Upadacitinib for the treatment of moderate to severe rheumatoid arthritis (RA)
Excerpt from paper to the Pharmacology and Therapeutics Advisory Committee (PTAC), February 2021

Costs and Savings

Estimated Incremental Total Cost of Listing

Patient numbers – in line with first-line bDMARDs

The supplier submitted a budget impact model for upadactinib using an epidemiological approach to estimate the prevalence of severe RA, along with market share assumptions. PHARMAC has re-estimated the budget impact of upadacitinib based on dispensing data from PHARMHouse for RA treatments. The estimates of patient numbers include the following assumptions:

- During 2020, there were 1182 patients receiving adalimumab, and 762 receiving etanercept (i.e. market share of approximately 60% adalimumab, 40% etanercept), corresponding to a total first-line anti-TNF market of 1944 patients;
- 4% annual market growth, based on market growth from 2016-2020;
- An estimate that the market will grow by an additional 10% with the introduction of a new (oral) agent. This estimated growth is higher than the 5% figure proposed by the supplier, but consistent with PTAC advice from August 2015 for subcutaneous tocilizumab, which considered that the listing of another non-IV treatment option could increase the total number of rheumatoid arthritis patients on biologics by up to 10%;
- Total market share of upadacitinib (as a proportion of all patients receiving first-line tsDMARD/bDMARD treatment) of 15%, eventually rising to 40%. This is a higher and faster uptake rate than proposed by the supplier, who proposed year 1 uptake of 6%, rising to 36%. Previous advice provided by PTAC in 2015 for subcutaneous tocilizumab considered up to 20% of adalimumab and etanercept patients may switch to a new agent to improve treatment response, and this higher uptake reflects a potential bolus of patients switching to upadacitinib shortly after listing;
- 40% of biologic-naïve patients are prescribed upadacitinib as a first-line tsDMARD/bDMARD treatment option by year 5 after listing.

Patient numbers are shown in the table below. 1081 patients are expected to receive upadacitinib each year by 2026.

Table 4: PHARMAC-estimated patient numbers if upadacitinib were to be listed with the same restrictions as adalimumab and etanercept.

Financial Year	2022	2023	2024	2025	2026
First-line tsDMARD/bDMARD RA market	2207	2404	2500	2599	2703
Market share - UPA	15%	25%	30%	35%	40%
Patients receiving UPA	331	601	750	910	1081

Estimated budget impact – in line with first-line bDMARDs

The net cost to the Pharmaceutical Schedule from the listing of upadacitinib is estimated to be Withheld in year 1, rising to Withheld by year 5. There is also a small rise in the net cost of pharmacy handling and distribution fees (which is calculated as 4% of the gross price of the pharmaceutical).

The analysis below also includes the cost of Herpes Zoster vaccination for all patients initiating upadacitinib, though the cost of this is very small compared to the other pharmaceutical costs, with a 5-year NPV of around Withheld. An additional nurse visit to administer the vaccine is also included in the BIA, at a 5-year NPV to other DHB budgets of approximately $20,000 as a result.

These results are shown in table 5 below. The estimated 5-year NPV for the proposal is Withheld under .

Table 5: Budget impact if upadacitinib were to be listed with the same restrictions as adalimumab and etanercept.

Financial Year	2022	2023	2024	2025	2026	5-year NPV (8%)
Patients receiving UPA	331	601	750	910	1081	
Net cost to pharm budgets	Withheld under	Withheld under	Withheld under	Withheld under	Withheld under	Withheld under
Net cost to other DHB budgets	Withheld under	Withheld under	Withheld under	Withheld under	Withheld under	Withheld under
Net cost to DHB budgets	Withheld under	Withheld under	Withheld under	Withheld under	Withheld under	Withheld under

Budget impact of upadacitinib if restricted to use in line with second-line bDMARDs

The supplier did not provide an estimate of budget impact for upadactinib if restricted to use after one prior bDMARD.

A Canadian study of patients initiating tofacitinib for RA reported that, three years after listing, 60% of patients initiating tofacitinib had received at least one prior bDMARD (and

approximately half of these patients had received at least 2 prior bDMARDs) (Pope et al. Rheumatology 2020; 59: 568-74).

Based on the Canadian uptake of tofacitinib, and the above estimate that upadacitinib would make up 40% of the first-line market if it were listed with the same restrictions as adalimumab and etanercept, PHARMAC staff estimate that upadacitinib would make up approximately 25% of the total non-IV market if restricted to use after use of at least one prior biologic. Given that market expansion with the listing of a new oral agent may be smaller if upadacitinib was restricted in line with second-line bDMARDs, a 5% market expansion is assumed.

The budget impact if listed in line with infliximab and rituximab only is shown below.

Table 6: budget impact if upadacitinib was restricted to use after an anti-TNF

Financial Year	2022	2023	2024	2025	2026	5-year NPV (8%)
Patients receiving UPA	215	344	477	620	645	
Net cost to pharm budgets	Withheld under	Withheld under	Withheld under	Withheld under	Withheld under	Withheld under
Net cost to other DHB budgets	Withheld under	Withheld under	Withheld under	Withheld under	Withheld under	Withheld under
Net cost to DHB budgets	Withheld under	Withheld under	Withheld under	Withheld under	Withheld under	Withheld under