of biologics for Dermatological conditions.

7.3.1. The Committee noted correspondence and feedback from the Named Patient Pharmaceutical Assessment (NPPA) regarding the use of secukinumab for hidradenitis suppurativa. The Committee considered that the clinical evidence supported the superiority of secukinumab over adalimumab for hidradenitis suppurativa in short term treatment but that the evidence was unclear as to which was more effective in the long term. The Committee recommended that Pharmac should assess hidradenitis suppurativa for addition to the secukinumab Special Authority with a similar access criteria to the current adalimumab criteria.

7.3.2. The Committee noted that for many of the biologics the renewal timeframes could be extended to simplify access as once people are established they are likely to continue use until the efficacy of the biologic agent reduces.

7.3.3. The Committee considered that the special authority for rituximab be extended to include all forms of pemphigus and pemphigoid including bullous and cicatricial.

7.3.4. The Committee noted that the reduced cost of adalimumab (Amgevita brand) compared to adalimumab (Humira) may create opportunities for increased dosages without posing significant financial risk to the Pharmaceutical Schedule. The Committee noted that adalimumab maximum dosing was previously 40mg per two weeks but had been changed to 40mg per week. The Committee considered that there would be a small group of people with psoriasis for whom 80mg per week would be a more effective treatment and that this increase in dosage would assist in preventing them transitioning off adalimumab to other biologics which are comparatively more expensive.

7.3.5. The Committee considered that there were a number of biologics available internationally for dermatological indications that are not currently Medsafe registered, or generally available in New Zealand including specifically interleukin (IL) inhibitors used for psoriasis and atopic dermatitis. The Committee recommended that Pharmac should investigate options and correspond with the relevant pharmaceutical suppliers to encourage them to submit applications to both Medsafe and Pharmac and make their medicines available to New Zealand. The Committee noted that dupilumab (an IL-4/13 inhibitor) for atopic dermatitis was available in Australia and that there was currently a significant gap in the treatment options for atopic dermatitis in New Zealand compared to many other countries.

Anti-acne preparations

7.4. The Committee noted the recommendation from the 2020 Dermatology Advisory Committee meeting (item 5.2) for allowing lifetime approval and removal of the renewal criteria from the isotretinoin Special Authority. The Committee noted that the requirement for yearly renewal was not clinically necessary and was originally drafted to prompt prescribers to consider if ongoing treatment was necessary due to teratogenicity. The Committee considered that the Special Authority was not the appropriate place for consideration of treatment continuation which form part of clinical best practice and reiterated its recommendation from 2020.

7.4.1. The Committee noted that due to the teratogenic effects of isotretinoin, young women would often have contraceptives prescribed alongside isotretinoin and that depending on their social and cultural background, this could result in a sense of whakama (*shame, embarrassment*) and result in some people not

taking isotretinoin and possibly, moving to less effective, non-funded medications. Due to this it was important for prescribers to be sensitive and culturally conscious and careful with the messages and education provided when prescribing isotretinoin.

7.5. The Committee noted correspondence from the health sector around adapalene gel requesting the removal of the per-prescription maximum. The Committee considered that this appeared to primarily be a cost-containment restriction and that there was no clinical reason for the current restriction.

Topical antibacterials

7.6. The Committee reviewed their 2020 recommendation that the part-charge on mupirocin ointment was appropriate due to the alternatives available and the desire to move away from topical antibacterial treatments due to anti-microbial resistance issues. The Committee considered that for Dermatological conditions mupirocin and other topical antibacterials should be phased out in favour of antiseptics due to the risk of anti-microbial resistance generation. The Committee noted however, that there may be a requirement for mupirocin ointment for other conditions such as its use in nephrology.

7.7. The Committee recommended that Pharmac consult with the health sector on a possible delisting of mupirocin and other topical antibiotics.

Topical antifungals

7.8. The Committee noted correspondence from the supplier of itraconazole oral liquid (Sporanox) that the product would be discontinued in late 2024 and stock would be available until approximately early 2025. The Committee considered that there would be an ongoing requirement for an oral liquid formulation for the treatment of children and that there was emerging data which showed an increase in systemic anti-fungal resistant tinea (ringworm) internationally and noted several cases already reported by New Zealand hospitals. Due to this it was important to maintain access to a wide portfolio of anti-fungal medications including itraconazole. The Committee considered that if no alternative supplier could be identified there would be a requirement for a compounded product and recommended Pharmac consult with the Extemporaneously Compounded Products Group.

7.9. The Committee noted the same rationale applied to the current supply issues for ciclopirox olamine and considered that Pharmac should continue to seek an alternative supplier for the product.

Emollients

7.10. Members noted that there is often a significant change in the texture, appearance or smell of emollients when there is a change in manufacturer or supplier. This can be distressing for those using these products frequently and suggested that Pharmac should consider it alongside other factors when deciding to fund new formulations, or brands in place of existing products.

7.11. Members noted the high comparative usage of Cetomacrogol with glycerol compared to other formulations within the group and considered that this was because of the formulation being available with a pump dispenser which greatly simplified use. Members considered that Pharmac should attempt to source more emollients with a pump dispenser where the formulation allowed.

Antineoplastics

7.12. The Committee noted that there was support for the funding of topical 2% lovastatin for treatment of porokeratosis and considered that Pharmac should investigate any potential supplier of the product.

Topical corticosteroids

7.13. The Committee reviewed the existing market for corticosteroids and combinations corticosteroids. The Committee considered that the majority of the existing formulations were required, especially the combinations which all had individual uses but that there was the potential for market consolidation with some of the different formulation sizes. The Committee considered that consolidation would be a significant project and require careful consultation at all stages.

7.14. The Committee considered that Pharmac should request an amendment to the current packaging for hydrocortisone with miconazole to clarify that it contains a topical steroid and long-term use should be restricted.

7.15. Members considered there was an ongoing need for a small size hydrocortisone ointment (15 g or less) and that Pharmac should continue attempting to source a product.

Parasiticidal preparations

7.16. The Committee noted the current unavailability of permethrin cream and considered that there were significant suitability advantages for a cream compared to a lotion formulation, especially for elderly people. The Committee recommended Pharmac continue to attempt to source a cream formulation.

7.17. The Committee noted their support for the amendment to the ivermectin for scabies Special Authority on 1 June 2023 to simplify access. The Committee considered that it would be appropriate to introduce a limit of three renewals within a short timeframe as a means to reduce the potential for continual re-treatment of ivermectin resistant scabies or incorrect diagnosis.

7.18. The Committee noted that there was an ongoing need for a topical ivermectin formulation for the treatment of rosacea.

Psoriasis and eczema preparations

7.19. The Committee noted that some use of calcipotriol would be for actinic keratoses and that a smaller pack size of 5-10 g would potentially reduce overall usage as only small amounts is required for this indication.

7.20. The Committee considered that the Special Authority criteria for tacrolimus ointment should be widened. The Committee noted that there was significant clinical benefit to using tacrolimus over moderate or potent topical steroids due to equivalent clinical effects and a superior side effect profile.

7.20.1. The Committee considered that the Special Authority for tacrolimus should be widened to include all types of facial eczema/dermatitis as the clinical evidence showed efficacy against many types of less common dermatitis and the current restriction to atopic dermatitis was overly narrow and excluded people with equivalent health impacts whose dermatitis was non-atopic.

7.20.2. The Committee considered that the Special Authority for topical tacrolimus should also be widened to include treatment of eczema/dermatitis at any anatomic site, i.e. as a direct alternative to potent TCS for any inflammatory dermatoses.

7.20.3. The Committee noted that a larger pack size should be considered if tacrolimus usage was to be widened to include non-facial conditions as the 30g tube would not be sufficient for whole-body usage.

7.20.4. The Committee noted that it was supportive of unrestricted access to tacrolimus ointment in line with mid/potent topical corticosteroids but acknowledged that there was a substantial price differential between tacrolimus

and many of the mid/potent steroids. The Committee considered that it was difficult to estimate the total increase in use that would result from an open listing of tacrolimus ointment but that it would be substantial and replace a significant proportion of the current mid/potent steroid use. The Committee considered that a gram for gram replacement of betamethasone prescriptions could be used as an indicator of likely use if tacrolimus ointment was open listed.

7.20.5. The Committee considered for cost containment purposes that a potential Special Authority for tacrolimus could restrict it to use after three months of appropriate use of a suitable mid/potent topical corticosteroids had not been effective or in case of steroid allergy.

7.20.6. The Committee noted that there was a significant outstanding health need for people with vitiligo, particularly people with darker skin tones as the psychosocial effects can be profound. The Committee noted their support for funding tacrolimus for treatment of vitiligo but that at present Pharmac was yet to receive an application for this indication.

7.20.7. The Committee noted that there were other appropriate indications for tacrolimus ointment including discoid lupus erythematosus and psoriasis and considered that Pharmac should investigate expansion of the Special Authority to include these indications.

Wart Preparations

7.21. The Committee noted that at present the only funded wart preparations were imiquimod and podophyllotoxin. The Committee noted that previously more formulations were funded and recommended that Pharmac investigate funding of a greater variety of formulations as the currently available preparations were difficult to use and resulted in larger use of cryotherapy in primary care.

8. Funding applications

8.1. The Committee reviewed the ongoing funding applications in the Dermatology Therapeutic Group and the changes to the Pharmaceutical Schedule that had been made since the 2020 Dermatology Subcommittee meeting.

8.1.1. The Committee considered its previous recommendation from 2015 that brimonidine tartrate 0.5% gel be funded for facial erythema of rosacea was still appropriate, noting that a product has since been approved by Medsafe

8.1.2. The Committee noted ongoing applications for both zinc paste and Lassar paste and considered that the previous recommendations were still appropriate and that they were clinically superior alternatives to zinc with castor oil which was the currently used product. The Committee recommended Pharmac approach suppliers about provision of both products noting that both agents can reduce the use of topical antibiotics and systemic agents.

8.1.3. The Committee noted that metronidazole gel would be suitable for treatment of fungating wounds and that there was a gel formulation currently available (Rozex).

8.1.4. The Committee noted that isotretinoin was the standard of care internationally for adjunctive treatment of neuroblastomas and recommended Pharmac investigate a listing for this indication and consult the Cancer Treatments Advisory Committee (CTAC) on an appropriate Special Authority.

9. Benzoyl peroxide for the treatment of acne vulgaris

Application

9.1. The Advisory Committee reviewed the application for benzoyl peroxide in the treatment of acne vulgaris and provided further information to aid in the economic assessment of benzoyl peroxide.

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

Discussion

Māori impact

9.3. The Committee discussed the impact of funding benzoyl peroxide for the treatment of acne vulgaris on Māori health areas of focus and Māori health outcomes. The Committee considered that it is unknown whether acne disproportionately affects Māori individuals compared to people of other ethnicities, though a higher proportion of Māori compared to non-Māori are among age groups where the prevalence of acne is highest. The Committee noted that Māori face barriers to accessing primary health care (New Zealand Health Survey 2021/22), and as treatment for acne is typically access in primary care, Māori may face disproportionate barriers to accessing acne treatments.

Background

9.4. The Dermatology Committee noted the application for benzoyl peroxide has been reviewed by the following Committees: Anti-infectives Advisory Committee, 2022; Dermatology Subcommittee, 2020, 2017, 2015, 2013; and PTAC, 2016.

9.4.1. In 2013, the Dermatology Subcommittee recommended the listing of topical benzoyl peroxide preparation with a medium priority, due to the unmet need for anti-acne options especially for pregnant individuals.

9.4.2. In 2014, PTAC recommended the listing of topical benzoyl peroxide preparation with a medium priority.

9.4.3. In 2015, the Dermatology Subcommittee recommended the listing of topical benzoyl peroxide preparation with a high priority, due to the unmet need for anti-acne options especially for pregnant individuals.

9.4.4. In 2016, PTAC noted a change in the treatment algorithm for acne since the Dermatology Subcommittee meeting in November 2015. Members considered a funding application on topical benzoyl peroxide should be brought to the Committee for its review.

9.4.5. In 2017, the Dermatology Subcommittee noted its 2015 recommendation to list a topical benzoyl peroxide product and reiterated that funding benzoyl peroxide would help to reduce antibiotic use in the treatment of acne. The Subcommittee considered that there was a lack of funded alternatives for individuals unable to use systemic therapy. Members noted that oral isotretinoin was contraindicated in pregnancy.

9.4.6. In 2020, the Dermatology Subcommittee reiterated its 2015 and 2017 recommendations to list benzoyl peroxide product. Members suggested that Pharmac approach the New Zealand Dermatological Society to request a funding application for topical benzoyl peroxide. The Subcommittee suggested that topical benzoyl peroxide could be funded as a Pharmacist-Only medicine (i.e. not requiring a doctor's prescription) to improve equity of access.

9.4.7. In 2022, the Anti-infectives Advisory Committee noted that due to the prevalence of acne that funded use of topical benzoyl peroxide could potentially be widespread. The Committee also considered that funding topical benzoyl peroxide would have positive equity and anti-microbial stewardship implications as currently people may receive non-funded alternatives (which are relatively expensive) or funded doxycycline, with negative anti-microbial stewardship implications. The Committee considered that Pharmac should attempt to source topical benzoyl peroxide and consider it for funding.

Health need

9.5. The Committee noted that acne is a chronic inflammatory disease of the pilosebaceous unit, which includes the hair follicle, hair shaft and the sebaceous gland. Four processes are believed to contribute to acne development: increased sebum production, follicular hyperkeratinisation, colonisation of skin bacteria, and inflammation.

9.6. The Committee noted acne vulgaris affects nearly all adolescents and adults at some time in their lives, with an 85% prevalence in those aged 12-24 years old and visible adult acne, experienced by 64% and 43% of individuals aged 20-29 and 30-39 years old, respectively.

9.7. The Committee noted that the acne is diagnosed clinically, and is phenotypically characterised by its severity; mild, moderate, or severe. The Committee noted that there is an emphasis to focus more on the experience of the individual and the impact of their quality of life to determine the severity of the acne.

9.8. The Committee noted that acne has a substantial impact on the physical, mental, and social well-being of the individual. The Committee noted that in a New Zealand cross-sectional study of 9,567 high school students, 'problematic acne' was self-reported by 14% of students. Compared to students without the condition, individuals with problematic acne were more likely to have clinically relevant depressive symptoms (OR=2.04; 95% CI, 1.70 to 2.45), clinical significant anxiety (OR=2.30; 95% CI, 1.74 to 3.00), suicidal ideation (OR=1.74; 95% CI, 1.54 to 1.97) and report that they had attempted suicide (OR=1.83; 95% CI, 1.51 to 2.22) (Purvis et al. J Paediatr Child Health. 2006; 42: 793-6).

9.9. The Committee noted that antibiotic resistance is associated with courses of antibiotics, used for the treatment of acne, increase the risk of antibiotic resistance developing in *Cutibacterium acnes* (formerly named *Propionibacterium acnes*) and other commensal bacteria. Community Health Pathways and The Australasian College of Dermatologists report that antibiotic monotherapy (topic or oral) is not recommended due to concerns around the development of antibiotic resistance. Although antibiotics have been important for managing moderate to severe acne, most treatment protocols suggest that they be used for a limited amount of time and should be used in combination with a non-topical antibiotic topical preparation such as benzoyl peroxide, retinoids or azelaic acid (Walsh et al. Lancet. 2016;16:e22-32).

Health benefit

9.10. The Committee noted that benzoyl peroxide is a bactericidal, oxidising agent, that has anti-inflammatory action and may reduce antibiotic resistance when combined with oral or topical antibiotic. The mechanisms of action are complementary to antibiotics and retinoids thus contribute to the synergistic activity.

9.11. The Committee noted that BPO is an effective treatment of acne vulgaris and should be applied to the entire affected area rather than as a spot treatment. The Committee

noted that health benefits would be noticed by the individual after a minimum 3 months of consistent use.

Suitability

9.12. The Committee noted their previous recommendation for a 2.5 or 5% (w/v) preparation of benzoyl peroxide are effective options for the treatment of acne and the lower incidence of irritation when compared to the 10% w/v benzoyl peroxide preparation. The Committee noted that BPO is an effective treatment for acne irrespective of whether a gel or cream preparation is used.

9.13. A Committee member noted people may experience whakama (*shame, embarrassment*) if prescribed acne treatments that are also oral contraceptives, or when contraceptives are co-prescribed with teratogenic treatments such as isotretinoin. As a topical treatment BPO may provide an alternative option for treatment.

Cost and savings

9.14. The Committee considered that if benzoyl peroxide was funded without restrictions in New Zealand, benzoyl peroxide would be used to treat acne of any severity. The Committee considered that funding benzoyl peroxide was unlikely to substantially increase the overall numbers of people accessing funded medications for acne.

9.15. The Committee considered that in the setting of mild to moderate acne, some individuals currently receiving topical retinoids may switch to receiving benzoyl peroxide. The Committee considered that for individuals starting funded treatment for acne, benzoyl peroxide would be used as the first line topical treatment of choice, ahead of other funded topical treatments such as adapalene.

9.16. The Committee considered that in the setting of severe acne, individuals currently receiving oral antibiotics or oral isotretinoin for acne may begin receiving benzoyl peroxide. Members noted the potential for benzoyl peroxide to aggravate the asteotoic effect of isotretinoin but that such an effect was uncommon at the lower doses of isotretinoin commonly used in New Zealand to treat acne. The Committee noted that benzoyl peroxide has synergistic effects when used with other anti-acne treatments and could be used with the intent of reducing the risk of developing antibiotic resistance.

9.17. The Committee considered that most new users of benzoyl peroxide in the first few years of funding would be people newly initiating funded treatment for acne rather than people switching from or already receiving other topical or oral therapies. The Committee noted that some individuals may be accessing privately funded benzoyl peroxide and may switch to publicly funded benzoyl peroxide. The Committee considered that the number of individuals in this group would be relatively small.

9.18. The Committee considered that the duration of treatment for benzoyl peroxide would vary between individuals, with roughly 50% of individuals discontinuing the treatment in the first two weeks due to skin irritation or perceived lack of efficacy. The Committee considered that the remaining proportion of individuals may continue to use benzoyl peroxide long-term.

9.19. The Committee noted that the natural history of acne among teenagers spans an average of four to five years, and long-term users of benzoyl peroxide were likely to have discontinued the treatment after this period.

Summary for assessment

9.20. The Advisory Committee considered that the table below summarises its interpretation of the most appropriate PICO (population, intervention, comparator,

outcomes) information for [the pharmaceutical] if it were to be funded in New Zealand for [the indication]. 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 Advisory 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	Individuals with mild to moderate acne, requiring first-line treatment	Individuals with moderate to severe acne, current receiving oral antibiotics, or other oral treatment for the condition
Intervention	Benzoyl peroxide gel, 25mg/g concentration, applied once daily. With or without other topical acne treatments: • Topical adapalene • Topical tretinoin • Topical clindamycin	Benzoyl peroxide gel, 25mg/g concentration, applied once daily. In addition to oral acne treatments: • Oral lymecycline • Oral doxycycline • Oral isotretinoin (seldom necessary)
Comparator(s) (NZ context)	No treatment, or other topical acne treatments: • Topical adapalene • Topical tretinoin • Topical clindamycin	Oral acne treatments: • Oral lymecycline • Oral doxycycline • Oral isotretinoin
Outcome(s)	Similar efficacy to other topical acne treatments • Yang et al. Cochrane Syst Database Rev. 2020: CD011154 reported that benzoyl period was non-inferior to other agents such as adapalene and clindamycin for the treatment of acne. Reduction in the risk of developing antibiotic resistance	

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 target population would receive currently (status quo – including best supportive care; dose, frequency, treatment duration/conditions for treatment cessation).

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

10. Alitretinoin for the treatment of severe chronic hand eczema in adults that is unresponsive to treatment with potent topical corticosteroids

Application

10.1. Advisory Committee reviewed the application for alitretinoin for the treatment of severe chronic hand eczema in adults that is unresponsive to treatment with potent topical corticosteroids.

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

Recommendation

10.3. The Advisory Committee **recommended** that alitretinoin for the treatment of severe chronic hand eczema in adults that is unresponsive to treatment with potent topical corticosteroids application be funded with a **high priority** within the context of dermatology treatments, subject to the following Special Authority criteria:

> **Initial application** from any relevant practitioner. Approvals valid for 6 months for applications meeting the following criteria:
> All of the following:
> 1. Patient has been diagnosed with severe chronic hand eczema
> 2. Patient is over 18 years of age; and
> 3. Patient has not received sufficient clinical benefit from an adequate trial of potent topical steroids; and
> 4. Patient is not of child-bearing potential; or
> 5. Patient is of child-bearing potential and the possibility of pregnancy has been excluded prior to commencement of treatment and patient has been counselled and understands the risk of teratogenicity if alitretinoin is used during pregnancy and that they must not become pregnant during treatment and for a period of one month after the completion of treatment
>
> **Renewal** from any relevant practitioner. Approvals valid for 6 months for applications meeting the following criteria:
> All of the following:
> 1. Patient is continuing to receive benefit; and
> 2. Patient is not of child-bearing potential; or
> 3. Patient is of child-bearing potential and the possibility of pregnancy has been excluded prior to commencement of treatment and patient has been counselled and understands the risk of teratogenicity if alitretinoin is used during pregnancy and that they must not become pregnant during treatment and for a period of one month after the completion of treatment;

10.4. In making this recommendation, the Advisory Committee considered:

10.4.1. The treatment paradigm for hand eczema can be difficult to deliver in the New Zealand healthcare setting due to the limited time and resources provided to New Zealand primary care providers, and limited access to dermatology services.

10.4.2. There is high quality evidence available showing the efficacy of alitretinoin for hand eczema.

10.4.3. If funded, alitretinoin would be utilised alongside other therapies including topical and systemic corticosteroids, other topical treatments, and possibly methotrexate or ciclosporin dependent on the disease response to treatment.

Discussion

Māori impact

10.5. The Committee discussed the impact of funding alitretinoin for the treatment of severe chronic hand eczema on Hauora Arotahi - Māori health areas of focus and

Māori health outcomes. The Committee noted/considered in 2012 it was reported that, the prevalence of severe eczema was 0.8% in European, and 2.1% in Māori adolescents aged 13-14 years of age (based on 2001-2003 data). This data indicated that the prevalence of eczema in Māori was 2.6 times higher than that of European adolescents at that time. (Clayton et al. Asia Pac Allergy. 2013;3:161-178) The Committee noted that although the study was not conducted in adults, it acknowledges that as many Māori are disproportionately affected by socioeconomic disadvantage, they may be less likely to have access to effective and sustained management of their condition, an inequitable situation that is not confined to tamariki - children alone. The Committee considered that some Māori may have manual labour focussed occupations, in particular involving wet-work (where hands do not stay dry) which is a risk factor for chronic hand eczema.

Background

10.6. The Committee noted the currently funded topical corticosteroids on the Pharmaceutical Schedule, and that the topical calcineurin inhibitors tacrolimus and pimecrolimus, are also funded under Special Authority criteria specifically for facial and eyelid eczema respectively. The Special Authority criteria requires people to have at least one of the following contraindications to topical corticosteroids: periorificial dermatitis, rosacea, documented epidermal atrophy or documented allergy to topical corticosteroids.

10.7. The Committee noted that Pharmac has also not previously received a funding application for any other treatments for severe chronic hand eczema in adults that is unresponsive to treatment with potent topical corticosteroids.

Health need

10.8. The Committee noted that hand dermatitis can be classified into several subtypes, including atopic, hyperkeratotic, vesicular, nummular, and pulpitis; and that the types are all treated similarly. The Committee noted that symptoms of hand eczema include fissures on the hands, which can cause severe pain and lead to the person not being able to use their hands, both in their occupation and for tasks for daily living (Sheehan. Uptodate. 2022). The Committee considered that the itch caused by hand eczema, particularly of the vesicular subtype, can be severe.

10.9. The Committee noted that the prevalence of hand eczema ranges between 1-5% of the global population (Agner et al. J Eur Dermatol Venereol. 2020;34:4-12) and members considered that approximately 1% was the most likely prevalence in New Zealand in their expert opinion. The Committee noted that the prevalence of hand eczema is approximately double in females compared to males (Agner et al. J Eur Dermatol Venereol. 2020;34:4-12). The Committee considered that this is likely due to females being more likely to work in occupations involving wet-work. The Committee considered that the condition more commonly effects people who work in industries involving wet-work, exposure to chemicals, and/or hand visibility Adiest et al, Contact dermatitis. 2002;152(1):93-98 *and* Cvetkovski et al, Br J Dermatol. 2005; 152(1):93-8.

10.10. The Committee considered that hand eczema has further costs and impacts beyond the treatment of immediate symptoms, including the impact on absence from work. It was also noted that people chronic hand eczema has a significant impact on health-related quality of life.

10.11. The Committee considered that although straightforward, the treatment paradigm for hand eczema can be difficult to deliver in the New Zealand healthcare setting due to the time required to educate those with hand eczema about its treatment and prevention. The Committee considered that education on recommended hand-care, skin protection programmes, and avoidance of factors that contribute to hand eczema

are important components of the hand eczema treatment paradigm. The Committee considered that emollients and silicon barriers on their own are often not sufficiently effective in treating hand eczema, and that topical steroids are required in most cases.

10.12. The Committee considered that other treatment options for hand eczema in New Zealand may include botulinum toxin A (Botox) (for hand eczema associated with hyperhidrosis, but not funded for this indication), and systemic therapies such as corticosteroids, methotrexate and ciclosporin. The Committee considered that phototherapy can be effective, but access is severely limited due to there being few phototherapy units across New Zealand.

10.13. The Committee considered that goals of treatment included improving symptoms of the disease, restoring form and function of the hands, and ensuring the hands continue to remain clear of eczema. The Committee considered the importance of setting individualised goals for those affected, for example being able to wash one's hair without pain or being able to participate in sports activities.

10.14. The Committee considered that the duration of treatment was dependent on the treatment being used and the individual circumstances of the person. The Committee noted that hand eczema is a chronic condition which may continue for 5-10 years or longer, and so treatment may be needed over that length of time. The Committee considered that treatments should be added over time, rather than replaced, for example adding a systemic therapy whilst also continuing with topical treatments.

Health benefit

10.15. The Committee considered that the Dermatology Life Quality Index (DLQI), is one of the ways the success of a treatment for hand eczema can be assessed with a decrease of at least 4 points being traditionally assessed as "effective". The Committee noted that a DLQI score of 15 being decreased to 11 still represents a significant impact upon the person's quality of life, so the goal of treatment is shifting to achieving a DLQI of <5 going forward.

10.16. The Committee noted the results from a United Kingdom (UK)-wide survey on the treatment of severe, chronic hand eczema (Smith et al. Clin Exp Dermatol. 2016;42:185-188). The Committee noted that psoralen combined with ultraviolet A (PUVA) and alitretinoin were identified as the most frequent first line treatment options for hyperkeratotic hand eczema, whereas oral corticosteroids were identified as the most frequent first-line treatment for vesicular hand eczema, followed by PUVA and alitretinoin. The Committee noted that retinoids were effective in almost 60% of people, whereas PUVA was effective in 28% of people.

10.17. The Committee noted that alitretinoin is a retinoid (vitamin A derivative) which binds to several retinoid receptor subtypes, regulates cell proliferation and differentiation, reduces epidermal thickness, normalises the expression of some skin barrier genes, and has dermal immunomodulatory and anti-inflammatory properties (New Zealand Formulary. NZF v127. 2023).

10.18. The Committee noted that acitretin is currently available and funded in New Zealand. The Committee considered the results of the following publications to assess the efficacy of acitretin for hand eczema:

- Thestrup-Pederson et al. Aca Derm Venereol. 2001;81:353-5,
- Capella et al. J Dermatolog Tret. 2004;15:88-93 ,
- Tan et al. J Dermatolog Treat. 2015;26:373-5
- O'Shea et al. J Drugs Dermatol. 2015;14:1389-91

- Song et al. Ann Dermatol. 2017;29:385-7

10.19. The Committee considered that the evidence for acitretin was of low quality but did show efficacy of the treatment through increased rates of clearance in comparison to methotrexate (O'Shea et al. J Drugs Dermatol. 2015;14:1389-91) and topical treatments (Capella et al. J Dermatolog Tret. 2004;15:88-93).It also showed reduced symptoms (Tan et al. J Dermatolog Treat. 2015;26:373-5, Thestrup-Pederson et al. Aca Derm Venereol. 2001;81:353-5, Song et al. Ann Dermatol. 2017;29:385-7).

10.20. The Committee also noted the results of a real-world retrospective study comparing the use of alitretinoin and acitretin (Politiek. Dermatol Ther. 2016;29:364-71). The Committee noted authors concluded that both treatments are effective options, but that fewer patients discontinued alitretinoin compared with acitretin due to adverse effects. The Committee considered that the result of most people discontinuing alitretinoin by 48 weeks may show that the condition cleared quicker than with acitretin.

10.21. The applicant noted results of the BACH trial (Ruzicka et al. Br J Dermatol. 2008;158:808-817), a randomised double-blind placebo-controlled multicentre conducted in 1032 people with severe CHE lasting >6 months refractory to previous topical steroid therapy with 409 people given alitretinoin 30 mg daily, 418 people given alitretinoin 10 mg daily, and 205 people given placebo, for 24 weeks. The Committee noted that at 24 weeks 47.7% patients taking 30mg alitretinoin group reported "clear" (22%) or "almost clear" (25.7%) physician global assessment (PGA) scores (P<0.001) and the 10mg alitretinoin group had a response of 27.5% clear (9.3%) or almost clear (18.2%) (P=0.004). The Committee noted that the response rates in both alitretinoin group were higher than the placebo response score 16.6% clear (2.9%) or almost clear (13.7%) (P=0.004) in each group, respectively. The Committee considered that trial was high quality evidence for the efficacy of alitretinoin for hand eczema.

10.22. The Committee noted the 2019 Cochrane systematic review on interventions for hand eczema which included 60 randomised controlled trials on various hand eczema treatments. The Committee considered other clinical studies that showed evidence for the efficacy of alitretinoin for hand eczema, including:

- Halioua et al. Eur J Dermatol. 2019;29:59-66: 112/274 (40.9%) PGA score clear/almost clear at the end of treatment
- FUGETTA (Augustin et al. J German Society Dermatol. 2016: 1261-1270): At week 24, PGA of clear/almost clear was 56% for 30mg and 42% for 10mg .
- Kwon et al. Ann Dermatol. 2016;28:364:70: 12/27 (44.4%) clear/almost clear responses after 12 weeks of treatment.
- PASSION (Diamant et al. J Dermatological treatment. 2016;26(6):577-583): At Week 12 and Week 24, 31.7% (n=200) and 29.8% (n=188), respectively, of all patients receiving at least one dose of alitretinoin (n=631) had a PGA status of clear/almost clear
- TOCCATA (Diepgen et al. Acta Derm Venereol. 2012;92:251-25): 56.7% of 680 PPGA clear/almost clear

10.23. The Committee considered results of a retrospective review comparing efficacy and safety of alitretinoin to ciclosporin (Jang et al. Acta Derm Vernereol. 2020;100:adv00043. The Committee noted that after 24 weeks of treatment, responder rates were 68.2% for alitretinoin and 40.9% for ciclosporin. The Committee also considered a prematurely discontinued randomised controlled trial comparing

alitretinoin to azathioprine (Voorberfg et al. Contact Dermatitis. 2022;87:366-8). At 24 weeks response rates were 64.3% for alitretinoin and 14.3% for azathioprine.

10.24. The Committee considered a retrospective study assessing the efficacy of 10 mg alitretinoin with Narrowband Ultraviolet B (UVB)Therapy for chronic hand dermatitis compared to alitretinoin 30 mg. At 16 weeks response rates were 68% alitretinoin + UVB, and 39% alitretinoin. The Committee considered that alliteration with UVB therapy would be a useful way to decrease alitretinoin adverse effects but considered that UVB therapy is not accessible for many New Zealanders.

10.25. The Committee considered that the adverse effects of alitretinoin are class-related and appear to be dose-related. The Committee noted that the most common side effects include headache, and that thyroid tests would be required before starting therapy.

Suitability

10.26. The Committee noted that the Medsafe Datasheet for alitretinoin (Zematane) indicates it is a powerful human teratogen inducing a high frequency of severe and life-threatening birth defects and is strictly contraindicated in pregnancy. Those of childbearing potential must meet all of the conditions of the Pregnancy Prevention Programme.

Cost and savings

10.27. The Committee considered that if funded, alitretinoin would be utilised alongside other therapies including topical and systemic corticosteroids, other topical treatments, and possibly methotrexate or ciclosporin, dependent on the disease's response to treatment (but that lesser amounts or lower doses of these treatment would be required). The Committee considered that around 50% of individuals would cease treatment after 6 months, and the remainder might continue treatment for approximately 1-2 years.

10.28. The Committee considered it is difficult to assess the number of people who would be eligible for funded treatment but considered that the uptake would be high (around 80% by Dermatologists and 20% by GPs).

10.29. The Committee considered that there was a risk that alitretinoin would be used outside of the funded indication, and that this should be accounted for in its evaluation.

Summary for assessment

10.30. The Advisory Committee considered that the table below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for alitretinoin if it were to be funded in New Zealand for chronic hand eczema unresponsive to potent topical corticosteroid treatment. 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 Advisory 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.

10.31. The Advisory Committee noted that elements of in the PICO (population, intervention, comparator, outcomes) for this application is unclear/uncertain at this time. The PICO may develop based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	Adults with severe chronic hand eczema unresponsive to potent topical corticosteroid treatment
Intervention	Alitretinoin 10 mg once per day initially, increasing by 10 mg per week to a maximum of 30 mg per day, for 12-24 weeks (in addition to an initial course of prednisone), with continued treatment if benefiting
Comparator(s) (NZ context)	Prednisone 0.5-1 mg/kg per day gradually reduced over 2-8 weeks, superpotent topical corticosteroids appropriately prescribed for 3-6 months, prednisone, with adjuvant systemic therapy (eg ciclosporin (2.5-5 mg/kg per day) methotrexate (10-15 mg/week), methotrexate, azathioprine, or phototherapy (<5% of cases)) for 6-12 months.
Outcome(s)	Physician Global Assessment of response - 'clear' or 'almost clear', Significant improvement in DLQI

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 target 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. Sirolimus for the treatment of facial angiofibromas associated with tuberous sclerosis complex

Application

11.1. The Advisory Committee reviewed the application for sirolimus in the treatment of facial angiofibromas associated with tuberous sclerosis complex.

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

Recommendation

11.3. The Advisory Committee **recommended** that sirolimus be listed with a **high priority** within the context of dermatology treatments subject to the following Special Authority criteria:

Initial application — (Facial angiofibromas) from any relevant practitioner. Approvals valid for 6 months for applications meeting the following criteria:

1. Patient has confirmed diagnosis of facial angiofibromas

Renewal application — (Facial angiofibromas) from any relevant practitioner. Approvals valid for life for applications meeting the following criteria:

Both:
1. Patient has confirmed diagnosis of facial angiofibromas
2. Patient has ongoing improvement in symptoms

11.4. The Advisory Committee recommendation was based on:

- The high health need of those with facial angiofibromas
- The lack of other treatments available in the public system
- The need to ensure equitable access to treatment

Discussion

Māori impact

11.5. The Committee considered the impact of funding sirolimus for the treatment of facial angiofibromas associated with tuberous sclerosis complex on Hauora Arotahi - Māori health areas of focus and Māori health outcomes. The Committee noted that whilst there was no published evidence on the prevalence of the condition in Māori, approximately four of the 32 requests for access to sirolimus, for all indications, via the Named Patient Pharmaceutical Assessment (NPPA) process were for Māori. The Committee noted access to medicines via the NPPA process may result in inequitable access due to the physician time and resource required for an application.

Background

11.6. The Committee noted its previous review (as the Dermatology Subcommittee) in November 2015 of an application for topical sirolimus consequent to NPPA applications for sirolimus ointment (rapamycin). That application involved a 0.1-1% ointment that was compounded by Optimus Healthcare compounding pharmacy. The Committee noted that the recommendation of deferral, subject to the outcome of a phase two study by Koenig et al on 177 patients with tuberous sclerosis complex associated facial angiofibromas treated with topical sirolimus (NCT01526356). This product was ranked in 2020. This application is now on the decline list due to the lack of a supplier, and the product not being able to be safely compounded in community pharmacy.

11.7. The Committee noted a further application for this pharmaceutical was received in January 2023, from a supplier for the same indication, but for a non-compounded product with a strength of 0.5%.

Health need

11.8. The Committee noted it had previously reviewed the health need of those with facial angiofibromas associated with tuberous sclerosis complex in November 2015.

11.9. The Committee noted facial angiofibromas are the most common presentation in tuberous sclerosis complex and are prevalent in 70-80% of those with the condition.

11.10. The Committee noted tuberous sclerosis complex is an autosomal dominant genetic disorder which is caused by a mutation in either the TSC1 gene or the TSC2 gene. It is a genetic multisystem disorder characterised by widespread hamartomas in several organs, including the brain, heart, skin, eyes, kidney, lung, and liver.

11.11. The Committee noted that the prevalence of tuberous sclerosis complex is estimated at between 0.7 – 8.8 per 100,000, and facial angiofibromas to be the most common presentation in tuberous sclerosis complex which are prevalent in 70-80% of people with tuberous sclerosis complex. The Committee noted in November 2015, that there could be 399 individuals in New Zealand with tuberous sclerosis complex (based on a 2004 estimate), and of that number, there may be 40-80 individuals in New Zealand with moderate/significant facial angiofibromas, with an additional seven new cases per year.

11.12. The Committee noted those with facial angiofibromas associated with tuberous sclerosis complex can experience frequent spontaneous and uncontrolled bleeding, and infections are common when the lesions are present around the eyes, nose, and mouth. Due to progressive growth, over time facial angiofibromas can impair vision and breathing, and have psychological consequences (emotional, social and self-image disorders), with uncontrolled growth potentially causing further cosmetic disfigurement (Crall et al. Pediatr Dermatol. 2016; 33:518-25).

11.13. The Committee noted the number and size of the facial angiofibromas increased through childhood, whilst in adulthood the lesions tended to be stable or grow at a slower rate.

11.14. The Committee considered that the effects of the condition were most distressing in young adults, and as such they had a higher health need.

11.15. The Committee noted a 2016 survey, undertaken in a children's hospital, suggested that those who received treatment for facial angiofibromas reported a significantly improved Children's Dermatology Life Quality Index (CDLQI) score compared to those not treated. The CDLQI score of untreated individuals was 9.5 compared to 3.83 in those who had received treatment (p=0.001). Those who were not treated had a CDLQI score that represented a moderate effect on quality of life, whilst those treated had a small effect (Crall et al. 2016).The largest proportion of those who were treated had been recommended to use topical rapamycin (47.3%) (Crall et al. 2016).

11.16. The Committee noted a US study provided by the supplier that reported gaps in the care for people with facial angiofibromas associated with tuberous sclerosis complex. 41% of people reported never receiving treatment for facial angiofibromas even though 74.3% had visited a dermatologist, indicating many people are unable to receive treatment. The Committee considered that underdiagnosis may also influence access to treatment in New Zealand for those affected, with the condition being hard to diagnose.

11.17. The Committee noted that there is minimal access to dermabrasion or laser therapies in the public health system, these treatments must be self-funded by the individual at significant cost.

11.18. The Committee considered that the health need of those with facial angiofibromas was higher than those on the body due to increased prominence of the angiofibromas, and the ensuing greater cosmetic impact.

Health benefit

11.19. The Committee noted sirolimus forms a complex which binds to and selectively inhibits mTORC1. The mTOR complex modulates aspects of the cell cycle, cell growth, proliferation and migration. mTORC1 inhibition reduces the dysregulated growth and differentiation observed in facial angiofibromas.

11.20. The Committee noted the Koenig et al, JAMA Dermatol. 2018;154:773-80 study of 179 individuals randomised to control, 0.1% or 1% topical treatment for 6 months, applied once daily. At 6 months the Angiofibroma Grading Scale mean improvement for 1% sirolimus was 16.7 points vs 11.0 for 0.1% sirolimus vs 2.1 points for vehicle only (P < .001 for 1% and 0.1% vs vehicle only). The Committee noted there were minimal adverse events. The Committee considered most improvement was observed in the first month of treatment, with most participants completing the trial. The Committee noted there was no drug detected in the serum of individuals.

11.21. Committee noted the Wataya-Kaneda et al, JAMA Dermatol. 2017;153:39-48 study that involved 36 people, of which 18 were children. Sirolimus gel concentrations of 0.05%, 0.1%, or 0.2% or placebo were applied twice daily for 12 weeks. The improvement factor was statistically significant in all active treatment groups receiving 0.2% sirolimus (mean [SD], 1.94 [0.68]; P < .001) but not in the adult subgroups receiving 0.1% (mean [SD], 0.88 [0.85]; P = .31) and 0.05% (mean [SD], 1.63 [1.11]; P = .09) concentrations of sirolimus. No significant adverse effects were observed. The Committee considered that whilst the study was small, it was well designed.

11.22. The Committee noted that low blood levels of sirolimus (<0.25 ng/mL) were detected in adults (1 [25%] in 0.1% and 2 [50%] in 0.2%) and children (1 [25%] in 0.05%, 2 [50%] in 0.1%, and 4 [100%] in 0.2%). The Committee noted that the authors

considered this may be due to the gel formulation being better absorbed than the ointment form.

11.23. The Committee noted the Wataya-Kaneda et al, JAMA Dermatol. 2018;154:781-788 study of 62 people, of which 27 were children, who were received either 0.2% sirolimus gel (n=30) or placebo (n=32) applied twice daily for 12 weeks. The response rates of the angiofibromas at weeks 4, 8, and 12 of treatment was 20% (95% CI, 8%-39%; P = .01), 43% (95% CI, 26%-63%; P < .001), and 60% (95% CI, 41%-77%; P < .001) with sirolimus vs 0% in placebo group. 0/ 31 in placebo group were rated improved or better, and 26 (84%) were rated unchanged. In the sirolimus group 5 (17%) and 13 (43%) were rated markedly improved and improved, respectively.

11.24. The Committee noted the following studies:

- Foster et al, Australas J Dermatol. 2012;53:52-6.
- Wataya-Kaneda et al, Br J Dermatol. 2011;165:912-6.
- Csoma et al, Pediatric Dermatology. 2019;36:S41-S42 (supplier provided)
- Amin et al, Int Sch Res Notices. 2017:8404378
- Tu et al, Australas J Dermatol. 2014;55:63-9
- Salido et al, J Eur Acad Dermatol Venereol. 2012;26:1315-8
- Viswanath et al, Indian J Dermatol. 2016; 61: 119
- Bae-Harboe et al, Lasers Surg Med. 2013;45:555-7
- Knopfel et al, Actas Dermosifiliogr. 2014;105:802-3
- Smith et al, BJD, 2012; 167 (s1); ppl127-141 (supplier provided)
- Ott et al, Int J Clin Pharm, 2013, 35;1331 (supplier provided)
- Wheless et al, J Child Neurol, 2013, 28;933:
- Wheeless et al, Child Neurol Open. 2019; 6:
- Truchuelo et al, Dermatol Online J. 2012;18:15
- Wataya-Kaneda et al, Arch Dermatol. 2012;148:138-9:
- DeKlotz et al, Arch Dermatol. 2011;147:1116-7.
- Haemel et al. Arch Dermatol. 2010;146:715-8
- Trujillano Ruiz et al, EJH Pharmacy 2016;23:A207.
- Okanishi et al, Front Med (Lausanne). 2020; 7: 1.
- Lee et al, Dermatology. 2018;234:13-22:
- Hatano et al, Orphanet J Rare Dis. 2020;15:133
- Wataya-Kaneda et al, Dermatol Ther (Heidelb). 2020;10:635-650
- Ebrahimi-Fakhari et al, Dermatol Ther (Heidelb), 2017; 7:175–179:
- Norrenberg et al, Br J Dermatol. 2018;179:208-209
- Safa et al, Oxford Medical Case Reports, 2017;7, 104–105 (supplier provided)
- Wang et al, Pediatr Dermatol. 2017;34:572-577.
- Tanaka et al, Br J Dermatol. 2013;169:1314-8.
- Cinar et al, Indian J Dermatol Venereol Leprol. 2017;83:27-32

- Pynn et al, Pediatr Dermatol. 2015;32:e120-3.
- Hwang et al, Journal of Dermatology, 2012 (supplier provided)
- Vasani et al, Indian J Dermatol. 2015; 60: 165–169.
- Park et al, Dermatology 2014;228:37–41:
- Rodrigo-Nicolas et al, J Am Acad Dermatol, 2013, P6521 (supplier provided)
- Kaufman Mcnamara et al, J Dermatolog Treat. 2012; 23: 46–48.
- Valerón-Almazán P, et al, Actas Dermosifiliogr. 2012;103:165—6:
- Malissen et al, J Am Acad Dermatol. 2017;77:464-472.e3
- Mutizwa et al, Br J Dermatol. 2011;165:922-3.
- Chen et al Br J Dermatol. 2020; 183:655-663

11.25. The Committee considered there to be a lack of long-term safety data (>5 years) regarding the adverse effects of topical sirolimus.

11.26. The Committee considered it was unclear which types of lesions respond to topical sirolimus, but facial hypomelanotic macules and some fibrous cephalic plaques have been observed to respond to treatment.

Suitability

11.27. The Committee noted sirolimus is administered as a topical preparation, once daily, ideally prior to sleep. The amount of topical preparation that needs to be applied is 6 mg/cm2/day to produce a thin confluent layer on the affected skin. The recommended amount should be explained by a pharmacist or prescriber to ensure that an adequate amount is administered.

Cost and savings

11.28. The Committee considered that individuals were likely to need long term uninterrupted treatment to maintain the clinical benefit, with the Committee noting the condition had a lifelong health need. In practical use the Committee estimated that many people will cease use as their condition improves, restarting after a period off treatment as the condition recurs. The Committee estimated an average time on treatment as 50% across the entire group of people using sirolimus for facial angiofibromas.

11.29. The Committee considered that the quantity of ointment used per week would be equal to their previous estimate for the 0.1% formulation, at 1-2g used per week. They considered that due to the higher strength, there is likely an efficacy gain over the 0.1% formulation.

11.30. The Committee noted health benefit evidence that reported a reduction in application frequency from three times weekly to once weekly did not adequately address the health needs of the individual, with the condition worsening upon reduction in treatment.

11.31. The Committee considered that while some people would receive surgical treatment privately, this was uncommon in the public system.

Funding criteria

11.32. The Committee considered that funding of this treatment through the NPPA pathway should not be restricted during the funding assessment process.

Summary for assessment

11.33. The Advisory Committee considered that the table below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for sirolimus if it were to be funded in New Zealand for facial angiofibromas associated with tuberous sclerosis complex. 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 Advisory 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	Individuals with facial angiofibroma associated with tuberous sclerosis complex.
Intervention	Sirolimus ointment 0.5%, applied as a thin film over affected area daily. Treatment expected to be ongoing
Comparator(s)	Surgical intervention for a limited number of individuals.
Outcome(s)	Improved appearance (reduced size and colour) of facial angiofibromas which is sustained while sirolimus treatment ongoing. Recurrence is usual after surgical interventions.

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 target 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.

12. Guselkumab for the treatment of moderate to severe plaque psoriasis

Application

12.1. The Advisory Committee reviewed the application for guselkumab in the treatment of moderate to severe plaque psoriasis.

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

Recommendation

12.3. The Advisory Committee **recommended** that Guselkumab be **listed** with a **high priority** within the context of first-line treatment of moderate to severe plaque psoriasis subject to the following Special Authority criteria:

Initial application – (severe chronic plaque psoriasis, first line biologic) application from a dermatologist. Approvals valid for 4 months for applications meeting the following criteria:

1. All of the following:
   1.1. Either:
      1.1.1. The patient has 'whole body' severe chronic plaque psoriasis with a Psoriasis Area and Severity Index (PASI) score of greater than 10; or
      1.1.2. The patient has severe chronic plaque psoriasis of the face, or palms of a hand or sole of a foot, or genital or flexural psoriasis present; and

1.2. The Patient has tried but had an inadequate response, or has experienced intolerable side effects from, at least three of the following (at maximum tolerated doses unless contraindicated): phototherapy, methotrexate, ciclosporin, or acitretin; and
1.3. A PASI assessment or Dermatology Life Quality Index (DLQI) assessment has been completed for at least the most recent prior treatment course, preferably while still on treatment but no longer than 1 month following cessation of each prior treatment course; and
1.4. The most recent PASI or DLQI assessment is no more than 1 month old at the time of application.

Renewal – (severe chronic plaque psoriasis) application from any relevant practitioner. Approvals valid for 6 months for applications meeting the following criteria:

1. All of the following:
   1.1. Either:
      1.1.1. Patient's PASI score has reduced by 75% or more (PASI 75) as compared to their baseline PASI prior to commencing guselkumab; or
      1.1.2. Patient has a Dermatology Life Quality Index (DLQI) improvement of 5 or more, as compared to their baseline DLQI prior to commencing guselkumab.

12.4. The Advisory Committee **recommended** that Guselkumab to be listed with a **high priority** within the context of second-line treatment of moderate to severe plaque psoriasis subject to the following Special Authority criteria:

Initial application – (severe chronic plaque psoriasis, second line biologic) application from a dermatologist. Approvals valid for 4 months for applications meeting the following criteria:

1. All of the following:
   1.1. The patient has had an initial Special Authority approval for adalimumab, etanercept or Secukinumab, or has trialled infliximab in accordance with the General Rules of the Pharmaceutical Schedule, for severe chronic plaque psoriasis; and
   1.2. Either:
      1.2.1. Patient has experienced intolerable side effects from adalimumab, etanercept, infliximab or secukinumab; or
      1.2.2. Patient has received insufficient benefit from adalimumab, etanercept, infliximab or secukinumab; and
   1.3. A PASI assessment or Dermatology Life Quality Index (DLQI) assessment has been completed for at least the most recent prior treatment course, preferably while still on treatment but no longer than 1 month following cessation of each prior treatment course; and
   1.4. The most recent PASI or DLQI assessment is no more than 1 month old at the time of application.

Renewal – (severe chronic plaque psoriasis) application from any relevant practitioner. Approvals valid for 6 months for applications meeting the following criteria:

1. Both:
   Either:
   1.1. Patient's PASI score has reduced by 75% or more (PASI 75) as compared to their baseline PASI prior to commencing guselkumab; or
   1.2. Patient has a Dermatology Life Quality Index (DLQI) improvement of 5 or more, as compared to their baseline DLQI prior to commencing guselkumab.

12.5. The Advisory Committee made the recommendations for the listing of guselkumab for first- and second-line therapy for individuals with moderate to severe plaque psoriasis due to:

- The high health need of these individuals, particularly when the previous biologic treatment has not provided the individual with adequate health benefit or the received health benefits of the treatment wanes with time.
- The less frequent dosing schedules, sustained efficacy, and clinical superiority of guselkumab compared to other funded options which would potentially offer individuals better treatment outcomes and a different mechanism to treat psoriasis if it was to be funded.

Discussion

Māori impact

12.6. The Committee noted the impact of funding guselkumab for the treatment of moderate to severe plaque psoriasis on Māori health areas of focus and Māori health outcomes. The Committee noted that there is limited evidence on the prevalence of moderate to severe psoriasis in the Māori population. The Committee noted a 2014 letter to the New Zealand Medical Journal reported that Māori and Pacific peoples were overrepresented in the numbers treated for psoriasis in the Auckland District Health Board (ADHB) over the last 5 years (2009–2014) (Lee and Lamb, N Z Med J. 2014;127:73-4). The Committee noted that as many Māori experience greater barriers to accessing the appropriate healthcare and treatments in comparison with European individuals and therefore considered there may be greater unmet health need for Māori individuals with plaque psoriasis.

Background

12.7. The Committee noted that it had previously reviewed an application in 2021 for risankizumab an interleukin-23 (IL-23) inhibiting biologic medicine. At the time this was recommended by the Dermatology Advisory Committee for listing on the Pharmaceutical Schedule with a high priority for both the first- and second-lines of treatment. The application for risankizumab was thereafter reviewed by PTAC in 2021 and was recommended for listing with a medium priority for first-line and high priority for second-line treatment. The Committee noted that as risankizumab and guselkumab both target the P19 subunit of IL-23, when considering the application for guselkumab, other currently unfunded biologics, namely, risankizumab and ustekinumab would also be discussed.

Health need

12.8. The Committee noted that chronic plaque psoriasis is an inflammatory skin disorder. Chronic plaque psoriasis is the most common type of psoriasis (approximately 80-90%). The Subcommittee noted that approximately 2% of the New Zealand population are affected, but that the majority of individuals have clinically mild psoriasis which is not extensive enough to warrant treatment with biologics.

12.9. The Committee noted that the interleukin 23 (IL-23) and interleukin 17 (IL-17) pathway is pivotal in the pathogenesis of psoriasis. IL-23 is a key regulator of IL-17 secretion.

12.10. The Committee noted that there are currently four biologic treatments, in two classes, funded for the treatment of moderate to severe plaque psoriasis in New Zealand: the three tumour necrosis factor alpha (TNF-α) inhibitors adalimumab, etanercept, and infliximab, and an IL-17A inhibitor secukinumab. The Committee considered that, although funded for this indication, infliximab is not the drug of choice for most clinicians as it requires a day stay infusion centre and incurs a significant cost in time and money to both the individual receiving treatment and the health sector. The Committee also considered that etanercept is less commonly used than adalimumab,

as it is less efficacious than the other funded biologic agents and it requires weekly administration.

12.11. The Committee noted that there are no funded IL-23 inhibitors available for the treatment of psoriasis and noted that the Pharmaceutical Schedule currently lists 'second-generation' biologics namely, etanercept, adalimumab, infliximab and secukinumab for the treatment of moderate to severe psoriasis. The Committee noted that Guselkumab is a third-generation biologic and considered to be associated with greater clinical efficacy for plaque psoriasis, which is sustained for greater periods of time, compared with the duration of second-generation biologics therapeutic efficacy.

12.12. The Committee noted that 30-60% of people with moderate to severe plaque psoriasis who were using biologics had discontinued treatment at 75 months due to loss of efficacy, with secukinumab having the lowest drug-survival (Egeberg et al. Br J Dermatol. 2018; 178:509-519). The Committee note the waning of therapeutic efficacy over time is a significant concern for individuals and clinicians. The Committee noted that if an individual has not received adequate health benefit from adalimumab, then they will change therapies and receive secukinumab, however, if this therapy does not provide individuals with significant relief from symptoms the clinician is limited to providing only best compassionate and supportive care for these individuals. The Committee noted that access to a funded third-generation biologic like guselkumab or risankizumab is needed in New Zealand to address this unmet health need.

12.13. The Committee considered that there is still a disproportionate impact of psoriasis on individuals who are not receiving adequate health benefit from the current biologic therapies. The Committee noted that psoriasis has a profound psychosocial effect, with individuals suffering from depression and anxiety. The Committee noted that plaque psoriasis is associated with levels of impairment leading to an inability to work, and that regaining the ability to work is an important outcome for affected individuals.

Health benefit

12.14. The Committee noted that guselkumab is a fully human immunoglobulin G1 lambda (IgG1λ) monoclonal antibody that binds with high-affinity and specificity to the p19 subunit of IL-23. This binding prevents the interaction of IL-23 with its corresponding receptor on the surface of the immune cell. This action is responsible for blocking the initiation of the IL-23 pathway and the subsequent release of other proinflammatory cytokines.

12.15. The Committee noted that the renewal criteria for biologics in the treatment of severe plaque psoriasis defines a sufficient response to treatment as a reduction in the Psoriasis Area Severity Index (PASI) rate response of 75% from baseline (PASI 75). The Committee considered that a PASI 75 response is now an older measure of success to treatment and improvements in therapeutics and protocols have resulted in PASI 90 rate response being considered to be a more significant goal for clinicians and the individuals with moderate-to-severe plaque psoriasis. The Committee noted that while a PASI score is clinically important, there is greater focus by clinicians in determining the health benefit of a treatment using the Dermatology life quality index (DLQI) in which provides clinicians with an understanding of the individual's experience with psoriasis before and after treatment.

12.16. The Committee noted the following studies demonstrating the health benefits of guselkumab for the treatment of moderate-to-severe psoriasis:

- Blauvelt et al. J Am Acad Dermatol. 2017; 76:405-17
- Reich et al. J Am Acad Dermatol. 2017; 76:418-431
- Papp et al. J Eur Acad Dermato Venereol. 2018; 32:1515-22.

- Reich et al. Lancet. 2019; 394:831-39
- Reich et al. Br J Dermatol. 2021; 185:1146-59
- Blauvelt et al. J Am Acad Dermatol. 2022; 86:827-834

12.17. The Committee considered that the evidence for guselkumab providing a clinically significant health benefit to individuals with plaque psoriasis is strong and would provide substantial improvement in the quality of life of those with moderate-to-severe plaque psoriasis. The Committee considered guselkumab clinical trials to have produced high quality data with a clear benefit which would also be experienced by individuals with plaque psoriasis in New Zealand. The Committee noted that in regard to the observed PASI 90 and PASI 100 responses guselkumab has superior therapeutic effects to the currently available biologic treatments for plaque psoriasis on the pharmaceutical schedule for plaque psoriasis and considered there to be a significant unmet health need that guselkumab would address.

12.18. The Committee noted a meta-analysis study comparing efficacy and safety of biologics used in the treatment of plaque psoriasis. The study analysed the results of sixty trials and reported on the PASI 90 score for psoriasis treatment options (Armstrong et al. JAMA Dermatol. 2020; 156:258-69):

12.18.1. In regards to short-term efficacy (week 10 to 16) the estimated PASI 90 response rates were 71.6% (95% credible interval [CrI], 67.5%-75.4%) for risankizumab, 67.3% (95% CrI, 62.5%-71.9%) for guselkumab; 61.4% (95% CrI, 57.2%-65.6%) for secukinumab; 57.4% (95% CrI, 52.2%-62.8%) for infliximab, 43.9% (40.2%-47.9%) for ustekinumab; 43.7% (95% CrI, 40.0%-47.4%) for adalimumab and 17.9% (CrI, 14.9%-21.4%) for etanercept. No significant differences in short-term efficacy among risankizumab and guselkumab were reported.

12.18.2. In regards to long-term efficacy (44 to 60 weeks of therapy recieved) the estimated PASI 90 response rates were 79.4% (95% confidence interval [CI], 75.5%-82.9%) for risankizumab, 76.5% (95% CI, 72.1%-80.5%) for guselkumab, 71.3% (95% CI, 64.2%-77.5%) for secukinumab, 52.4% (95% CI, 47.1%-57.7%) for ustekinumab, 46.2% (95% CI, 38.6%-53.9%) for adalimumab, 40.1% (95% CI, 30.0%-51.1%) for infliximab, 33.4% (95% CI, 28.5%-38.7%) for etanercept. Significantly higher PASI 90 response rates were reported in guselkumab and risankizumab and secukinumab compared to adalimumab, infliximab, etanercept and ustekinumab.

12.19. The Committee considered the clinical efficacy and sustained therapeutic duration of guselkumab and risankizumab to be superior to the currently available therapeutics in New Zealand. The Committee considered that the evidence appears to suggest guselkumab and risankizumab have improved long-term drug survival compared to the currently funded biologics for psoriasis. The Committee noted that guselkumab and risankizumab have the same mechanism of action and noted the therapeutic efficacy and safety profiles of both guselkumab and risankizumab to be equivalent. The Committee noted that either of these two pharmaceuticals would provide significant health benefit to individuals with moderate-to-severe plaque psoriasis in both first- and second-line treatment. The Committee noted that if either option was listed guselkumab or risankizumab would likely become the preferred first-line option for treatment for individuals with moderate-to-severe plaque psoriasis.

Suitability

12.20. The Committee noted that guselkumab is administered as a subcutaneous injection, the supplier indicates a person could self-inject following appropriate training by a healthcare professional. The recommended dose of guselkumab for adults with

moderate to severe plaque psoriasis is 100mg by subcutaneous injection at weeks 0 and 4, and thereafter every 8 weeks. While other biologics can also be administered subcutaneously, including etanercept, adalimumab and secukinumab, as these are administered at a higher frequency than guselkumab (once weekly, fortnightly, and monthly respectively), the latter would lower the number of injections an individual must receive or undertake. The Committee considered that the longer duration between administration would be more convenient for individuals with psoriasis.

Cost and savings

12.21. The Committee noted that most people treated with a biologic for psoriasis received either adalimumab or secukinumab with the former having the greater market share. The Committee considered that uptake of guselkumab would likely be similar to uptake of risankizumab should either be funded, due to the similar efficacy between the two. The Committee considered that if guselkumab were available in a first line setting, that the majority of patients would start on it due to the strong evidence of benefit. The Committee considered that there may be slight differences in frequency of administration between guselkumab and risankizumab that may impact uptake if both were to be funded. The Committee also considered that the evidence supported a superior efficacy for both guselkumab and risankizumab compared to ustekinumab for plaque psoriasis. The Committee considered that few people received etanercept or infliximab.

Summary for assessment

12.22. The Advisory Committee considered that the table below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for guselkumab if it were to be funded in New Zealand for psoriasis. 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 Advisory 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	First-line: People with severe chronic plaque psoriasis (defined as a PASI score >10 or psoriasis of the face, palm or sole of foot) who have experienced intolerable side effects from, are contraindicated to or have received inadequate benefit from, prior systemic therapy. Second-line: As above, with the additional requirement of having also trialled at least one prior biologic therapy.
Intervention	Guselkumab 100mg at weeks 0 and 4, and thereafter every 8 weeks delivered via subcutaneous injection. In case of treatment non-response, people may proceed to a subsequent line biologic.
Comparator(s) (NZ context)	Other listed biologic treatments: • Adalimumab: 80mg initially followed by 40mg every two weeks thereafter; delivered as subcutaneous injection (currently ~50% market share) • Secukinumab: 300mg weekly for five weeks and monthly thereafter; given as 2x 150mg subcutaneous injections. (currently ~42% market share) • Etanercept: 50mg twice per week for 12 weeks, then once per week thereafter (currently ~4% market share) • Infliximab: 5mg/kg given as an IV infusion followed by additional 5mg/kg infusion doses at 2 and 6 weeks (currently ~4% market share)

	If all biologic treatments fail, people receive Best Supportive Care
Outcome(s)	Greater rates of PASI 75 / 90 / 100 response, as per VOYAGE 1&2 and ECLIPSE; this results in improved quality of life. Rates of PASI response are assumed to be equivalent to risankizumab.

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 target 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.

13. Ustekinumab for the treatment of chronic plaque psoriasis

Application

13.1. The Advisory Committee reviewed the application for ustekinumab for the treatment of chronic severe plaque psoriasis.

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

Recommendation

13.3. The Advisory Committee **recommended** that ustekinumab be funded with a **high priority** as a first-line biologic treatment, or **medium priority** as a second-line biologic treatment, for those with severe chronic plaque psoriasis within the context of dermatology treatments, subject to the following Special Authority criteria:

> **Initial application – (severe chronic plaque psoriasis) First line biologic** only from a dermatologist.
> Approvals valid for 4 months for applications meeting the following criteria:
> All the following:
> 1. Patient has "whole body" severe chronic plaque psoriasis with a Psoriasis Area and Severity Index (PASI) score of greater than 10, where lesions have been present for at least 6 months from the time of initial diagnosis or
> 2. Patient has severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot, where the plaque or plaques have been present for at least 6 months from the time of initial diagnosis:
>
> And
> 3. Patient has tried, but had an inadequate response (see Note) to, or has experienced intolerable side effects from, at least three of the following: phototherapy, methotrexate, ciclosporin or acitretin
>
> And
> 4. A PASI assessment or Dermatology Life Quality Index (DLQI) assessment has been completed for at least the most recent prior treatment course, preferably while still on treatment but no longer than 1 month following cessation of each prior treatment course.
>
> And
> 5. The most recent PASI or DLQI assessment is no more than 1 month old at the time of application.
>
> **Renewal – (severe chronic plaque psoriasis)** from any relevant prescriber.
> Approvals valid for 6 months for applications meeting the following criteria:
> Both:
> 1. Either:
>
> 1.1. Patient's PASI score has reduced by 75% of more (PASI 75) as compared to baseline PASI prior to commencing ustekinumab; or

1.2. Patient has a Dermatology Life Quality Index (DLQI) improvement of 5 or more, as compared to baseline DLQI prior to commencing ustekinumab.

And

2. Either:
   - 2.1. Ustekinumab is to be administered at a maximum dose of 45mg every 12 weeks; or
   - 2.2. For patients with body weight greater than 100 kg ustekinumab to be administered at a maximum dose of 90mg every 12 weeks.

Second line biologic
Initial application – (severe chronic plaque psoriasis) second line biologic only from a dermatologist.
Approvals valid for 4 months for applications meeting the following criteria:
All the following:

1. Patient has had an initial Special Authority approval for adalimumab, etanercept or secukinumab or has trialled infliximab for severe chronic plaque psoriasis and experienced either intolerable side effects or received insufficient benefit.

   And

2. A PASI assessment or DLQI assessment has been completed for at least the most recent prior treatment course, preferably while still on treatment but no longer than 1 month following cessation of each prior treatment course.

   And

3. The most recent PASI or DLQI assessment is no more than 1 month old at the time of application.

Renewal – (severe chronic plaque psoriasis) from any relevant prescriber. Approvals valid for 6 months for applications meeting the following criteria:
Both:

1. Either:
   - 1.1. Patient's PASI score has reduced by 75% of more (PASI 75) as compared to baseline PASI prior to commencing ustekinumab; or
   - 1.2. Patient has a Dermatology Life Quality Index (DLQI) improvement of 5 or more, as compared to baseline DLQI prior to commencing ustekinumab.

And

2. Either:
   - 2.1. Ustekinumab is to be administered at a maximum dose of 45mg every 12 weeks; or
   - 2.2. For patients with body weight greater than 100 kg ustekinumab to be administered at a maximum dose of 90mg every 12 weeks.

13.4. The Advisory Committee recommended the criteria based on:

- The unmet health need of those with severe chronic plaque psoriasis
- Weight based dosing regimen that may offer health benefits to those with a weight of over 100kg.
- The subcutaneous formulation and reduced dosing frequency which reduces infusion time and treatment burden.
- The sustainability of the treatment over time.

Discussion

Māori impact

13.5. The Committee discussed the impact of funding ustekinumab for the treatment of chronic plaque psoriasis on Hauora Arotahi - Māori health areas of focus and Māori health outcomes. The Committee noted that a 2014 letter to the New Zealand Medical Journal reported that Māori and Pacific peoples were overrepresented in the numbers that had been treated for psoriasis in the Auckland District Health Board (ADHB) over the 5 year period (2009–2014 (Lee and Lamb, N Z Med J. 2014;127:73-4).

13.6. The Committee noted the subcutaneous formulation, and reduced dosing frequency, would be of benefit.

Background

13.7. The Committee noted that PTAC had reviewed an application for ustekinumab in May 2011 for the treatment of individuals with severe chronic plaque psoriasis, where it recommended funding of the 45mg dose if cost neutral to other funded biologics, and the 90mg dose if cost neutral to the 45mg dose.

13.8. The Committee noted that an application was received in December 2014 requesting ustekinumab be funded for the treatment of plaque psoriasis. PTAC reviewed this application in May 2015 and recommended ustekinumab be funded only if cost neutral to adalimumab.

13.9. The Committee noted additional evidence and pricing were provided by the supplier in August 2022. Pharmac staff sought advice on the new evidence and the proposed use of ustekinumab as a first- or second-line biologic for the treatment of severe plaque psoriasis.

Health need

13.10. The Committee noted it had previously reviewed the health need for those with chronic plaque psoriasis in November 2020.

13.11. The Committee noted PTAC have previously considered that psoriasis is a significant health concern in New Zealand. The PTAC members noted estimates of 76,000 to 114,000 individuals in New Zealand with chronic plaque psoriasis, of whom perhaps 380-570 do not respond adequately to non-biologic systemic treatments (May 2015).

13.12. The Committee noted that those with psoriasis are currently treated with phototherapy, acitretin, methotrexate and/or ciclosporin. Under current Special Authority restrictions, those with moderate to severe chronic plaque psoriasis (PASI >10) must have tried, but had an inadequate response to, or experienced intolerable side effects from, at least three of phototherapy, methotrexate, ciclosporin, or acitretin treatment, prior to biologic treatment.

13.13. The Committee noted that many individuals will start on adalimumab as their first biologic, and then switch to either another anti-TNF (such as etanercept) or to secukinumab (an IL-17 inhibitor).

13.14. The Committee noted a 2014 letter to the New Zealand Medical Journal that reported a review of those treated in the Auckland District Health Board (ADHB) between 2009–2014, that found that of 511 people treated for psoriasis, 26.42% of individuals were of Māori and Pacific ethnicity. As a comparison, the general ADHB population at the time was comprised of 19.1% Māori and Pacific peoples and 52% New Zealand Europeans (Lee and Lamb, N Z Med J. 2014;127:73-4).

Health benefit

13.15. The Committee noted ustekinumab is a human IgG1kappa monoclonal antibody directed against interleukins (IL) - 12 and IL-23.

13.16. The Committee noted the following studies:

- Ozyurt et al, Turkish journal of medical sciences, 2022, 52:7
- Graier et al, Br J Dermatol, 2021, 184;996-997
- Cozzani et al, 2020, J Am Acad Dermatol, 82, 1, 37-43
- Shalom et al, JEADV, 2020, 34, 1524-1528:
- Kashimoto et al, J Dermatol. 2020 Jan;47:33-40

- Mourad & Gniadecki, 2021, Front. Med. 7:625755
- Marinas et al, Australas J Dermatol. 2018;59:e11-e14
- No et al, J Dermatolog Treat. 2018; 29:460-466
- Vilarrasa et al J Am Acad Dermatol. 2016;74:1066-72
- Huang et al, Front Pharmacol. 2022; 13:880985
- Tokuyama et al, Tokai J Exp Clin Med. 2020;45:230-235.
- Puig et al, J Dermatolog Treat. 2020;31:344-351
- Langley et al, Br J Dermatol. 2015;172:1371-8
- Zachariae et al, Eur J Dermatol. 2022;32:530-535
- Bagel et al J Eur Acad Dermatol Venereol. 2021; 35:135-142
- Blauvelt et al, J Am Acad Dermatol. 2017;76:60-69.e9
- Damiani et al, Dermatol Ther. 2019;32:e12793
- Landells et al, J Am Acad Dermatol. 2015;73;594-603
- Bai et al, J Immunol Res. 2019;2546161
- Mahil et al Br J Dermatol. 2020;183:638-649
- Bilal et al, J Dermatolog Treat. 2018;29:569-578
- Sun et al, Pediatr Dermatol. 2022;39:42-48
- Sbidian et al Cochrane Database Syst Rev. 2022;5:CD011535.
- Jabber-Lopez et al, J Invest Dermatol. 2017;137:1646-1654
- Lee et al, J Dermatol. 2019;46(9):752-758
- Augustin et al J Eur Acad Dermatol Venereol. 2017;31:294-303
- Beroukhim et al, J Dermatolog Treat. 2016;27:552-555

13.17. The Committee considered the quality and strength of evidence to be good, including randomised clinical trials, with long term follow up data.

13.18. The Committee considered the populations and endpoints considered within the pivotal trials to be relevant to New Zealand. The Committee considered that since the initial application for ustekinumab clinical practice and expectations of treatment efficacy had changed and efficacy endpoints of PASI 90 are currently more relevant than PASI 75. The Committee noted there were some differences between publications results, however the Committee considered it was likely that at weeks 44-60, using an endpoint of PASI 90, ustekinumab was broadly comparable to adalimumab. The Committee considered that long-term durability was likely to be slightly better with ustekinumab compared to funded agents such as adalimumab and secukinumab.

13.19. The Committee noted in first line biologic treatment ustekinumab had the longest drug survival rate compared to adalimumab, etanercept, ixekizumab, and secukinumab. (Graier et al. Br J Dermatol 2021.184, pp1094–1105). The Committee noted the Lin et al, Sci Rep. 2018;8:16068 meta-analysis that also reported ustekinumab was associated with the highest drug survival in those who had and had not received previous biologic treatments.

13.20. The Committee noted a publication reporting there was no difference in drug survival in second line treatment between ustekinumab and secukinumab, infliximab, adalimumab and etanercept (Cozzani et al. J Am Acad Dermatol. 2020;82:37-44).

13.21. The Committee noted a meta-analysis comparing health benefit of biologics in first line treatment, this reported risankizumab and guselkumab offered greater efficacy at weeks 44-60 in improvement of PASI 90 score compared to ustekinumab, at 79.4, 76.5 and 52.4% respectively (Armstrong et al. JAMA Dermatol. 2020;156:258-69).

13.22. The Committee noted that ustekinumab has a weight-based dosing, with 45mg recommended for those under 100kg, and 90mg for those with a weight greater than 100kg. The Committee considered a significant number of people with psoriasis in New Zealand have a weight greater than 100 kg and would benefit from weight-based dosing including Māori and Pacific peoples with psoriasis,

Suitability

13.23. The Committee considered that the subcutaneous formulation offers an advantage over infliximab, which is administered by infusion, by reducing the time needed for administration and travel for those undergoing treatment. The Committee noted the subcutaneous formulation would result in a reduction in the demand for infusion services for individuals who would otherwise have received infliximab intravenous infusions.

13.24. The Committee noted ustekinumab offered a reduced dosing frequency, with maintenance dosing every 12 weeks, in comparison to etanercept, adalimumab and secukinumab which are administered once weekly, fortnightly, and monthly respectively.

Summary for assessment

13.25. The Advisory Committee considered that the table below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for ustekinumab if it were to be funded in New Zealand for first- or second-line treatment of chronic severe plaque psoriasis. 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 Advisory 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 with moderate-to-severe chronic plaque psoriasis (defined as a PASI score >10 or psoriasis of the face, palm or sole of foot) who have experienced intolerable side effects from, are contraindicated to having or have received inadequate benefit from prior systemic therapy in first line, and/or at least one prior biologic therapy.
Intervention	Ustekinumab 45mg at weeks 0 and 4, then every 12 weeks via subcutaneous injection. A 90mg dose would be used for those over 100kg. In case of non-response, people would proceed to subsequent biologics.

Comparator(s) (NZ context)	Other listed biologic treatments: • Adalimumab 80mg at week 0, then 40mg every other week (currently ~50% market share) • Secukinumab 300mg each week for the first 4 weeks, 300mg once per month thereafter (currently ~42% market share) • Etanercept 50mg twice per week for 12 weeks, then once per week thereafter (currently ~4% market share) * • Infliximab 5mg/kg at weeks 0, 2 and 6, then every 8 weeks thereafter, via intravenous infusion (currently ~4% market share) If all biologic treatments fail, people receive best supportive care
Outcome(s)	Greater rates of PASI 75 / 90 / 100 response resulting in improved quality of life: Short-term PASI response rates derived from the key trials, e.g. PHOENIX 1 (Leonardi et al. Lancet 2008;371(9625): 1665-74), PHOENIX 2 (Papp et al. Lancet, 2008:371(9625):1675-84) and UltIMMa-1&2 (Gordon et al. Lancet. 2018;392:650-61). Longer term drug survival derived from cohort study. (Yiu et al. JAMA Dermatology, 2022;158(10):1131-41) and/or 5-year follow-up of PHOENIX trials (Langley et al. Br J Dermatol., 2015;172(5):1371-83) Likely that: - Short-term effectiveness of ustekinumab similar to adalimumab - Long-term persistence on therapy likely to be greater than adalimumab (though this is more uncertain)
Table definitions: Population, the target population for the pharmaceutical; Intervention, details of the intervention pharmaceutical; Comparator, details the therapy(s) that the target population would receive currently (status quo – including best supportive care); Outcomes, details the key therapeutic outcome(s) and source of outcome data.	

14. Adalimumab for Flexural or Genital Psoriasis

Application

14.1. The Advisory Committee reviewed the application for adalimumab for the treatment of flexural or genital psoriasis.

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

Recommendation

14.3. The Advisory Committee **recommended** access to adalimumab be amended to include the treatment of genital or flexural psoriasis with a high priority within the context of dermatology treatments subject to the following Special Authority criteria (additions in **bold**):

> **Initial application — (Plaque psoriasis - severe chronic)** only from a dermatologist.
> Approvals valid for 4 months for applications meeting the following criteria:
> Either:
> 1. Both:
> 1.1. Patient has had an initial Special Authority approval for etanercept for severe chronic plaque psoriasis; and
> 1.2. Either:
> 1.2.1. Patient has experienced intolerable side effects; or
> 1.2.2. Patient has received insufficient benefit to meet the renewal criteria for etanercept for severe chronic plaque psoriasis;
> Or

2. All of the following:
    2.1. Either:
        2.1.1. Patient has "whole body" severe chronic plaque psoriasis with a PASI score of greater than 10, where lesions have been present for at least 6 months from the time of initial diagnosis; or
        2.1.2. Patient has severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot, where the plaque or plaques have been present for at least 6 months from the time of initial diagnosis; or
        2.1.3. Patient has severe chronic localised genital or flexural plaque psoriasis where the plaques or lesions have been present for at least 6 months from the time of initial diagnosis, with a Dermatology Life Quality Index (DLQI) score greater than 10; and
    2.2. Patient has tried, but received insufficient therapeutic effect from, or has experienced intolerable side effects from, at least three of the following (at maximum tolerated doses unless contraindicated): phototherapy, methotrexate, ciclosporin, or acitretin; and
    2.3. A PASI assessment or DLQI assessment has been completed for at least the most recent prior treatment course but no longer than 1 month following cessation of each prior treatment course and is no more than 1 month old at the time of application.

Renewal — (Plaque psoriasis - severe chronic) from any relevant practitioner. Approvals valid for 2 years for applications meeting the following criteria:
Either:

1. Both:
    1.1. Patient had "whole body" severe chronic plaque psoriasis at the start of treatment; and
    1.2. Either:
        1.2.1. The patient has a PASI score which is reduced by 75% or more, or is sustained at this level, when compared with the pre-treatment baseline value; or
        1.2.2. The patient has a DLQI improvement of 5 or more, when compared with the pre-treatment baseline value; or
2. Both:
    2.1. Patient had severe chronic plaque psoriasis of the face, or palm of a hand or sole of a foot at the start of treatment; or
    2.2. Either
        2.2.1. The patient has a reduction in the PASI symptom subscores for all 3 of erythema, thickness and scaling, to slight or better, or sustained at this level, as compared to the treatment course baseline values; or
        2.2.2. The patient has a reduction of 75% or more in the skin area affected, or sustained at this level, as compared to the pre-treatment baseline value or
        2.2.3. The patient has a DLQI improvement of 5 or more, when compared with the pre-treatment baseline value; or
3. Both;
    3.1. Patient had severe chronic localised genital or flexural plaque psoriasis; and
    3.2. Either
        3.2.1. The patient has a reduction of 75% or more in the skin area affected, or sustained at this level, as compared to the pre-treatment baseline value or
        3.2.2. Patient has a Dermatology Quality of Life Index (DLQI) improvement of 5 or more, as compared to baseline DLQI prior to commencing adalimumab

14.4. The Advisory Committee noted

- The high health need of those with genital or flexural psoriasis
- The sensitive psychosocial aspects of genital and flexural psoriasis.
- The lack of current treatments, and the unsuitability of topical creams, and cultural considerations of topical application.

Discussion

Māori impact

14.5. The Committee discussed the impact of funding adalimumab for the treatment of genital or flexural psoriasis on Hauora Arotahi - Māori health areas of focus and Māori health outcomes. The Committee noted a 2014 letter to the New Zealand Medical Journal which reported that reported Māori and Pacific peoples were overrepresented in the numbers treated for psoriasis in the Auckland District Health Board (ADHB) over the last 5 years (2009–2014) (Lee and Lamb, N Z Med J. 2014;127:73-4).

Background

14.6. The Committee noted no treatments have previously considered for this specific type of psoriasis, but other pharmaceuticals have been considered, and funded, for the broader indication of chronic plaque psoriasis.

Health need

14.7. The Committee noted flexural psoriasis, also known as inverse or intertriginous psoriasis, is characterised by thickened areas of skin localised to the skin folds and genitals. Common sites of flexural psoriasis are the armpits, groin, and natal cleft.

14.8. The Committee noted the pathogenesis does not differ from plaque psoriasis. The Committee noted that the skin appears macerated and can often become infected with *Candida*. The condition may be present exclusively, or in combination with classical plaque psoriasis lesions in other body areas (Micali et al, Clin Cosmet Investig Dermatol. 2019; 12: 953–959).

14.9. The Committee noted that those with genital or flexural psoriasis had a high health need due to the condition being very distressing, and due to the location of the symptoms also causing high levels of embarrassment.

14.10. The Committee noted approximately 2% of the population are affected by psoriasis, with a recent study reporting an occurrence of 1.58% (0.5-5.73%) in Australasia (Parisis et al, BMJ. 2020; 369: 1590). Of this population, involvement of the genitals is relatively common occurring in 29-40% of all individuals, with the prevalence broadly increasing with the severity of the psoriasis (Egeberg et al, BMC Dermatol. 2020;20:3; Kelly et al, Am J Clin Dermatol. 2019; 20:639-646). Psoriasis that is largely confined to the genitals, occurs in approximately 2-5% of individuals with psoriasis, although this may be under diagnosed, with approximately half of those with genital lesions not discussing their symptoms with their physician (Yang et al, Psoriasis (Auckl). 2018; 8: 41–47). It has been estimated that flexural psoriasis affects between 6.8-36% of those with psoriasis (Van de Kerkhof et al, J Dermatolog Treat. 2007;18:351-60).

14.11. The Committee considered this form of psoriasis was under reported by those with the condition.

14.12. The Committee noted approximately 72% of individuals with genital psoriasis feel uncomfortable about dating and 60% report that this disease has prevented them from pursuing an intimate relationship (Yang et al, 2018).

14.13. The Committee noted psoriasis is detrimental to the quality of life of the person who is affected. It is often linked with social stigmatisation, loss of self-confidence, pain, discomfort, physical disability, and psychological distress. Many of those with psoriasis report moderate to extreme feelings of anxiety, anger, and depression and higher frequency of suicidal ideation (Sarker et al, Indian Dermatol Online J. 2016; 7: 481–488).

14.14. The Committee noted those with genital psoriasis also report chronic intense itching, burning skin and pain, with a worsening of symptoms following intercourse (Ryan et

al, J Am Acad Dermatol. 2015;72:978-83). Individuals with genital psoriasis had more impairment in quality of life and sexual health as determined by the Dermatology Life Quality Index (P < .0001), the Centre for Epidemiological Studies-Depression Scale (P = .01), and the Relationship and Sexuality Scale (P < .0001) (Ryan et al, 2015).

14.15. The Committee noted that most individuals are treated with topical corticosteroids. However, these have adverse effects including skin atrophy, and are usually administered sparingly for short periods of time. The Committee also noted that thin skin and constant occlusion of this environment cause topical medications to have increased penetration in the groin area, increasing the risk of systemic side effects (Beck et al, Dermatol Ther (Heidelb). 2018; 8: 509–525). The Committee noted individuals progress to systemic treatments including acitretin or methotrexate, and occasionally cyclosporin however these are not commonly used.

14.16. The Committee noted a 2014 letter to the New Zealand Medical Journal which reported that a review of people treated in the Auckland District Health Board (ADHB) over the last 5 years (2009–2014) had found that of 511 people treated for psoriasis, 26.42% of individuals were of Māori and Pacific ethnicity. As a comparison, the general ADHB population was comprised of 19.1% Māori and Pacific peoples and 52% New Zealand Europeans at the time (Lee and Lamb.2014).

Health benefit

14.17. The Committee noted adalimumab binds to tumour necrosis factor (TNF) and neutralises the biological function of TNF by blocking its interaction with the p55 and p75 cell surface TNF receptors. Increased levels of TNF are found in psoriasis plaques, which contribute to the inflammatory response, to the proliferation and decreased maturation of keratinocytes and to the associated vascular damages that are characteristic of the disease.

14.18. The Committee noted health benefit evidence for adalimumab for the treatment of plaque psoriasis was reviewed by PTAC in 2008, which recommended it be given a medium priority for funding, whilst noting other biologics may be acceptable.

14.19. The Committee noted the Burlando et al, Dermatol Ther. 2020;33:e13110 study that examined which biologic therapy is more effective on genital psoriasis in 74 women, of which 34% had genital psoriasis. Of 10 that received anti-TNF therapies (8 adalimumab, 1 etanercept, 1 certolizumab) four individuals reached PASI 90. Improved responses were also reported in those that received secukinumab, ixekizumab and ustekinumab.

14.20. The Committee noted the Ješe et al, Acta Dermatovenerol Alp Pannonica Adriat. 2014;23:21-3 study of one male with inverse psoriasis. At 6 months follow up after adalimumab treatment, psoriatic lesions had resolved, and quality of life measures (Health Assessment Questionnaire: Patient-Reported Outcomes Measurement Information and Dermatology Life Quality Index) were significantly improved.

14.21. The Committee considered other biologic treatments including etanercept, infliximab, ustekinumab and guselkumab would be beneficial to those who have flexural or genital psoriasis. The Committee considered that treatment of genital and flexural psoriasis should be similar to those who have chronic plaque psoriasis, or who have psoriasis located on the hands, feet or face.

Suitability

14.22. The Committee noted adalimumab is a prefilled syringe or pen that enables individuals to self-administer their treatment, if appropriate, with medical follow-up as necessary, after proper training in subcutaneous injection technique.

14.23. The Committee noted other treatments require daily oral or topical administration. In addition, these topical administrations can be painful or uncomfortable when administered to the skin.

14.24. The Committee noted that for some individuals, topical administration to the skin, in areas affected by genital or flexural psoriasis, may not be suitable for religious or cultural reasons.

Cost and savings

14.25. The Committee considered many individuals would already be receiving biologic treatment for psoriasis in other regions of the body, and it was common for people with this subtype of psoriasis to present with whole-body disease. The Committee considered that less than 10% of those with psoriasis would only present with flexural or genital psoriasis.

14.26. The Committee considered a small percentage with flexural psoriasis or genital psoriasis may not reach the current Special Authority criteria threshold PASI score (greater than 10) for biologic treatment. The Committee considered that PASI scores did not accurately reflect the disease severity of those with flexural or genital psoriasis, as the PASI typically reflected disease activity for those with whole body psoriasis. The Committee considered that whilst DLQI would be most reflective of disease severity, the change in PASI scores for whole body psoriasis could be used to model an estimate of benefit for these groups, however DLQI would be a better measure of treatment success.

14.27. The Committee considered it was likely that the health gains for this subpopulation would be similar to those treated with biologics for whole body psoriasis. However, the Committee considered that it was uncertain whether the quality-of-life impacts associated with a PASI 75 could be used as a proxy for the quality-of-life improvement associated with a DLQI improvement for this disease subtype.

14.28. The Committee considered some individuals may still prefer to use topical products.

14.29. The Committee considered that similar health benefit gains would be observed in those with genital or flexural psoriasis treated with adalimumab as those with whole body chronic severe plaque psoriasis or where it is located on the hands, feet, and face.

14.30. The Committee considered the frequency of dosing would likely be similar for this group as for those with chronic plaque psoriasis or those with psoriasis of the hands, feet, and face.

Funding Criteria

14.31. The Committee noted dermatology life quality index (DLQI) score is more appropriate when assessing health benefit for genital or flexural psoriasis.

14.32. The Committee considered that the if the adalimumab Special Authority criteria were to be amended, they should align with the Special Authorities for other biologic treatments for plaque psoriasis, allowing subsequent treatment of genital or flexural psoriasis with those agents as well.

Summary for assessment

14.33. The Advisory Committee considered that the table below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for adalimumab if it were to be funded in New Zealand for flexural or genital psoriasis. 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 Advisory 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 with severe flexural or genital psoriasis who are intolerant of, contraindicated to or have experienced inadequate benefit from prior systemic therapy.
Intervention	Adalimumab subcutaneous injection • Initial dose of 80 mg (via two 40 mg injections) • Subsequent dose is 40 mg every fortnight, starting one week after initial dose. Treatment is discontinued if the individual does not experience a DLQI improvement of 5 or more. Other biologic treatments currently funded for psoriasis.
Comparator(s)	Best supportive care in the form of topical therapies
Outcome(s)	Greater rates of DLQI improvements, resulting in 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 target population would receive currently (status quo – including best supportive care); Outcomes, details the key therapeutic outcome(s) and source of outcome data.	