Ivax Pharmaceuticals UK

Sponsor Submission to the National Institute for Health and Clinical Excellence

Clinical and cost-effectiveness of QVAR for the treatment of chronic asthma in adults and children aged 12-years and over

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IVAX

EXECUTIVE SUMMARY

Background

- Asthma is a complex chronic disease of the airways resulting in symptoms including cough, wheeze and breathlessness. It is estimated that over 4.6 million people suffer from asthma in England and Wales. The prevalence of asthma is increasing, leading to an increased burden from the condition on healthcare resources.
- In recent years there have been large increases in both general practice consultations and hospital admissions relating to asthma. It has been estimated that asthma costs the National Health Service (NHS) more than £889 million each year. The largest component of this cost is attributable to asthma medication.
- Current management guidelines produced by the British Thoracic Society (BTS) and Scottish Intercollegiate Guidelines Network (SIGN) recommend that inhaled corticosteroids (ICS) are used in patients requiring regular preventer therapy (Step 2).
- Beclometasone dipropionate (BDP) is an ICS that has a proven track record of efficacy and safety. In the UK it is most commonly delivered via a CFC-propelled metered dose inhaler (MDI). However, as a result of international concern with regards to the effects of CFCs on the environment, and in accordance with the Montreal Protocol (which the UK government has ratified) the production of CFCs is to be phased out over the next few years.
- BDP formulations that require delivery via CFCs are currently considered essential medicines but can be replaced when two alternative independent CFC-free products are available. Although the UK has ratified the Montreal Protocol, it remains one of the few European countries that have not yet adopted these recommendations. However, since two commercially licensed CFC-free products are now available, it is likely that CFC-BDP will no longer be deemed as essential and manufacturing allocations will be reduced accordingly until final phase out has been achieved.
- QVAR® is a CFC-free formulation of BDP with hydrofluoroalkane (HFA) as propellant that was developed to facilitate the phasing out of CFCs. In this submission it will be termed QVAR to differentiate it from other HFA-BDP since the formulation, dose administration and clinical benefits are different to other products that will be available.
- The average particle size of QVAR is approximately one quarter that of CFC-BDP and other currently licensed formulations of HFA-BDP. This results in a higher proportion of the drug being deposited in the lungs, and QVAR having an equivalent therapeutic effect at about half the daily dose of CFC-BDP.
- QVAR is available in a range of inhaler devices: an MDI (as recommended by the BTS/SIGN guidelines) and the breath-actuated inhalers, Autohaler and Easi-Breathe. The Easi-Breathe breath-actuated inhaler was developed to aid patient coordination by actuating during inhalation without the need for simultaneous manual firing of the inhaler. Studies show that patients find the Easi-Breathe easier to use than standard metered dose inhalers and they prefer it.

Clinical effectiveness

- BDP is an effective treatment for asthma. Cochrane collaboration meta-analyses suggest BDP has comparable efficacy to the same dose of budesonide, and half the daily dose of fluticasone propionate in terms of some of the outcomes measured.
- It is important that QVAR is dosed at the correct ratio compared to the other ICS:

QVAR : BDP	1:2
QVAR : fluticasone propionate	1:1
QVAR : budesonide	1:2

- QVAR is at least as effective as BDP when given at half the daily dose, in terms of a range of pulmonary function outcomes (forced expiratory volume in 1 second [FEV_1], forced vital capacity [FVC], morning peak expiratory flow rate [am PEF], evening peak expiratory flow rate [pm PEF], and forced expiratory flow between the 25% and 75% forced vital capacity levels [$FEF_{25–75\%}$]). In addition, patients treated with QVAR showed greater improvements in some of the patient-reported outcomes such as days without cough and the percentage of symptom-free days.
- In terms of a range of efficacy parameters (am PEF, pm PEF, FEV_1, asthma symptoms, β_2-agonist use), QVAR is at least as effective as twice the dose of budesonide. In one study, patients treated with QVAR had significantly greater changes from baseline than those treated with double doses of budesonide in the percentage of days free from wheeze, shortness of breath, chest tightness and daily asthma symptoms after 8 weeks of treatment.
- QVAR is at least as effective as fluticasone at the same daily dose. A Cochrane meta-analysis found that lung function was not significantly different between QVAR and the same dose of fluticasone in patients with moderate to severe asthma. Clinical trials also suggest that QVAR is at least as effective as fluticasone at the same dose, in improving patient-reported outcomes, such as cough, shortness of breath, chest tightness and nights without sleep disturbance.
- Improvements in quality of life (QoL) are similar in patients treated with QVAR as those treated with BDP and fluticasone. In one large, long-term study improvements from baseline in the overall Asthma Quality of Life Questionnaire (AQLQ) were consistently higher for QVAR than BDP and this difference reached statistical significance at month 12.
- The BTS/SIGN guidelines recommend prescribing the lowest effective ICS dose. At half the conventional BDP dose, QVAR represents an important therapeutic advantage for asthma patients and their physicians who seek improvements in symptom relief with a favourable safety profile.

Cost-effectiveness

- A number of published studies suggest that the treatment of chronic asthma with ICS is cost-effective. The relative cost-effectiveness of different ICS varies between analyses.
- Three published cost-effectiveness analyses compare QVAR with alternative treatments from a UK NHS perspective.
- Results suggest that QVAR is more cost-effective than BDP in terms of symptom-free days. In a population with stable asthma, QVAR resulted in

more symptom-free days at reduced cost, making it the dominant treatment strategy. In addition, the cost of QVAR to achieve a clinically significant improvement in health-related QoL was approximately half that for BDP (£13.24 per week vs £29.38 per week, respectively).

- This suggests that switching patients away from CFC-propelled ICS, in accordance with the Montreal Protocol, can be achieved with some improvements in efficacy and without a significant increase in costs to the NHS.
- QVAR provides similar improvements to fluticasone propionate in the percentage of symptom-free days, at a lower total healthcare cost and appears to be more cost-effective in patients with poorly controlled moderate to severe asthma.
- QVAR provides significantly greater improvements than budesonide, in the percentage of symptom-free days, at a lower total healthcare cost.
- QVAR is therefore a dominant strategy in the treatment of patients with asthma.
- This suggests that in the transition away from CFC inhalation devices, QVAR is both a clinically effective and cost-effective option when compared with the alternatives currently available.

Implications for the NHS

- Recent data for England and Wales suggest that the prevalence of asthma is around 4.6 million.
- BDP is the current mainstay of ICS therapy for asthma: approximately 77% of those patients who are prescribed an ICS receive BDP of which around 15% of these are prescribed QVAR. At the time of the enactment of the Montreal Protocol, when CFC-based BDP will no longer be manufactured, only HFA based alternatives will be available.
- At the time of the withdrawal of CFC-based BDP, a total switch to QVAR would result in only a modest 6% cost increase.
- However QVAR would result in an overall cost saving if it is substituted for more costly ICS alternatives such as products containing fluticasone propionate and budesonide.