PHARMAC
TE PĀTAKA WHAIORANGA

PHARMACEUTICAL SCHEDULE APPLICATION

To: Rheumatology Special Advisory Committee

From: Funding Application Advisor

Date: March 2023

Upadacitinib – for the treatment of psoriatic arthritis (PsA) following inadequate benefit from at least one biologic [P-001741] and for the treatment of PsA following inadequate benefit from at least two biologics [P-001774]

SUMMARY OF PHARMACEUTICAL			
Brand Name	RINVOQ	**Chemical Name**	Upadacitinib
Indications	For the treatment of psoriatic arthritis in adults which has responded inadequately to prior bDMARD use	**Presentation**	15 mg modified-release tablet
Therapeutic Group	Immunosuppressants	**Dosage**	15 mg once daily
Supplier	AbbVie Ltd	**Application Date**	November 2021
MOH Restrictions	Prescription medicine	**Proposal type**	Widen listing
Current Subsidy	Gross $1,271 per 28 15mg tablets (net S 9(2)(b) per 28 tablets)	**Proposed Restriction**	Special Authority
Proposed Subsidy	Same as above	**Approved by Medsafe for this indication**	Yes

MOH, Ministry of Health; NPV, Net Present Value.

QUESTIONS TO COMMITTEE

Note to Committee members: These questions have been identified by Pharmac staff as being particularly relevant to the application. Please feel free to provide additional information as appropriate.

In May 2022, PTAC considered that Pharmac should seek further advice regarding upadacitinib for psoriatic arthritis (PsA) from the Rheumatology Advisory Committee regarding the Committee's views of several topics. These are listed below, along with general questions for the Committee from Pharmac staff.

Topics for consideration referred from PTAC:

1. The sequencing of bDMARD treatments for PsA
2. Whether or not people with PsA who experience smaller responses to treatment from treatment (eg a 20% improvement) would remain on their treatment
3. The benefits and risks of second line versus third line use of upadacitinib for PsA and where upadacitinib would be used in the treatment paradigm, if funded
4. The appropriate comparator for upadacitinib third-line use, if funded
5. Secukinumab first-line use and whether upadacitinib would be used second line following first line secukinumab
6. Whether there is an existing group of people who would switch to upadacitinib second line and third line upon listing and what size that group might be
7. Are the proposed Special Authority criteria appropriate for the second-line treatment of PsA? If not, how should these be amended?
8. Are the proposed Special Authority criteria appropriate for the third-line treatment of PsA? If not, how should these be amended?

General questions from Pharmac staff

Need

9. Noting the previous consideration by PTAC in May 2022 of the health needs of individuals with PsA and those of their families and whānau and wider society, does the Committee have any additional considerations regarding these health needs?
10. Does the Committee have any further considerations on the effect of PsA on Māori, Pacific peoples, or other groups experiencing health inequities in New Zealand?

Health benefit

11. Noting the prior consideration by PTAC in May 2022, does the Committee have any further comment on any additional health benefit or additional risks compared with other funded treatment options?
12. Currently, what proportion of people receive secukinumab second-line? And what proportion receive a second-line anti-TNF instead of secukinumab?
13. If listed second-line, would upadacitinib be used as a second-line treatment in the majority of individuals with PsA?

14. What proportion of individuals with PsA would receive a second anti-TNF instead of upadacitinib?

Costs and savings

15. After secukinumab was listed, approximately 10% of people with PsA (150 individuals) switched to secukinumab within the first year of listing. Would the Committee expect a larger or smaller group of people with PsA would take up upadacitinib within the first year of listing?

16. Is it reasonable to assume that individuals who experience a smaller response to treatments (eg 20% improvement) would remain on upadacitinib treatment?

General

17. Is there any data or information missing from the application, in particular clinical trial data and commentary?

Recommendations

18. Should upadacitinib be listed in the Pharmaceutical Schedule for the **second-line** treatment of PsA?

    - Name the Factors for Consideration particularly relevant to a positive or negative recommendation and explain why each is relevant.
    - If listing is recommended, what priority rating would you give to this proposal? **[low / medium / high / only if cost-neutral]**?

19. Should upadacitinib be listed in the Pharmaceutical Schedule for the **third-line** treatment of PsA?

    - Name the Factors for Consideration particularly relevant to a positive or negative recommendation and explain why each is relevant.
    - If listing is recommended, what priority rating would you give to this proposal? **[low / medium / high / only if cost-neutral]**?

20. Should Pharmac seek any further advice to inform its assessment of this application? If so, what advice and from whom?

21. Does the Committee have any recommendations additional to the application?

PURPOSE OF THIS PAPER

The purpose of this paper is to seek the Committee's advice regarding an application from AbbVie Ltd for the use of upadacitinib for psoriatic arthritis (PsA).

In May 2022, PTAC considered upadacitinib (Rinvoq) for the **second-line** treatment for adults with PsA who have received inadequate benefit from one prior biologic disease modifying antirheumatic drug (bDMARD). PTAC also considered the potential benefits and risks of upadacitinib for the **third-line** treatment for adults with PsA who have received inadequate benefit from prior disease modifying antirheumatic drugs including two bDMARDs.

In making their recommendations, the PTAC recommended that Pharmac refer several questions to the Rheumatology Advisory Committee, seeking their specialist advice. These questions are included at the start of this paper.

DISCUSSION

BACKGROUND

Consideration of upadacitinib for PsA

Pharmac received an application for upadacitinib for PsA in November 2021. PTAC reviewed this application in May 2022. The clinical advice paper and relevant excerpt of the record related to the meeting are attached in Appendix 1.

PTAC considered that upadacitinib would most likely be used as a third-line treatment following secukinumab, however they considered that second-line use of upadacitinib would be expected if funding permitted this and considered that upadacitinib could gradually replace a portion of the current secukinumab second-line market. The Committee also considered that there was unlikely to be an existing group of individuals with PsA who would switch to upadacitinib second-line or third-line upon its listing. The Committee recommended Pharmac seek advice from the Rheumatology Advisory Committee regarding treatment sequencing of upadacitinib, these topics are included at the start of this paper.

At this time, PTAC recommended upadacitinib be listed in the Pharmaceutical Schedule for third-line treatment of PsA with a **high** priority**,** and that upadacitinib be listed in the Pharmaceutical Schedule for the second-line treatment of PsA only if **cost-neutral** to secukinumab.

Previous consideration of other treatments for PsA

Table 1: Summary of consideration of treatments for PsA.

Pharmaceutical	Mechanism of action	Treatment line/detail	Status
Adalimumab	Tumour necrosis factor (TNF) inhibitor	First biologic line	Funded in 2009. Access criteria amended in 2011. Current criteria here.
Etanercept	TNF inhibitor	First biologic line (allowing eligible patients to access adalimumab and etanercept in any order)	Funded in 2010. Current criteria here.

Golimumab	TNF inhibitor	Second-line	PTAC recommended declining the application. Inactive application was declined by Pharmac in 2020.
Infliximab	TNF inhibitor	Second or third line	Funded. Current criteria here.
Secukinumab	Inhibitor of proinflammatory cytokine interleukin-17A (IL-17A)	First and second biologic line	Funded for first-line or second-line in 2021. Current criteria here.

Consideration of upadacitinib for other indications

Upadacitinib has previously been considered by PTAC as follows:

- Moderate to severe rheumatoid arthritis (recommended with **medium** priority by PTAC in February 2021)
- Moderate to severe atopic dermatitis (recommended with **high** priority by PTAC in November 2021)
- Ankylosing spondylitis, second line biologic (recommended by PTAC in May 2019, only if **cost neutral** to secukinumab) – *to be considered at this meeting*
- Ankylosing spondylitis, third line biologic (recommended with a **low** priority by PTAC in May 2019 – *to be considered at this meeting*

Upadacitinib was listed in Section B and Section H of the Pharmaceutical Schedule in 2021 in response to a tocilizumab stock shortage in 2021 as a later-line treatment for rheumatoid arthritis, subject to funding criteria. This issue has now been resolved, however upadacitinib remains listed in these sections of the Schedule. Funding of a wider group of people with rheumatoid arthritis remains under assessment.

Need

Description of the disease

Psoriasis is a common skin disease occurring in 3% of adults and <1% of children. PsA is a heterogenous inflammatory musculoskeletal disease which occurs in about 20-30% of people with psoriasis (Fitzgerald et al. Nat Rev Dis Primers. 2021;7:59; Karmacharya et al. Best Pract Res Clin Rheumatol. 2021;35:101692). Further description of PsA is available in the PTAC May 2022 clinical advice paper. (Appendix 1)

Epidemiology

PsA affects males and females equally. The supplier has stated that the prevalence of psoriasis is 3% in the adult population; of these, the supplier estimates 15-25% have PsA

and about a quarter of those receive an insufficient benefit from conventional synthetic DMARDs (csDMARDs). As of September 2021, there were 860 people with PsA in New Zealand who were prescribed a bDMARD for PsA, with annual growth of bDMARD prescribing of 9%. Based on 30% of people with PsA receiving an inadequate response from bDMARDs, approximately 307 individuals would be eligible for second-line biologic treatment.

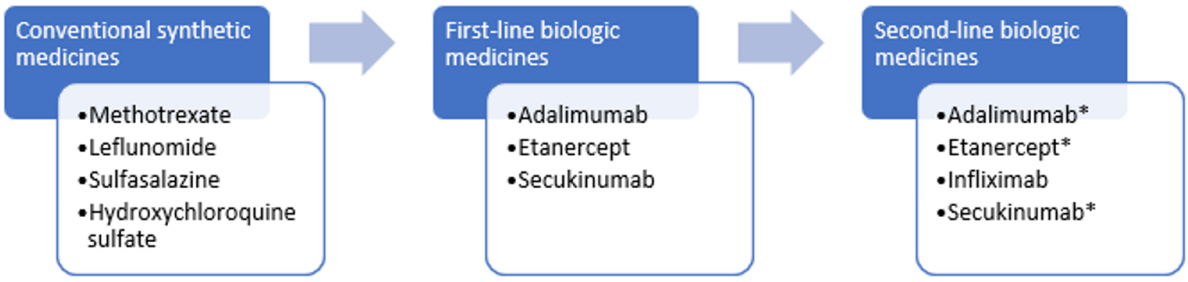
The health need of the person

The health need of individuals with PsA is detailed in the PTAC May 2022 clinical advice paper (Appendix 1).

The availability and suitability of existing medicines, medical devices, and treatments

There are currently several funded conventional synthetic and biologic DMARDs available to treat PsA. People with a confirmed diagnosis of PsA will have tried two or more csDMARDs before using adalimumab and/or etanercept. The supplier considers that most people with PsA will commence on adalimumab or etanercept in the first line, with secukinumab used in the second line setting.

The current options in the supplier's proposed treatment paradigm for individuals with PsA, is as follows (shown below in **Figure XX**):



Source: Adapted from PHARMAC 2021a
Note: *if not trialled in first line

Figure 1: Illustration of current clinical management of PsA in New Zealand as permitted by Pharmac Special Authority criteria Proposed treatment paradigm (Source: Supplier application).

Pharmac staff consider the current treatment sequence for such patients could be:

1. *First line anti-TNF (typically adalimumab) → 2. Secukinumab → 3. Second anti-TNF → supportive care.*

Both the supplier's and Pharmac staff's views of the location of each agent in the treatment paradigm are outlined below in **Table 2**.

We seek the Committee's view of this treatment sequence paradigm.

Table 2: Potential location and sequence of treatments in PsA treatment paradigm

Treatment	Supplier view of location in PsA paradigm	Pharmac staff view of location in PsA	Patients on treatment – 2022	Market share

		paradigm		
Adalimumab	First-line	First-line	818	54%
Etanercept	First-line	First-line	395	26%
Secukinumab	Second-line	First- or second- line	235	15%
Infliximab	Third-line	Second-line	79	5%

The health need of family, whānau, and wider society

Pharmac acknowledges that there may be a health need for other people as a result for caring for individuals with PsA.

In May 2022, PTAC considered that PsA impacts on an individual's function/activities and employment, which in turn impacts their family and whānau, particularly as the disease progresses and pain and mobility worsen.

The impact on the Māori health areas of focus and Māori health outcomes

Analysis of the ethnicity of people receiving biologic treatment for PsA across the 2020 and 2021 financial years suggested that 7.6% of those receiving biologics for PsA were Māori.

In May 2022 PTAC considered that there was no specific evidence of a disproportionate impact from PsA on Māori.

The impact on the health outcomes of population groups experiencing health inequities

Analysis of the ethnicity of people receiving biologic treatment for PsA across the 2020 and 2021 financial years suggested that 2% of patients receiving biologics for PsA were of Pacific ethnicity.

In May 2022 PTAC that there was no specific evidence of a disproportionate impact from PsA on Pacific peoples, or other groups experiencing health inequities

The impact on Government health priorities

The treatment of PsA, which is a long-term condition, aligns with the current Government health priorities.

Health Benefit

Details of the pharmaceutical under consideration

Clinical Pharmacology and Mechanism of Action

JAK1 is important in inflammatory cytokine signals while JAK2 is important for red blood cell maturation and JAK3 signals play a role in immune surveillance and lymphocyte function.

Upadacitinib is an oral, and reversible inhibitor of Janus Kinase-1 (JAK1), which is more potently inhibited by upadacitinib compared to JAK2 and JAK3 (Source: Rinvoq Data Sheet).

New Zealand Regulatory Approval

Upadacitinib is Medsafe-approved for the treatment of active PsA in adults whose condition has responded inadequately to conventional therapy.

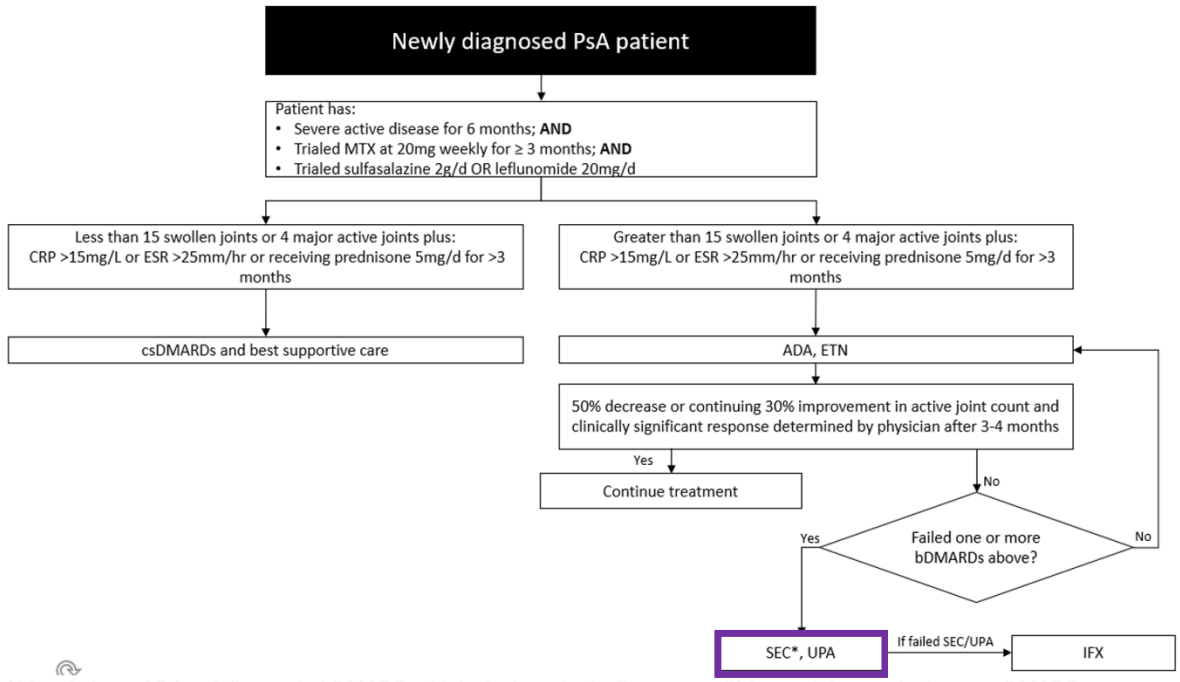
Recommended Dosage

The recommended dose of upadacitinib for PsA is one 15 mg modified release tablet once daily by mouth, taken with or without food. The supplier proposes ongoing treatment for PsA, with no maximum treatment duration stated. The 30 mg once daily dose was included in upadacitinib clinical trials, however S 9(2)(b)(ii), 9(2)(ba)(i) & 9(2)(j) S 9(2)(b)(ii), 9(2)(ba)(i) & 9(2)(j).

Proposed Treatment Paradigm

The supplier proposes upadacitinib be listed for second-line, and third-line treatment of PsA, after treatment with a TNFi (ie adalimumab or etanercept). This would therefore be an alternative option to secukinumab in the second line with a different mechanism of action and mode of administration. The proposed treatment paradigm is presented in **Figure 2**, with upadacitinib (UPA) shown in the bold purple box.

Pharmac staff seek the Committee's view of whether this reflects where upadacitinib would be expected to be accessed in the treatment paradigm, if it were to be funded for PsA (ie would people prefer to try it earlier than depicted, ahead of other treatments in the paradigm?).



Abbreviations: ADA, adalimumab; bDMARDs, biological synthetic disease modifying anti rheumatic drugs; csDMARDs, conventional synthetic disease modifying anti rheumatic drugs; CRP, C-reactive protein test; ESR, Erythrocyte sedimentation rate; ETN, etanercept; IFX, infliximab; MTX, methotrexate; PsA, psoriatic arthritis; SEC, secukinumab; UPA, upadacitinib
* Secukinumab can also be used first line but this is expected to occur only in a small number of patients with skin involvement.

Figure 2: Proposed treatment paradigm (Source: Supplier application).

Proposed Special Authority Criteria

In May 2022, PTAC recommended that seek the Rheumatology Advisory Committee's views regarding what elements should comprise the Special Authority criteria for second-line and third-line use of upadacitinib for PsA.

Second-line treatment

The supplier has proposed the following Special Authority criteria for upadacitinib for the **second-line treatment of PsA**. Pharmac staff have made minor additions, as shown in **bold**, to ensure consistency with other current Special Authority criteria**.** Pharmac staff consider that the proposed criteria would allow for upadacitinib to be accessed in several treatment lines. The final criterion specifying a maximum dose may be intended to manage the risk of anti-drug antibodies with biologics and mitigate the risk of increased dosing, which also may or may not be relevant for upadacitinib. We seek the Committee's advice on whether the proposed criteria would be appropriate for upadacitinib including these particular points.

> **Initial application — (psoriatic arthritis – second-line biologic)** only from a rheumatologist **or practitioner on the recommendation of a rheumatologist**. Approvals valid for 6 months for applications meeting the following criteria:
> Both:
> 1. The patient has had an initial Special Authority approval for adalimumab **and/**or etanercept for psoriatic arthritis; and
> 2. Either
>   2.1. The patient has experienced intolerable side effects from **a reasonable trial of** adalimumab **and/**or etanercept **and/or secukinumab**; or
>   2.2. The patient has received insufficient benefit from adalimumab or etanercept to meet the renewal criteria for adalimumab or etanercept for psoriatic arthritis.

Renewal — (psoriatic arthritis – second-line biologic) only from a rheumatologist or practitioner on the recommendation of a rheumatologist. Approvals valid for 6 months for applications meeting the following criteria:
All of the following:
1. Either:
    1.1. Following 3 to 4 months' initial treatment, the patient has at least a 50% decrease in active joint count from baseline and a clinically significant response to treatment in the opinion of the physician; or
    1.2. The patient demonstrates at least a continuing 30% improvement in active joint count from baseline and a clinically significant response to prior upadacitinib treatment in the opinion of the treating physician; and
2. Upadacitinib to be administered at doses no greater than 15 mg **daily**.

Third-line treatment

Pharmac staff have drafted the following Special Authority criteria for **third-line treatment of PsA,** based on the above criteria for second-line:

Initial application — (psoriatic arthritis – third-line biologic) only from a rheumatologist **or practitioner on the recommendation of a rheumatologist**. Approvals valid for 6 months for applications meeting the following criteria:
Both:
1. The patient has had an initial Special Authority approval for at least two biologic therapies for psoriatic arthritis (adalimumab, etanercept, secukinumab, and/or infliximab); and
2. Either
    2.1. The patient has experienced intolerable side effects from **a reasonable trial of** two prior biologic therapies; or
    2.2. The patient has received insufficient benefit to meet the renewal criteria for the prior biologic therapies for psoriatic arthritis.

Renewal — (psoriatic arthritis – third-line biologic) only from a rheumatologist or practitioner on the recommendation of a rheumatologist. Approvals valid for 6 months for applications meeting the following criteria:
All of the following:
1. Either:
    1.1. Following 3 to 4 months' initial treatment, the patient has at least a 50% decrease in active joint count from baseline and a clinically significant response to treatment in the opinion of the physician; or
    1.2. The patient demonstrates at least a continuing 30% improvement in active joint count from baseline and a clinically significant response to prior upadacitinib treatment in the opinion of the treating physician; and
2. Upadacitinib to be administered at doses no greater than 15 mg **daily**.

International Recommendations

Table 3: International recommendations regarding the funding of upadacitinib for PsA

Country (HTA Agency)	Date	Outcome	Reason
Australia (PBAC)	March 2021	✓ The PBAC recommended upadacitinib for "the treatment of severe active PsA in patients who have failed to achieve an adequate response to conventional DMARDs".	Cost-effectiveness of upadacitinib would be acceptable if it were cost minimised to the lowest cost bDMARD for this indication. Nominated comparator of tofacitinib was reasonable, however all other bDMARDs currently listed for PsA were also relevant alternative therapies. Indirect comparison support a conclusion that upadacitinib is of non-

Country (HTA Agency)	Date	Outcome	Reason
			inferior comparative effectiveness to tofacitinib (both American College of Rheumatology (ACR) 20 and 50 response.
Canada (CADTH - CDEC)	August 2021	✓ The CADTH recommended upadacitinib for "the treatment of adults with active PsA who have had an inadequate response or intolerance to methotrexate or other DMARDs". ✓ Upadacitinib may be used as monotherapy or in combination with methotrexate or other nonbiologic DMARDs.	Evidence that upadacitinib is more effective than placebo at improving PsA symptoms. May meet some of the needs that are important to patients (reduced joint pain, clearing psoriasis, improving health-Related quality of life (HRQOL). Evidence to suggest upadacitinib is more effective than other reimbursed therapies. Budget impact ranged from $2.5m in savings to $3.1m cost.
Scotland (SMC)	No evidence of consideration by the SMC for PsA at the time this paper was written.		
England/Wales (NICE)	February 2022	✓ The NICE recommended upadacitinib for patients with PsA who have had 2 conventional DMARDs and at least 1 biological DMARD, or for whom TNFi are contraindicated ✓ Upadacitinib may be used as monotherapy or in combination with methotrexate	Evidence that upadacitinib is more effective than placebo for treating PsA and may be similarly as effective as adalimumab Results of an indirect comparison are uncertain but suggest that upadacitinib is likely to work as well as other bDMARDs Upadacitinib was not cost-effective vs some bDMARDs for people who had not had a biological DMARD before Upadacitinib was cost effective for people who had had at least 1 biological DMARD or who could not have TNF-alpha inhibitors

The health benefits to the person, family, whānau and wider society

Evidence Summary

The supplier has provided indirect evidence claiming non-inferior efficacy and comparable safety of upadacitinib versus its nominated comparator, secukinumab, for the second biologic line of treatment of PsA. A summary of the evidence is provided in the May 2022 PTAC clinical advice paper. The summary of key evidence for upadacitinib and evidence for secukinumab for the second-line treatment of PsA table from the May 2022 clinical advice

paper (Appendix 1) reviewed at the May 2022 PTAC meeting included the following citations:

- Mease et al. Ann Rheum Dis. 2020;80:312-20
- Mease et al. Rheumatol Ther. 2021;8:903-19
- McInnes et al. Lancet. 2015;386:1137-46
- McInnes et al. Rheumatology (Oxford). 2017;56):1993-2003
- McInnes et al. Lancet. 2020;2:E227-35
- Nash et al. Arthritis Res Ther. 2018;20:47
- Mease et al. Ann Rheum Dis. 2018;77:890-897
- van der Heijde et al. Rheumatology (Oxford). 2020;59:1325-34
- Mease et al. RMD Open. 2021;7:e001600

Secukinumab - FUTURE 2, 3 and 5

PTAC previously considered evidence from FUTURE-1 and FUTURE-2, and from six other studies using data from secukinumab trials to compare against other biologic treatments, in February 2018. Notes on these considerations are included in the May 2022 clinical advice paper (Appendix 1).

Indirect treatment comparison

The supplier application incorporated an indirect treatment comparison of upadacitinib 15 mg vs secukinumab 300 mg which concluded that, at weeks 12 and 24, upadacitinib 15 mg was non-inferior to secukinumab 300 mg in terms of ACR20/50/70 response, although point estimates favoured upadacitinib.

In May 2022 PTAC considered that secukinumab would be the appropriate comparator for upadacitinib second-line treatment, however, that it was unclear what was the appropriate comparator for upadacitinib in the third line and considered that Pharmac should seek the Rheumatology Advisory Committee's view.

Upadacitinib for first-line (1L) treatment, third-line (3L) treatment, and treatment sequencing

In May 2022 PTAC also reviewed the evidence for upadacitinib for first-line treatment, and third-line treatment and associated treatment sequencing. Their discussion is outlined in the background section of this document and is available in full in the record excerpt (Appendix 1).

International guidelines

The 2020 Assessment of SpondyloArthritis international Society (ASAS)-EULAR recommendations for the management of axial spondyloarthritis recommends that in people with peripheral arthritis and an inadequate response to at least one csDMARD and at least one bDMARD, or when a bDMARD is not appropriate, a JAK inhibitor may be considered (eg upadacitinib) (Gossec et al. Ann Rheum Dis. 2020;79(6):700-712).

Literature Search

Pharmac staff conducted an updated PubMed search on 23/02/2023 to identify any additional publications regarding upadacitinib for second-line treatment of PsA, further evidence for upadacitinib specifically in the third line, and any publications regarding sequencing/switching of biologic treatments that were not identified by the supplier, or the original literature search detailed in the May 2022 clinical advice paper (Appendix 1). Results were limited to articles published since April 2022 to prevent overlap with previous search results. Full text articles are included in Appendix 2.

Table 4: Pharmac literature searches.

Search terms	Results
upadacitinib and psoriatic arthritis	*Note: All of the publications in this table include analyses of the SELECT-PsA 1 trial, which was previously excluded as evidence by Pharmac staff due to the indication not currently being under consideration*. Safety profile of upadacitinib over 15,000 patient years across Rheumatoid arthritis (RA), PsA, ankylosing spondylitis (AS), and atopic dermatitis (AD) (Burmester et al. RMD Open. 2023;9(1):e002735) • Included 907 individuals with PSA treated with upadacitinib 15 mg daily • In PsA, the rate of AEs was numerically higher with upadacitinib (244.8) vs adalimumab (229.9) • Rrates of death were higher with upadacitinib 15 mg compared with adalimumab, owing to increased COVID-19-related deaths in patients taking upadacitinib • Most common upadacitinib related AE as upper respiratory tract infection • Serious infections with upadacitinib occurred at similar rates between RA, PsA, and AD and infrequently led to discontinuation. • Identified no new safety risks compared with previous reports JAK inhibitors – review of safety data in PsA (Nash. J Dermatol. 2022;49(6 suppl 1):44-47). • Included upadacitinib trials: SELECT-PsA 1 and 2 • Concluded people with PsA are at lower risk of morbidity than patients with RA for a number of reasons, including lower corticosteroid usage, lower age group, and fewer co-morbidities. Systematic review and meta-analysis of JAK inhibitors for psoriatic arthritis (Harkins et al. Int J Rheum Dis. 2023;26(1):31-42). • Included upadacitinib trials: SELECT-PsA 1 and 2 • No relevant information further to 2022 clinical advice paper identified Post hoc analysis of the SELECT-PsA 1 and 2 trials(Mease et al. Rheumatol Ther. 2022;9(4):1181-1191) • 1386 patients were analysed. • Disease control was achieved at 24 weeks in upadacitinib 15 mg-treated patients across both studies: LDA/MDA was achieved by 25-48% of patients receiving upadacitinib 15 mg versus 2-16% of patients receiving placebo • Remission rates were 714% with upadacitinib 15 mg versus 04% with placebo. • All responses were sustained at 56 weeks. Pooled data of SELECT-PsA 1 and 2 (Nash et al. Rheumatology. 2022;61(8):3257-3268) • Placebo-subtracted treatment effects for a 20% improvement in ACR criteria at week 12 were 33.7% (95% CI 24.4 to 43.1) and 34.0% (95% CI 27.9 to 40.1) for upadacitinib 15 mg daily monotherapy and combination therapy, respectively, and 45.7% (95% CI 36.9 to 54.5) and 39.6% (95% CI 33.7 to 45.5) for upadacitinib daily 30 mg monotherapy and combination therapy, respectively
upadacitinib AND psoriatic arthritis AND subsequent	Nil relevant

Search terms	Results
upadacitinib AND psoriatic arthritis AND second line upadacitinib AND psoriatic arthritis AND sequential upadacitinib AND psoriatic arthritis AND paradigm upadacitinib AND psoriatic arthritis AND algorithm upadacitinib AND psoriatic arthritis AND retreatment	
psoriatic arthritis AND treatment AND sequence; filtered by: publication date 2018-2022	Nil relevant

Consequences for the health system

Upadacitinib is an oral treatment that could be administered both in the community and hospital settings. It would not require injection education or administration by infusion, like other treatments for PsA.

In May 2022 PTAC considered that there would be no substantial impact to healthcare workers if upadacitinib were funded for PsA, due to the suitability benefit of upadacitinib discussed below.

Suitability

The features of the medicine or medical device that impact on use

In May 2022 PTAC noted that oral upadacitinib would have a suitability benefit over subcutaneous secukinumab, which is generally self-administered by the individuals themselves or is administered at home or in the community by health workers in a small number of cases. PTAC considered that the suitability of upadacitinib as an oral treatment would be of benefit especially to Māori and people who live in rural areas, who may find it more suitable and accessible than alternative treatments that are injected subcutaneously.

Costs and savings

Costs and savings to pharmaceutical expenditure

The current confidential net price of upadacitinib is $S 9(2)(b) per 28 x 15 mg tabs, corresponding to an annual cost of $S 9(2)(b) . S 9(2)(b)(ii), 9(2)(ba)(i) & 9(2)(j) S 9(2)(b)(ii), 9(2)(ba)(i) & 9(2)(j) S 9(2)(b)(ii), 9(2) .

Key questions to inform Pharmac's economic modelling

Prevalent pool

PTAC considered it unlikely that there would be a prevalent pool of individuals who would switch to upadacitinib upon listing.

When secukinumab was listed, approximately 150 people switched to secukinumab within the first year, corresponding to ~10% of biologic-treated individuals.

We seek the Committee's advice on whether there would be a similar prevalent pool of people who would switch with the listing of upadacitinib, taking into account available treatments and the potential preference of individuals for upadacitinib.

Use of secukinumab in clinical practice

According to PharmHouse data, approximately 20% of people on secukinumab received secukinumab without the box being ticked by an applicant that says they have previously received another biologic. This is in line with the rate of first line secukinumab treatment in other jurisdictions, where reported rates vary between 13-37% (Letarouilly et al. Rheumatol 2021;60: 2773-82; Ramonda et al. RMD Open 2021;7: e001519).

Among those that do not receive secukinumab first-line, it is also uncertain whether secukinumab is typically used after failure of one or two prior anti-TNFs, which then informs whether secukinumab is used second- or third-line.

We seek the Committee's views on the current use of secukinumab in a first, second-, and third-line setting, as well as whether this is likely to evolve over time.

Pharmac estimate of treatment sequencing

A key point of uncertainty in the economic modelling is treatment sequencing of biologics for PsA. This applies both with current treatments, and also what the sequencing might be with the listing of upadacitinib.

Pharmac's estimate of the percentages of people receiving different treatments in the current treatment paradigm is shown below, with arrows depicting which treatments in the pathway individuals might progress on to next.

We seek the Committee's advice on:

- Whether the figure below accurately reflects the current treatment paradigm, and if not, where any potential amendments need to be made;
- The extent to which upadacitinib would be used in the second or third line setting, if listed second-line; and
- Whether upadacitinib would be used second-line among people that used secukinumab in the first-line setting

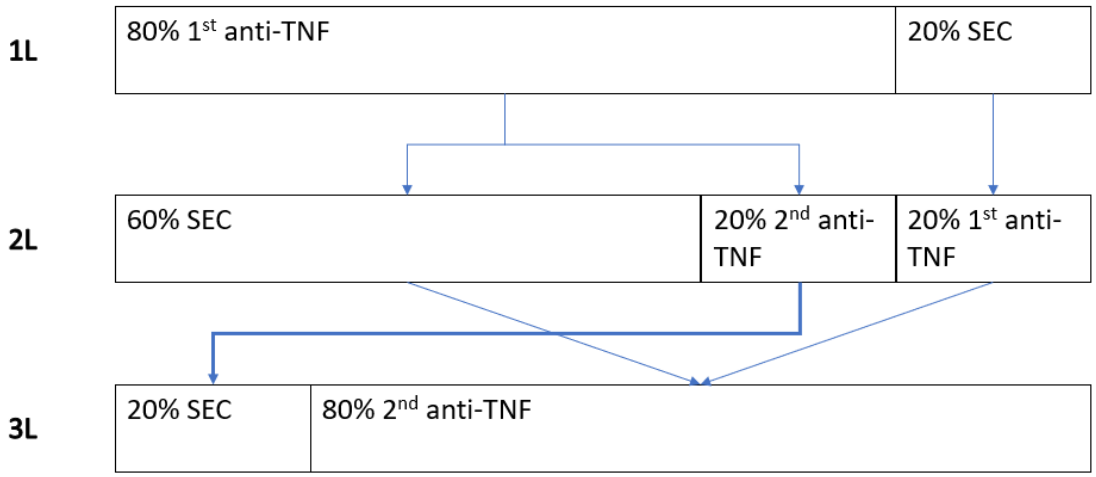


Figure 3: Pharmac staff's estimate of the treatment sequencing of biologics in PsA. SEC = secukinumab.

APPENDICES

Appendix 1:

- Upadacitinib for psoriatic arthritis clinical advice paper. May 2022.
- PTAC record excerpt - Psoriatic Arthritis. May 2022.

Appendix 2:

- Burmester et al. 2023.
- Nash. 2022.
- Harkins et al. 2022.
- Mease et al. 2022.
- Nash et al. 2022.

THE FACTORS FOR CONSIDERATION

Factors are presented here in the order they appear in the paper, without implying any ranking or relative importance.

NEED

- The health need of the person
- The availability and suitability of existing medicines, medical devices and treatments
- The health need of family, whānau, and wider society
- The impact on the Māori health areas of focus and Māori health outcomes
- The impact on the health outcomes of population groups experiencing health disparities
- The impact on Government health priorities

HEALTH BENEFITS

- The health benefit to the person
- The health benefit to family, whānau and wider society
- Consequences for the health system

SUITABILITY

- The features of the medicine or medical device that impact on use by the person
- The features of the medicine or medical device that impact on use by family, whānau and wider society
- The features of the medicine or medical device that impact on use by the health workforce

COSTS AND SAVINGS

- Health-related costs and savings to the person
- Health-related costs and savings to the family, whānau and wider society
- Costs and savings to pharmaceutical expenditure
- Costs and savings to the rest of the health system