6.10 ADALIMUMAB, Injection 20 mg in 0.2 mL pre-filled syringe, Injection 40 mg in 0.4 mL pre-filled pen, Injection 40 mg in 0.4 mL pre-filled syringe, Injection 80 mg in 0.8 mL pre-filled pen, Injection 80 mg in 0.8 mL pre-filled syringe, Humira®, and UPADACITINIB, Tablet 15 mg, Rinvoq®, AbbVie Pty. Ltd.

1 Purpose of Submission

1.1 The Category 3 submission sought to:

- change the restriction level of PBS-listed adalimumab in three strengths 20 mg in 0.2 mL, 40 mg in 0.4 mL and 80 mg in 0.8 mL (Humira®) for RA and ankylosing spondylitis (AS) from Authority Required (Written) for initial treatment to Authority Required (Telephone/Electronic), and for any continuing phase to Authority Required (Streamlined).
- change the restriction level of PBS-listed adalimumab in three strengths 20 mg in 0.2 mL, 40 mg in 0.4 mL and 80 mg in 0.8 mL (Humira®) for psoriatic arthritis (PsA), hidradenitis suppurativa (HS), chronic plaque psoriasis (CPP), Crohn Disease (CD) and Fistulising Crohn Disease (FCD) from Authority Required (Written) to Authority Required (Streamlined) for subsequent continuing treatment.
- change the restriction level of PBS-listed adalimumab in three strengths 20 mg in 0.2 mL, 40 mg in 0.4 mL and 80 mg in 0.8 mL (Humira®) for ulcerative colitis (UC) Authority Required (Written) to Authority Required (Telephone/Electronic) for Subsequent Continuing treatment.
- change the restriction level of PBS-listed upadacitinib 15 mg tablets (Rinvoq®) for rheumatoid arthritis (RA) from Authority Required (Written) to Authority Required (Streamlined) for subsequent continuing treatment.

1.2 Table 1 summarises the requested changes.

Table 1 Summary of the requesting listing changes for upadacitinib and adalimumab

Indication	Treatment Phase	Current Authority Required	Proposed Authority Required
Adalimumab (Humira)			
RA	Initial	Written	Telephone/Electronic
	Any Continuing[a]	Written	Streamlined
PsA	Subsequent Continuing	Written	Streamlined
AS	Initial	Written	Telephone/Electronic
	Any Continuing[a]	Written	Streamlined
HS	Subsequent Continuing	Written	Streamlined
CPP	Subsequent Continuing	Written	Streamlined
UC	Subsequent Continuing	Telephone/Electronic	Streamlined
CD	Subsequent Continuing	Written	Streamlined
FCD	Subsequent Continuing	Written	Streamlined
Upadacitinib (Rinvoq)			
RA	Subsequent Continuing	Written	Streamlined

Table reproduced from the submission (p. 5). Abbreviations: RA, rheumatoid arthritis; PsA, psoriatic arthritis; AS, ankylosing spondylitis; HS, hidradenitis suppurativa; CPP, chronic plaque psoriasis; UC, ulcerative colitis; CD, Crohn's Disease; FCD, Fistulising Crohn's Disease.
[a] The sponsor noted that the *Review Of PBS Authority Required (Written) Listings: Tranche 6* from PBAC March 2022 recommended changes to the subsequent continuing treatment phase but not the first continuing treatment phase restrictions for RA and AS (Recommendations made by the PBAC – March 2022 – PBAC Outcomes p. 60-62). As such they are requesting the change be applied to any continuing treatment phase.

2 Background

2.1 Adalimumab is currently listed for RA, PsA, AS, HS, CPP, UC, CD and FCD, as well as other indications for which changes have not been requested. For Humira, the originator brand of adalimumab, most restrictions for the requested indications require written authority for both initial and continuing treatment (Table 2). Balance of supply listings (not depicted) require Telephone/Electronic authority.

Table 2 Summary of the current authority required for adalimumab (Humira) by indication and treatment phase.

	Treatment Phase		
Indication	**Initial**	**First Continuing**	**Subsequent Continuing**
RA	Written	Written	Written
PsA	Written	Written	Written
AS	Written	Written	Written
HS	Written	Written[a]	Written[a]
CPP	Written	Written	Written
UC	Written	Telephone/Electronic	Telephone/Electronic
CD	Written	Written	Written
FCD	Written	Written	Written

Abbreviations: RA, rheumatoid arthritis; PsA, psoriatic arthritis; AS, ankylosing spondylitis; HS, hidradenitis suppurativa; CPP, chronic plaque psoriasis; UC, ulcerative colitis; CD, Crohn's Disease; FCD, Fistulising Crohn's Disease.
[a] Note that HS does not have a "first continuing" and "subsequent continuing" treatment phase, only Continuing treatment

2.2 Rinvoq is the sole brand of upadacitinib listed on the PBS. Its listings for the treatment of RA are Authority Required (Written) for initial and continuing phases of treatment and Telephone/Electronic Authority Required for balance of supply.

Registration status

2.3 Adalimumab 40 mg in 0.4 mL PFS and PFP, 20 mg in 0.2 mL PFS and 80 mg in 0.8 mL PFS and PFP are ARTG for the relevant indications under consideration. Specifically rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), hidradenitis suppurativa (HS), chronic plaque psoriasis (CPP), ulcerative colitis (UC) and Crohn's disease (CD).

2.4 Upadacitinib was first registered in the ARTG on 17 January 2020. Its registration includes the indication: "for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to, one or more disease-modifying anti-rheumatic drugs (DMARDs)" (Product Information for RINVOQ upadacitinib 15 mg modified release tablet blister pack, ARTG ID 312687).

Previous PBAC consideration

2.5 At its July 2021 meeting, the PBAC considered tranche 3 of the *Review of PBS Authority Required (Written) listings* (the Review), which included adalimumab in the treatment of CD, FDC and UC. The PBAC did not recommend any changes to the Authority Required levels (Table 3). For all considered indications, including CD, FDC and UC, the PBAC considered "a restriction change across PBS indications could be considered

once biosimilars are well established and utilisation has stabilised" (Review of Authority Required (Written) PBS listings Tranche 3, July 2021 PBAC Meeting Outcomes).

2.6 At its March 2022 PBAC meeting, the PBAC considered tranche 6 of the Review. Both adalimumab and upadacitinib were considered among other treatments for various rheumatological, dermatological and vascular conditions. However, upadacitinib was not included in the Review for RA due to the recency of PBS listing and immaturity of PBS data (Tranche 6 Review of Written Authority PBS Listing, March 2022).

2.7 The submission referred to the recommended listings from the *Review of PBS Authority Required (Written) listings – Tranche 6* for the biosimilar brands of adalimumab as the source of the requested change in Authority required for adalimumab (Humira®) and upadacitinib.

2.8 Adalimumab authority levels were reviewed for listings for the treatment of AS, PsA, RA, HS and CPP. The PBAC recommended changes to some Authority Required listings, however, it made separate recommendations for originator brands, including Humira. The PBAC only recommended one change for patients with RA being prescribed Humira; the subsequent continuing treatment phase to change from Authority Required (Written) to Authority Required (STREAMLINED), per Table 3.

2.9 The PBAC did not recommend changes to the authority level for other indications or treatment phases for Humira as "the PBAC was mindful of supporting the differential between biosimilar and originator brands and of encouraging the prescribing of biosimilars where appropriate." (Tranche 6 Review of Written Authority PBS listings, March 2022 PBAC Meeting Outcomes).

2.10 The changes recommended to adalimumab in the Review of Written Authority PBS listings referenced by the submission have not been implemented at this time.

Table 3 Summary of the PBAC recommended changes to authority required for adalimumab (Humira) by indication and treatment phase in the Tranche 6 review March 2022

	Treatment Phase		
Indication	**Initial**	**First Continuing**	**Subsequent Continuing**
RA[a]	Written (No Change)	Written (No Change)	~~Written~~ STREAMLINED
PsA[a]	Written (No Change)	Written (No Change)	Written (No Change)
AS[a]	Written (No Change)	Written (No Change)	Written (No Change)
HS[a]	Written (No Change)	Written[b] (No Change)	Written[b] (No Change)
CPP[a] (adult)	Written (No Change)	Written (No Change)	Written (No Change)
UC[c]	Written (No Change)	Telephone/Electronic (No Change)	Telephone/Electronic (No Change)
CD[c]	Written (No Change)	Written (No Change)	Written (No Change)
FCD[c]	Written (No Change)	Written (No Change)	Written (No Change)

Abbreviations: RA, rheumatoid arthritis; PsA, psoriatic arthritis; AS, ankylosing spondylitis; HS, hidradenitis suppurativa; CPP, chronic plaque psoriasis; UC, ulcerative colitis; CD, Crohn's Disease; FCD, Fistulising Crohn's Disease.
a Considered in March 2022 review of Tranche 6 Authority required listings
b Note that HS does not have a "first continuing" and "subsequent continuing" treatment phase, only Continuing treatment
c Considered in July 2021 review of Tranche 3 Authority Required listings.

For more detail on PBAC's view, see section 5 PBAC outcome.

3 Requested listing

3.1 The submission requested the following changes to the existing restrictions regarding authority type for the following indications. A summary of the affected drugs and PBS items is presented, by indication.

3.2 Suggested additions from the Department are in *italics* and deletions are in strikethrough.

Table 4: Requested Authority Required Restriction Changes

Drug, Strength & Form	Indication	PBS Item Codes	Sponsor Requested Authority
Adalimumab			
Adalimumab (Humira) - 40 mg/0.4 mL injection pen device - 40 mg/0.4 mL injection syringe	Rheumatoid arthritis	12429E 12390D 12400P 12430F	**Initial treatment 1, 2, 3 –** Authority Required (Telephone/Electronic) **Continuing treatment (first and subsequent continuing)** – Authority Required (STREAMLINED)
Adalimumab (Humira) - 40 mg/0.4 mL injection pen device - 40 mg/0.4 mL injection syringe	Ankylosing spondylitis	12376J 12363Q 12361N 12442W	**Initial treatment 1, 2, 3 –** Authority Required (Telephone/Electronic) **Continuing treatment (first and subsequent continuing)** –Authority Required (STREAMLINED)

Adalimumab (Humira) - 40 mg/0.4 mL injection pen device - 40 mg/0.4 mL injection syringe	Psoriatic arthritis	12375H 12398M	**Subsequent continuing treatment** – Authority Required (STREAMLINED)
Adalimumab (Humira) - 40 mg/0.4 mL injection pen device - 80mg/0.8mL injection pen device - 80mg/0.8mL injection syringe	Hidradenitis suppurativa	12414J 12448E 12408C	**Subsequent continuing treatment** – Authority Required (STREAMLINED)
Adalimumab (Humira) - 40 mg/0.4 mL injection pen device - 40 mg/0.4 mL injection syringe	Chronic plaque psoriasis	12377K 12422T	**Subsequent continuing treatment** – Authority Required (STREAMLINED)
Adalimumab (Humira) - 40 mg/0.4 mL injection pen device - 40 mg/0.4 mL injection syringe - 20 mg/0.2 mL syringe	Ulcerative colitis	12358K 12391E 12337H	**Subsequent continuing treatment** – Authority Required (STREAMLINED)
Adalimumab (Humira) - 40 mg/0.4 mL injection pen device - 40 mg/0.4 mL injection syringe - 20 mg/0.2 mL syringe	Crohn's disease	12341M, 12389C 12410E 12413H 12424X	**Subsequent continuing treatment** – Authority Required (STREAMLINED)
Adalimumab (Humira) - 40 mg/0.4 mL injection pen device - 40 mg/0.4 mL injection syringe	Fistulising Crohn's disease	12446C 12405X	**Subsequent continuing treatment** – Authority Required (STREAMLINED)
Upadacitinib			
Upadacitinib (Rinvoq) - 15 mg modified release tablet	Rheumatoid arthritis	11979L *New*	***First Continuing treatment*** *– Authority Required (Written)* ***Subsequent continuing treatment*** *– Authority Required (STREAMLINED)*

3.3 Upadacitinib 15 mg for RA is currently listed on the PBS as one continuing treatment phase. If changes are recommended to the continuing treatment phase the PBAC is asked to advise if these should be aligned with the existing listings for abatacept, baricitinib, certolizumab, golimumab, tocilizumab and tofacitinib which include a First continuing treatment Authority Required (Written) and subsequent continuing treatment Authority Required (STREAMLINED).

For more detail on PBAC's view, see section 5 PBAC outcome.

4 Consideration of the evidence

Sponsor hearing

4.1 There was no sponsor hearing for this item.

Consumer comments

4.2 The PBAC noted and welcomed the input from individuals (1) via the Consumer Comments facility on the PBS website. The PBAC noted the input related primarily to the individual's support for the ongoing access to adalimumab and upadacitinib on the PBS, however they did not indicate whether there was also support for the requested changes in authority levels for the two drugs.

Estimated PBS utilisation and financial implications - Upadacitinib

4.3 For consideration of upadacitinib, the submission presented 25 months of utilisation data from May 2021 to May 2022. The sponsor provided a graphical analysis of the trends in utilisation in the RA market, covering "the 10 years prior to upadacitinib listing, in the 6 years following tofacitinib listing and for the 2 years following the upadacitinib listing". The figure is reproduced as Figure 1.

4.4 The submission argued that the utilisation trends had not been impacted by the presence of upadacitinib. The submission argued that the listing of the drug "may have caused some market disruption by substituting for other medicines but has not driven market growth".

4.5 These claims were reiterated in the sponsor's pre-PBAC response. The sponsor provided utilisation data that included an additional 4 months' data for upadacitinib use in RA. The argument was made that the new market growth trends calculated by pre-PBAC response was not significantly different to that in the submission, and that the listing of upadacitinib was not influential to the trend.

4.6 The submission also argued that since the price of upadacitinib was equivalent to the lowest-cost comparator, that some script replacement may be a net cost benefit to the PBS. The submission also argued that this is of magnitude as it posits that "upadacitinib is currently one of the most effective RA treatments". *See paragraph 4.7 for the PBAC's consideration of upadacitinib's effectiveness compared to other agents.*

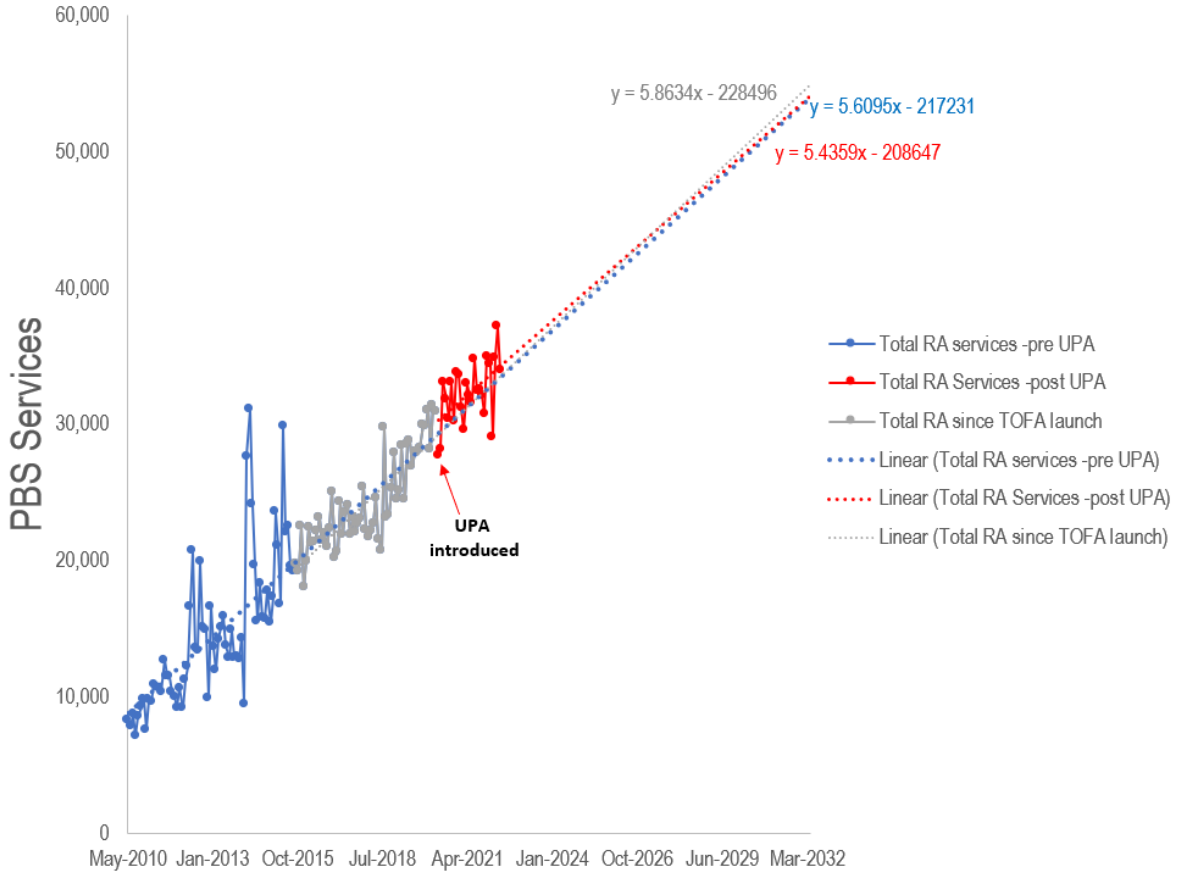
4.7 The PBAC recommended the listing of upadacitinib on a cost-minimisation basis against the least costly biological disease modifying anti-rheumatic drug (bDMARD) for rheumatoid arthritis (RA) (Para. 7.1, upadacitinib Public Summary Document [PSD], PBAC meeting November 2019). The PBAC considered the claims that upadacitinib is non-inferior to baricitinib in terms of effectiveness and safety and non-inferior in terms of safety compared to adalimumab, were adequately supported by the clinical evidence presented in the submission. The PBAC considered the claim of superior effectiveness versus adalimumab was not fully supported by the evidence (Para. 7.5, upadacitinib PSD, PBAC meeting November 2019).

4.8 In respect to these arguments, the submission then argued that it would be "reasonable to reduce the administrative burden for patients, clinicians, and Services Australia by extending the authority required changes to upadacitinib at the earliest opportunity, given that it is not more expensive than other treatment options and that more than 24 months of data following the May 2020 launch demonstrate that it has not driven further market growth". Upadacitinib was listed on a CMA to baricitinib with equi-effective doses of upadacitinib 15 mg daily = baricitinib 4 mg daily (Para. 6.26, upadacitinib PSD, November 2019). The current DPMQ for upadacitinib continuing treatment phase for severe active RA (11979L) is $1271.46 (AEMP October 2022 = $1149.97) which is equal to baricitinib (11443G) $1271.46 (AEMP October 2022 = $1149.97).

4.9 In considering Tranche 6 of the Review, the PBAC recommended that originator brands for treatment of RA have the authority level for subsequent continuing phase changed from Written to Streamlined, but there was not sufficient data for upadacitinib to be considered at that time.

4.10 The PBAC noted that PBS data showed a large increase in the number of patients initiating RA treatment in 2021, largely driven by adalimumab and upadacitinib. The PBAC considered it was not yet clear whether the listing of upadacitinib was contributing to an increase in utilisation in the RA market and, as such, was not of a mind to change the restriction level based on the data provided.

Figure 1 Rates of market growth in rheumatoid arthritis before and after May 2020



Source: Submission main body (p 7). PBS Item Reports, http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp (see attached Excel workbook for workings). Abbreviations: UPA: upadacitinib; RA: rheumatoid arthritis; TOFA: tofacitinib.

Estimated PBS utilisation and financial implications - Adalimumab

4.11 The submission did not provide any utilisation data to support the request to change the authority levels of adalimumab (Humira®) to match those of the biosimilar brands of adalimumab for RA, PsA, AS, HS, CPP, UC, CD and FCD.

4.12 The submission argued "aligning of authority requirements for adalimumab and biosimilars would likely lead to savings to the PBS via price disclosure". The PBAC noted that the proposed changes do not align with the Government's biosimilar policy.

4.13 The submission argued that for the year 2021, adalimumab biosimilars accounted for approximately 16% of the market share. When removing Humira® from the calculation, the submission argues that 100% of the market share is attributable to biosimilar brands. The submission argues that "uptake drivers that aim to increase market share of biosimilars will no longer be relevant or effective in driving savings for the Commonwealth". The submission argues that cost savings would be more likely to occur if biosimilar brands and originator brands were to compete on price, through a "freely competitive market" which would be enabled by aligning the authority required levels.

4.14 The submission argued that there is no clinical reason to apply different levels of Authority Required to different brands of the same drug. The submission added that alignment of restrictions would "reduce administrative burden across all indications and help minimise confusion for patients and clinicians while a number of authority required changes are implemented across many immunology indications".

4.15 The submission argued that the reasoning presented supported the Department's biosimilar policies to "to encourage a healthy competitive market that results in lower costs and ultimately supporting a viable long-term market for these medicines". The PBAC noted that the current policy framework provides for biosimilar uptake drivers and it is not a matter for the PBAC to develop another policy in this regard, that is a matter for Government.

4.16 The submission referred several times to a need to align the authority level for all indications. However, in considering tranche 3 and 6 of the Review, the PBAC did not recommend changes to the authority status for all indications, regardless of their originator or biosimilar status. The PBAC only recommended changes for the biosimilar brands of adalimumab in the treatment of AS and RA. All other indications were not recommended for a change to the Authority Required level. However, for the other indications, biosimilar brands are generally listed at an authority required level lower than the originator brand as part of the biosimilar uptake driver policy.

For more detail on PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

5.1 The PBAC did not recommend the requested changes to the Authority Required levels of the adalimumab brand, Humira, for rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, hidradenitis suppurativa, chronic plaque psoriasis, ulcerative colitis or Crohn's disease.

5.2 The PBAC noted that in the case of adalimumab, the changes requested would contradict its previous recommendations and would not align with the Government's biosimilar policy. The PBAC further noted biosimilar uptake driver policy was a matter for Government. The PBAC reaffirmed its position to align its recommendations with Government biosimilar policy.

5.3 The PBAC did not recommend changes to the Authority Required level for upadacitinib in the continuing phase listings for treatment of severe active rheumatoid arthritis to those recommended by the PBAC in March 2022 for other originator brands for this indication.

5.4 The PBAC considered there remained uncertainty about the contribution of upadacitinib to growth in the RA market. Therefore, the PBAC was unable to support the submission's claim that the change to authority level would have no financial impact based on the data provided.

5.5 The PBAC considered a resubmission may be lodged at any future standard due date for PBAC submissions using the standard re-entry pathway.

5.6 The PBAC noted that this submission is not eligible for an Independent Review. Independent Review is only available for submissions requesting to list the drug on the PBS or an extension of the listing of an already listed drug (indication or eligible population).

Outcome:
Not recommended

6 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

7 Sponsor's Comment

Upadacitinib: AbbVie is disappointed in the PBAC's decision not to extend the Tranche 6 recommendation of streamlined authority for subsequent continuing prescriptions to upadacitinib in rheumatoid arthritis despite the provision of 28 months of data. This means that upadacitinib will be the only product in the RA market with additional prescriber and patient administrative burden.

Adalimumab: AbbVie's position is that it would be appropriate for Humira to have a reduced prescriber administrative burden. AbbVie will continue to work with the Department and the Minister for Health and Aged Care to seek a change to the authority level for Humira.