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Submission of the Australasian College of Dermatologists

Pharmaceutical Benefits Scheme (PBS) Post-Market Review of biologics for severe chronic plaque psoriasis: Report to the Pharmaceutical Benefits Advisory Committee (PBAC)

Feb 2018

This submission outlines the response of the Australasian College of Dermatologists (ACD) to the draft report of the PBS post-market review of biologics for severe chronic plaque psoriasis (CPP).

The College welcomes the opportunity to respond to this review, noting that the public consultation period of two weeks is inadequate to undertake a thorough review of this comprehensive body of work. Thus, this submission presents a high level overview and the College trusts that this will be taken into account when stakeholder submissions are considered by PBAC. In addition, the College is aware that the Reference Group has not yet met to discuss their review of this report in its entirety. This raises concerns about whether this draft adequately reflects the collective views of the Reference Group and indeed about the consultation process more broadly.

The College notes that this detailed report has been conducted to address four Terms of Reference (ToR):

1. Review of current national and international clinical guidelines for CPP, viewed in the context of PBS restrictions for the use of biologics for this condition;

2. Update of recent clinical evidence of safety, efficacy and quality of life measures not considered by PBAC in previous sponsor application assessments;

3. Estimates of CPP prevalence and analysis of the actual biologic utilisation rates in Australia, to evaluate consistency with expected uptake and length of treatment based on clinical trial data;

4. Based on findings from ToR 1, 2 and 3, review of the cost-effectiveness of biologics. This analysis has yet to be performed. Outcomes from any subsequent cost utility model will be dependent on preselected inputs including changes to eligibility criteria and prevalence estimates.

The ultimate aim of this post-market review is to identify whether amendments to PBS restrictions may be warranted based on clinical evidence and stakeholder input, and supported by economic analysis.

In previous submissions to the post-market review and input into the Stakeholder Forum, the College has raised a number of issues relating to the availability and management of biologics via the PBS, including restrictions, compatibility with clinical trial eligibility, toxicity criteria, and other administrative concerns. The College is encouraged by the progress of the post-market review and anticipates that these issues will be addressed, allowing for timely and equitable access to biologics for those patients most likely to benefit and achieve long-term disease control.

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Tor 1 and 2

The College is satisfied that recent clinical guidelines and relevant published trial data have been captured in the analysis (ToR 1 and 2). Particular caution needs to be given to the tendency to over-interpret low powered studies with small patient numbers, or to extrapolate results across different clinical scenarios. The College looks forward to the opportunity to provide feedback once the report in its entirety has benefitted from Expert Reference Group review.

The report however does highlight the lack of alignment between PBS restrictions and international guidelines, as well as the Australian consensus statement. These restrictions are not reflective of usual best practice care and the College argues strongly for PBAC to consider the evidence in support of the following restrictions:

- Failure of two of four prior treatments (phototherapy, methotrexate, cyclosporine, acetritin); OR deletion of cyclosporin A from the list of required treatment failures given the toxicity risks i.e. failure of two of three prior treatments (phototherapy, methotrexate, acetritin)
- Reduction of the PASI threshold to PASI >10 and inclusion of quality of life measure (DLQI > 10)
- Involvement of: genitalia; palms and/or soles; major parts of the scalp; onycholysis or onychodystrophy of at least two fingernails.

The authors raise the concern that PASI lacks specificity at the lower end of the scale, and thus would be problematic as a measure for mild disease. However the requirement of ΔPASI 75 for treatment continuation necessitates the use of this measure of objective disease severity at the lower end of its range, and is currently the sole indictor of treatment pass/fail for the PBS. Subjective disease severity (DLQI) will be all the more important as a co-indicator in this regard. Furthermore, in the case whereby a patient does not reach ΔPASI 75 but exhibits improved quality of life (i.e. DLQI <5) then the College recommends the treatment regimen may be adjusted at the discretion of the treating dermatologist, as described in the Australian consensus statement, rather than discontinue as per PBS restrictions.

Finally, under the current restrictions, patients who fail to respond to three biologics must cease therapy for a minimum of five years. This is no longer considered an appropriate cut-off – given that there are currently six biologics on the market – all of which have different affinities for their biological target (TNF-alpha, interleukins) – and with several agents in clinical trial, a patient should not be considered to have exhausted treatment options after three biologics. There is no evidence to suggest that a patient will not respond to a fourth agent; data from the Australian Psoriasis Registry shows some patients (less than 10%) are undergoing treatment with a fourth, fifth or sixth biologic, having switched for reasons other than treatment failure. Flexibility is thus required in clinical decision making and current PBS restrictions do not permit a tailored treatment approach, inhibiting patient access unnecessarily.

ToR 3

ToR 3 presents an analysis of biologic utilisation rates based on unit record level PBS data from July 2013. As biologics have been available in Australia since 2006, it is unclear as to why only recent data were included in the analysis. Since 2013, the results show an increase over time of both prescription and patient

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numbers; by 2016, 5,144 patients were prescribed a biologic. The upper and lower CPP prevalence estimates in Australia were wide, ranging from 7,787 to 359,984 patients with PASI >15. The impact of prevalence estimates with such wide upper and lower limits on cost utility modelling is of concern to College, as the use of biologics are unlikely to demonstrate cost-effectiveness in the upper limit scenario especially in the context of an expanded eligible population. The College acknowledges the paucity of national and international prevalence data however consideration may need to be given to adjusting the methodology used to generate Australian prevalence estimates.

Of note, evidence from extension studies suggests manageable adverse effects in patients receiving biologic treatment in the longer term. Indeed, PBS data showed that patients are continuing treatment for longer than anticipated, suggesting an acceptable long-term safety profile. It is important here to note that trial data reports efficacy of biologic monotherapy, however in real-world application, patients may be treated with a biologic agent plus topical agents, phototherapy, and/or methotrexate. This may be a confounding factor which allows patients to maintain PASI 75 response and continue on biologic treatment beyond expected duration for improved disease control.

ToR 4

To address ToR 4, the review puts forward three options for consideration by PBAC regarding alterations to PBS restrictions. Ultimately, these options could be used to determine cost utility modelling inputs as described in Option 4b. In addition, the role of biosimilars with equivalent efficacy and safety must be noted - indeed, in the context of an expanded eligible patient population, biosimilars represent a viable option to address budgetary issues and increase patient access, and should be considered in any future economic or market evaluation. Furthermore, cost-effectiveness should not be limited to data supplied through application for individual agents, rather should look across the market.

The College is supportive of PBAC undertaking a cost-effectiveness analysis in which the PBS restrictions are expanded to include:

- Failure of two of four prior treatments (phototherapy, methotrexate, cyclosporine, acetritin); or failure of two or three prior treatments (phototherapy, methotrexate, acetritin)
- PASI >10 and/or DLQI >10
- Involvement of genital, scalp, nail and palms/soles.

These amendments align with ACD's consensus statement on treatment goals for psoriasis and in the view of the College, there is insufficient additional clinical evidence described in this review which would argue against this expansion. However as highlighted above, there are concerns around prevalence overestimates which may skew cost-effectiveness outcomes. The College looks forward to the opportunity to provide comment on cost utility modelling inputs prior to the commencement of the analysis to address ToR 4.