AstraZeneca welcomes the opportunity to provide comments on the draft Terms of Reference for the Post-Market Review of medicines to treat chronic obstructive pulmonary disease (COPD).

COPD is a serious long-term condition that affects over 5% of people aged over 55 years of age. In addition to distressing respiratory symptoms such as shortness of breath, cough and wheeze, it is associated with co-morbidities such as cardiovascular disease and diabetes mellitus. The treatment of a patient with COPD should be multidisciplinary and holistic, with the principal goals of therapy to stop smoking, to optimise function through symptom relief with medications and pulmonary rehabilitation, and to prevent or treat aggravating factors and complications.

An MBS item for pulmonary rehabilitation and pulmonary maintenance exercise is currently being considered by the MSAC which would be a welcome additional treatment option for COPD patients. One of the proposed inclusion criteria for the pulmonary rehabilitation service is that a patient's pharmacotherapy is optimised. Therefore, it is important that clinicians can access COPD medicines in a clinically-appropriate manner, to ensure their patients have the best opportunity to manage their disease holistically with a combination of medication and pulmonary rehabilitation services.

The draft Terms of Reference are each addressed below.

1. *Compare the prescribing restrictions for PBS-listed COPD medicines for consistency with the current clinical guidelines*

There is an inconsistency in regard to the list of medicines to be included in the review. Specifically, the single-agent LABAs are not included in the list, and the single-agent ICS are in the list. Yet neither of these are indicated for COPD despite both being included in local treatment guidelines. It may be beneficial to either include both classes in the review or exclude both classes.

The PBAC may want to consider including antibiotics to the list of relevant COPD medications. Antibiotics have a role to play in the treatment of some exacerbations of COPD.

2. *Review the clinical outcomes that are most important or clinically relevant to people with COPD and the extent to which these outcomes are included in the evidence previously provided to PBAC on the cost-effectiveness of these medicines*

No comment.

3. *Review the published literature on the efficacy and safety of monotherapy and combinations of LABA/ LAMA, ICS/ LABA and LAMA + ICS/ LABA (separate items or fixed dose combinations) for treatment of COPD*

The PBAC should note there is a large volume of clinical data for these treatments across a range of COPD severities and any review needs to allow ample time to ensure proper collation and interpretation.

4. *Review the published literature on the safety of prolonged (> 6 weeks) ICS use for COPD that PBAC has not previously considered.*

It is unclear why prolonged ICS use is specified as > 6 weeks in this ToR. The Australian clinical guidelines do not recommend use of ICS for a specified period of time, either as monotherapy or as a fixed dose combination with LABA.

It should be clarified if ICS in combination with LABA will be reviewed separately to ICS alone under this ToR.

5. *Analyse the current utilisation of PBS listed COPD medicines to identify the extent of co-prescribing and use that is inconsistent with clinical guidelines and/or PBS restrictions. Evaluate if the current utilisation of multiple therapies and the latest evidence relating to safety and efficacy justifies a review of cost-effectiveness for some or all medicines indicated for COPD.*

The first LAMA/ LABA fixed-dose combination was listed on the PBS 1 November 2014, with a second one listed 1 December 2014 and two more receiving positive recommendations at the July 2015 PBAC meeting. Any utilisation review conducted before 24 months of data is available for all four LAMA/ LABA agents is likely to misrepresent the longer-term pattern of use of these medicines.

Other comments

The PBAC may wish to consider an additional ToR to identify effective interventions that result in improvement of prescribing and quality use of medicines for COPD. This may be particularly relevant in an environment where there are several recent new treatment options and more anticipated, including biologic agents. A similar ToR was included in the review of asthma medicines for children.