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# Health Technology Assessment of Respiratory Biologics: Highlighting the Differences in Value Assessment of Asthma Interventions Globally

**Reductions in asthma exacerbations and CS use** are the **primary clinical decision drivers for HTAs** when considering **reimbursement of biologic therapies** for asthma

Digital poster

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## Background

- Asthma is a widespread chronic condition, affecting the QoL of millions of patients globally and posing a significant economic burden[1]
- Inadequate resolution of chronic airway inflammation in asthma contributes to poor symptom control, unpredictable exacerbations and declining lung function[2]
- Patients with uncontrolled severe asthma are often treated with recurrent OCS bursts; however, they are associated with adverse outcomes[3]
- Biologic therapies have emerged as an important treatment option for patients with severe asthma, particularly those who respond inadequately to conventional therapies, and have been shown to reduce exacerbations and OCS use, and improve QoL and lung function[4]
- However, despite their clinical potential, there are considerable challenges related to market access, with variations in regulatory approval, HTA decisions and reimbursement criteria across different countries
- Understanding the market access landscape for biologics in asthma and regional variations in decision making will help to better align clinical trial outcomes with payer expectations to ensure timely access to innovative treatments for patients and maximise the therapeutic impact of biologics in a real-world setting

## Aims

To evaluate and highlight differences in the value placed on clinical and economic evidence provided to HTA bodies, used to gain reimbursement

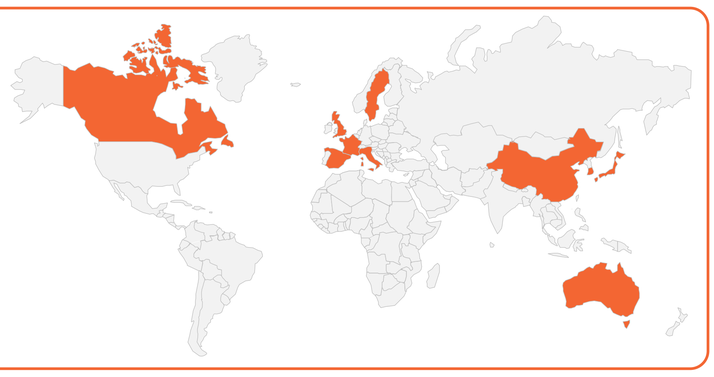
## Methods

GSK ID 222239: Study design

National HTA decisions from 2009 to 2024 for biologics for asthma were extracted from the Clarivate Context Matters Market Access platform*

**Biologics of interest:**
Benralizumab
Dupilumab
Mepolizumab
Omalizumab
Reslizumab
Tezepelumab

**HTAs of interest:**
Australia (PBAC)
Canada (CADTH)
China (NHSA)
England (NICE)
France (HAS)
Germany (G-BA)
Italy (AIFA)
Japan (CHUIKYO)
Scotland (SMC)
South Korea (HIRA)
Spain (AEMPS)
Sweden (TLV)



*Documents preceding 2009 and some regional HTA documents were obtained manually from appropriate websites

**Key areas of focus**

| | |
|---|---|
| Regulatory approvals | Regulatory approval status for all biologics and label differences highlighted between markets (where applicable) |
| HTA evaluations | Reimbursement recommendations and benefit rating (where relevant) for all in-scope biologics in all countries of interest (where available) |
| Restrictions applied | Reimbursement restrictions applied by HTA agencies for in-scope biologics |
| Clinical decision drivers | Key clinical results that influenced reimbursement decisions |
| Outcomes measures | Clinical trial outcomes measures cited in HTA evaluations |
| PROs | PROs and clinical outcomes assessments mentioned in HTA evaluations |

## Results

Table 1: **In total, 131 HTA decisions across 12 countries were included in the assessment**

| Market | Australia | Canada | China | England | France | Germany | Italy | Japan | Scotland | South Korea | Spain | Sweden | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Agency | PBAC | CADTH | NHSA | NICE | HAS | G-BA | AIFA | CHUIKYO | SMC | HIRA | AEMPS | TLV | |
| Benralizumab | 4 | 2 | 0 | 1 | 2 | 2 | 1 | 1 | 1 | 0 | 1 | 1 | 16 |
| Dupilumab | 1 | 2 | 0 | 1 | 3 | 4 | 1 | 1 | 2 | 0 | 2 | 4 | 21 |
| Mepolizumab | 9 | 2 | 1 | 2 | 5 | 3 | 2 | 2 | 2 | 2 | 2 | 4 | 36 |
| Omalizumab | 9 | 2 | 2 | 3 | 3 | 0 | 2 | 1 | 3 | 10 | 2 | 1 | 38 |
| Reslizumab | 0 | 2 | 0 | 1 | 2 | 2 | 1 | 0 | 1 | 0 | 1 | 0 | 10 |
| Tezepelumab | 0 | 1 | 0 | 1 | 1 | 2 | 1 | 1 | 1 | 0 | 1 | 1 | 10 |
| Total | 23 | 11 | 3 | 9 | 16 | 13 | 8 | 6 | 10 | 12 | 9 | 11 | 131 |

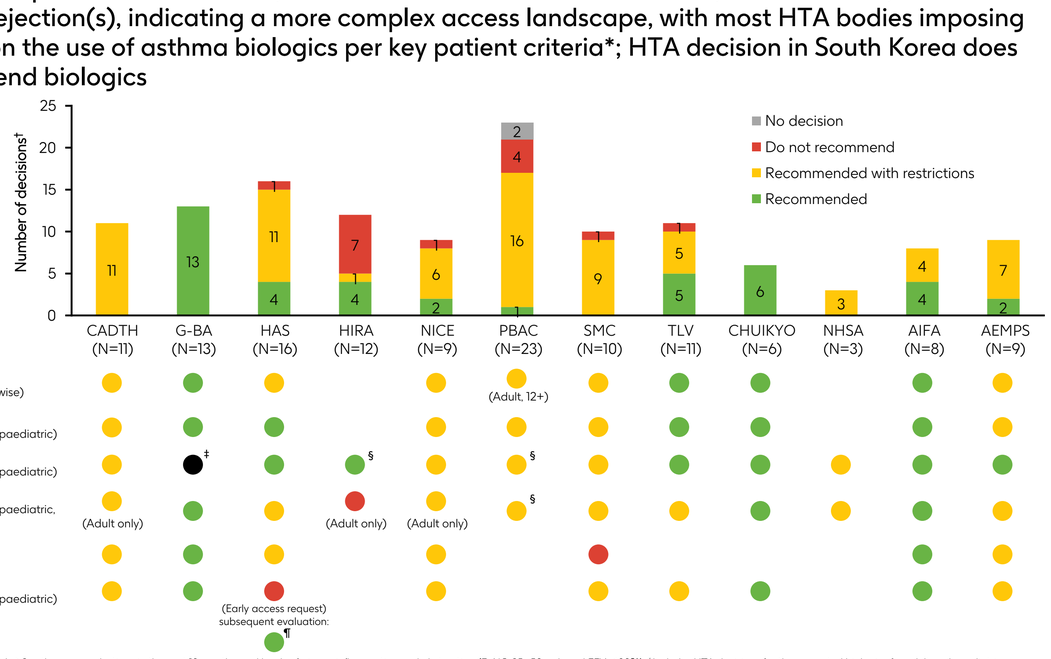
*Note:* *G-BA decisions for omalizumab prior to AMNOG (2010) were not included in the analysis*

Table 2: **Regulatory approvals for asthma*: Biologics with asthma regulatory approvals are mostly labelled as add-on maintenance treatments in adult and paediatric patients with disease inadequately controlled by conventional therapies (e.g. OCS) and/or LABA**

| Drug | FDA | EMA | MHRA | HC | TGA | MFDS | PMDA | NHSA |
|---|---|---|---|---|---|---|---|---|
| Omalizumab | Jun 2003† Jul 2016‡ | Oct 2005† Jul 2009‡ | Oct 2005† Jul 2009‡ | Nov 2004† Apr 2017‡ | Jul 2015† Feb 2016‡ | May 2007‡ | Jan 2009§ Aug 2013‡ | Aug 2017† |
| Mepolizumab | Nov 2015† Sep 2019‡ | Dec 2015§ Aug 2018‡ | Dec 2015§ Aug 2018‡ | Dec 2015§ Mar 2020‡ | Feb 2016† Feb 2020‡ | Mar 2016§ | Mar 2016† Feb 2020‡ | Dec 2023† |
| Reslizumab | Mar 2016§ | Aug 2016§ | Aug 2016§ | Jul 2016§ | Jul 2017§ | Sep 2017§ | | |
| Benralizumab | Nov 2017† | Jan 2018§ | Jan 2018§ | Feb 2018§ | Apr 2018† | Jun 2019§ | Jan 2018 | |
| Dupilumab | Oct 2018† Oct 2021‡ | May 2019† Apr 2022‡ | May 2019† Jul 2022‡ | Nov 2020† | May 2019† | Jun 2020† | Mar 2019 | |
| Tezepelumab | Dec 2021† | Sep 2022† | Sep 2022† | Oct 2022† | | | Sep 2022 | |

*Up to Dec 2023; †Represents ≥12 years of age; ‡Represents ≥6 years of age; §Represents ≥18 years of age

Figure 1: **Most decisions for reimbursement have recommended the use of biologics for adult and paediatric patients with asthma, either with or without restrictions and, in some cases, after initial rejection(s), indicating a more complex access landscape, with most HTA bodies imposing restrictions on the use of asthma biologics per key patient criteria*; HTA decision in South Korea does not recommend biologics**




*Including BEC 150–500 cells/μL, ≥2 asthma exacerbations in the past 12 months, and levels of airway inflammation and obstruction (FeNO 25–50 ppb and $FEV_1$ ≤80%); †Includes HTA decisions for the presented biologics for adult and paediatric populations, where relevant. In some cases, other factors are contributing to the total number of evaluations exceeding the number of drugs (e.g. some biologics had an initial submission and a resubmission); ‡The original omalizumab approval pre-dates AMNOG implementation, thus there is no G-BA early benefit assessment documentation; §Drug was initially rejected before receiving reimbursement approval; ¶The original early access request for tezepelumab was rejected due to insufficient evidence. However, the drug was recently evaluated in France with a positive reimbursement decision for adults and adolescents

Figure 2: **The most commonly cited outcome measures reported across HTA decisions were asthma exacerbations, patient QoL and OCS use**

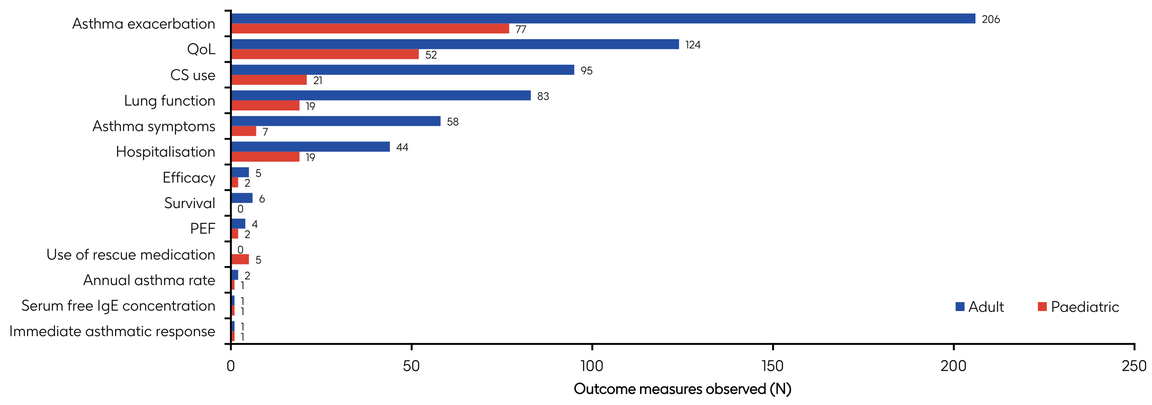
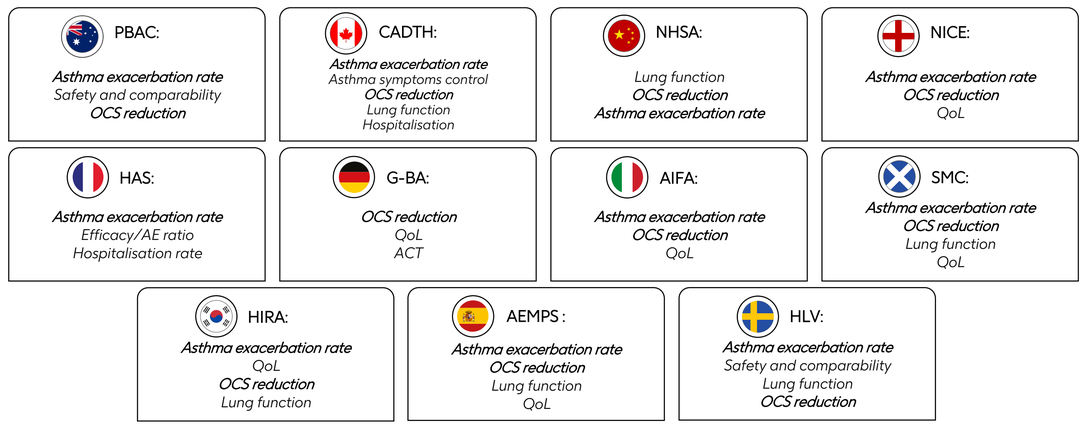



Figure 3: **Clinical decision drivers cited across all HTAs were asthma exacerbation rates (see note on Germany*) and reduction in OCS (except France); lung function, hospitalisation, asthma symptom control, QoL and safety were considered supporting clinical decision drivers**




*Note:* *Most widely reported clinical decision drivers across HTA agencies are highlighted in bold*
*In some circumstances (e.g. for benralizumab), the G-BA evaluation considered trial data where the clinical endpoint for asthma exacerbations was operationalised as a worsening of asthma symptoms that resulted in administration of OCS (or an increase in the dose of existing OCS therapy) for ≥3 days, a visit to an ER requiring treatment with OCS, or hospitalisation for asthma. Additionally, G-BA cited a lack of evaluable data (e.g. related to exacerbations) for some biologic studies due to misalignment with the agency's preferred active comparator*

Figure 4: **Asthma exacerbation reduction was cited as a clinical decision driver for all biologics; OCS reduction and improved lung function were also frequently listed as clinical decision drivers across biologics**

| Biologic | Top clinical decision drivers cited in descending order based on the number of mentions |
|---|---|
| Benralizumab | **Reduction in asthma exacerbations; OCS reduction**; PRO; QoL |
| Dupilumab | **Change from baseline in $FEV_1$; annualised event rate of severe asthma exacerbations**; PRO; QoL |
| Mepolizumab | **Reduction in steroid use;** reduction in asthma exacerbations |
| Omalizumab | **Reduction in asthma exacerbations;** reduction in hospitalisation/ER visits; change from baseline in $FEV_1$ |
| Reslizumab | **Reduction in asthma exacerbations**; improved lung function |
| Tezepelumab | **Reduction in asthma exacerbations; improved lung function**; OCS reduction; PRO; QoL |

*Note:* *Top clinical decision drivers cited per biologic are highlighted in bold*

## Conclusions

- These findings show that **most HTA decisions recommended biologics for the treatment of asthma**, with or without restrictions; China, Italy and South Korea have conducted fewer HTAs for biologics compared with other countries, perhaps due to stricter regulatory frameworks, variations in healthcare priorities, or cost-effectiveness concerns in these regions
- The **most valued clinical decision drivers across HTAs were reductions in asthma exacerbations** (see note for Germany*) **and OCS use** (except in France)
- **QoL and PROs were reported as an outcome** across HTAs except Australia, Canada, China, France and Sweden
- These results can **guide evidence-generation strategies**, aiding in reimbursement and optimising outcomes for biologics in asthma

*In some circumstances (e.g. for benralizumab), the G-BA evaluation considered trial data where the clinical endpoint for asthma exacerbations was operationalised as a worsening of asthma symptoms that resulted in administration of OCS (or an increase in the dose of existing OCS therapy) for ≥3 days, a visit to an emergency room requiring treatment with OCS, or hospitalisation for asthma. Additionally, G-BA cited a lack of evaluable data (e.g. related to exacerbations) for some biologic studies due to misalignment with the agency's preferred active comparator*

## Abbreviations

ACT, appropriate comparator treatment; AE, adverse event; AEMPS, *Agencia Española de Medicamentos y Productos Sanitarios* (Spanish Agency for Medicines and Medical Devices); AIFA, *Agenzia Italiana del Farmaco* (Italian Medicines Agency); AMNOG, Arzneimittelmarkt-Neorudnungsgesetz; BEC, blood eosinophil count; CADTH, Canadian Agency for Drugs and Technologies in Health; CHUIKYO, Central Social Insurance Medical Council; EMA, European Medicines Agency; CS, corticosteroid; ER, emergency room; FDA, Food and Drug Administration; FeNO, fractional exhaled nitric oxide; $FEV_1$, forced expiratory volume in 1 second; G-BA, Federal Joint Committee; HAS, *Haute Autorité de Santé* (High Authority for Health); HC, Health Canada; HIRA, Health Insurance Review and Assessment Service; HTA, Health Technology Assessment; IgE, immunoglobulin E; LABA, long-acting $\beta_2$-agonist; MHRA, Medicines and Healthcare products Regulatory Agency; MFDS, Ministry of Food and Drug Safety; NHSA, National Healthcare Security Administration; NICE, National Institute for Health and Care Excellence; OCS, oral corticosteroid; PBAC, Pharmaceutical Benefits Advisory Committee; PEF, peak expiratory flow; PMDA, Pharmaceuticals and Medical Devices Agency; ppb, parts per billion; PRO, patient-reported outcome; QoL, quality of life; SMC, Scottish Medicine Consortium; TGA, Therapeutic Goods Administration; TLV, *Tandvårds-OCH & läkemedelsförmånsverket* (Dental and Pharmaceutical Benefits Agency).

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## Disclosures

**WA** and **KH** are employed by GSK and hold financial equities in GSK. **PL**, **JC** and **LD** are employees of Clarivate Analytics, which received funding from GSK to conduct this analysis.



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