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Evaluation of Health Technology Assessment Decisions and Outcomes Landscape for Biologic Therapies in Chronic Rhinosinusitis with Nasal Polyps

Improvements in **key clinical outcomes**, such as NP score and nasal obstruction, are the primary **clinical decision drivers** for HTA when considering reimbursement of biologic therapies for CRSwNP

Digital poster

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Background

- CRSwNP is a chronic inflammatory disease of the nasal mucosa and paranasal sinuses, mainly caused by the presence of type 2 inflammation; patients with CRSwNP experience an underappreciated disease burden, negatively impacting their QoL and mental health[1,2]
- Identifying patients at a high risk of disease recurrence and appropriately referring and managing them are essential steps to prevent further disease progression and tissue damage[2]
- The current treatment paradigm involves corticosteroids and/or sinonasal surgery; however, these options may be associated with AEs and complications, as well as the recurrence of NP, especially in patients with comorbid type 2 inflammatory diseases.[1] This highlights the need for new effective therapies[2]
- Biologics have emerged as a promising treatment option for patients with CRSwNP, reducing the need for corticosteroids and surgery and improving patient outcomes[3]
- However, the clinical efficacy and cost effectiveness of biologics are assessed differently by various HTA bodies, necessitating a comprehensive evaluation to guide future evidence generation to support broader access and more consistent treatment approaches

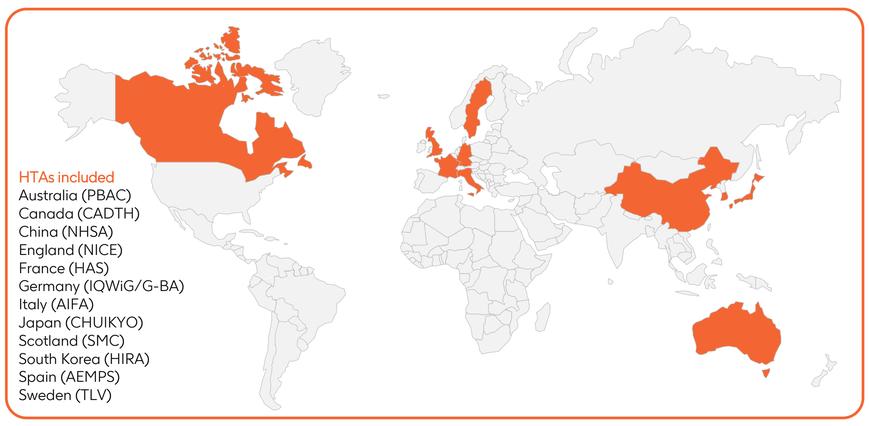
Aims

- To evaluate submissions and HTA decisions for biologic therapies for patients with CRSwNP
- To understand differences in clinical value and clinical decision drivers across HTA bodies and inform future evidence generation

Methods

Data extracted from HTA decisions for biologics for CRSwNP therapy published between 2009 and 2024

Biologics included
Dupilumab
Mepolizumab
Omalizumab
Tezepelumab



Data were extracted by authors from the Cortellis Context Matters HTA tracking database combined with hand-searching HTA bodies to ensure all decision documents were captured and up to date. Extraction and analysis were quality checked by senior Clarivate team members

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 trials' outcomes measures cited in HTA evaluations
PROs	PROs and clinical outcomes assessments mentioned in HTA evaluations

Results

Table 1: **In total, 13 HTA decisions across seven countries were included in the assessment***

Market	England	Scotland	France	Germany	Italy	Spain	Sweden	Canada	Australia	South Korea	Japan	China	Total
Agency	NICE	SMC	HAS	G-BA	AIFA	AEMPS	TLV	CADTH	PBAC	HIRA	CHUIKYO	NHSA	
Dupilumab	0	0	1	1	1	1	0	0	0	0	1	0	5
Mepolizumab	0	0	1	1	1	1	0	1	2†	0	0	0	7
Omalizumab	0	0	0	0	1	0	0	0	0	0	0	0	1
Total	0	0	2	2	3	2	0	1	2	0	1	0	13

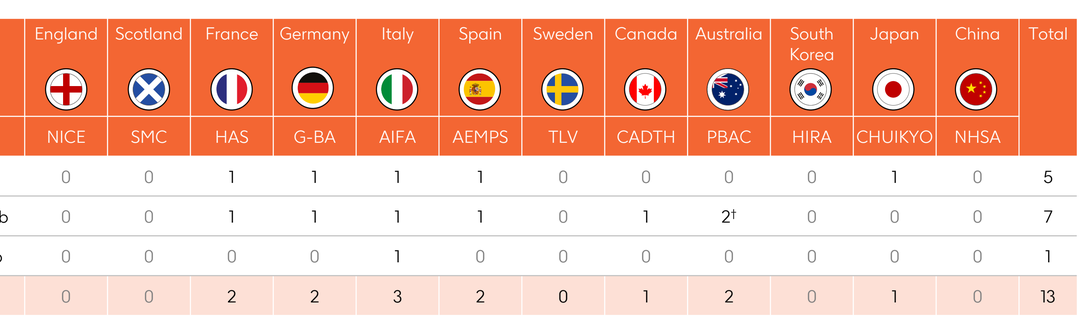
**No relevant HTA decisions were identified for tezepelumab; †Includes both the initial mepolizumab PBAC submission (negative recommendation in 2021) and the resubmission to PBAC (positive recommendation with restrictions in 2022)*

Table 2: **Regulatory approvals for CRSwNP: Biologics with CRSwNP regulatory approvals are authorised as add-on maintenance treatment for the adult population (≥18 years of age) with an inadequate response to nasal corticosteroids and/or surgery***

Biologic†	England	Scotland	France	Germany	Italy	Spain	Sweden	Canada	Australia	South Korea	Japan	China
	MHRA	EMA	EMA	EMA	EMA	EMA	EMA	HC	TGA	MFDS	PMDA	NMPA
Dupilumab	✓ 19/09/2019	✓ 19/09/2019	✓ 19/09/2019	✓ 19/09/2019	✓ 19/09/2019	✓ 19/09/2019	✓ 19/09/2019	✓ 12/08/2020	✓ 13/08/2021	✓ March 2021	✓ 25/03/2020	
Mepolizumab	✓ 16/09/2021	✓ 16/09/2021	✓ 16/09/2021	✓ 16/09/2021	✓ 16/09/2021	✓ 16/09/2021	✓ 16/09/2021	✓ 05/11/2021	✓ 11/01/2022		Awaiting approval‡	
Omalizumab	✓ 25/06/2020	✓ 25/06/2020	✓ 25/06/2020	✓ 25/06/2020	✓ 25/06/2020	✓ 25/06/2020	✓ 25/06/2020	✓ 19/07/2021	✓ 12/03/2021	✓ April 2021		

**Up to March 2024; †No relevant HTA decisions were identified for tezepelumab; ‡At the time of analysis, it was since approved in August 2024[4]*

Figure 1: **The majority of decisions for reimbursement have recommended the use of biologics for patients with CRSwNP, either with or without restrictions**



**Decision made pre-AMNOG so no benefit assessment exists; †Includes both the initial mepolizumab PBAC submission (negative recommendation in 2021) and the resubmission to PBAC (positive recommendation with restrictions in 2022)*

Figure 2: **The most commonly cited clinical decision drivers of HTA decisions (presented most to least common) were impacts on QoL (favourable or net), improvement in NP score, and relief of nasal obstruction and related symptoms. Reduced time to or need for surgery and/or corticosteroid use were cited as additional meaningful clinical decision drivers by G-BA, HAS and PBAC. A serious AE occurrence rate of ≤10% was also strongly considered in HTA decisions**

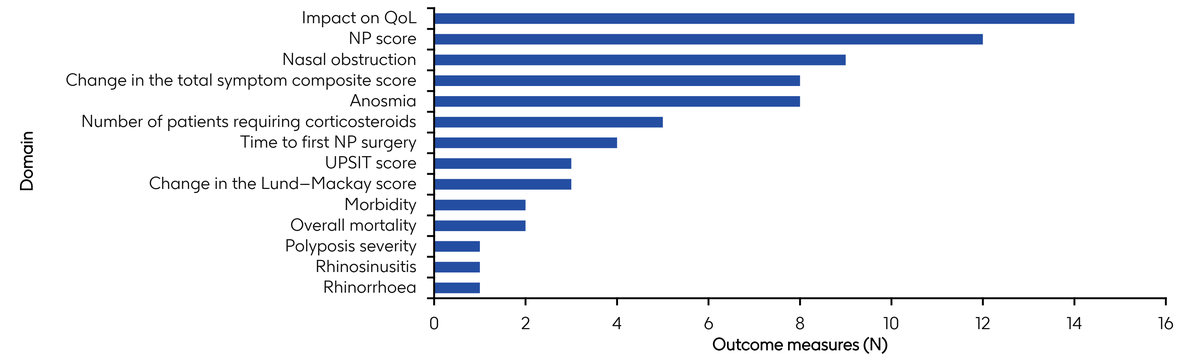


Table 3: **Improvement in NP score and nasal obstruction were the most common clinical decision drivers for dupilumab and mepolizumab; reduced corticosteroid use and time to first NP surgery were also commonly cited for mepolizumab. NP improvement was the main clinical decision driver for omalizumab. PROs were also common clinical decision drivers, with SNOT-22 the preferred measure; EQ-5D and SF-36 were also mentioned as exploratory endpoints**

Outcomes	Dupilumab		Mepolizumab	Omalizumab	
	SINUS-24	SINUS-52	SYNAPSE	POLYP 1	POLYP 2
Clinical efficacy					
NP score	●*	●*	●*	●*	
Nasal obstruction improvement	●*	●*	●*		
Anosmia improvement	●*	●*	●*		
Polyposis severity improvement			●*		
Reduction in corticosteroids and other interventions (e.g. surgery)			●*		
Total symptom composite score improvement	●*	●*	●*		
Rhinorrhoea	●*	●*			
Rhinosinusitis	●*	●*			
Change in Lund–Mackay score	●*				
PROs					
SNOT-22	●*	●*	●*	●*	
EQ-5D	●*	●*			
SF-36			●*		

**Represents a statistically significant difference between intervention and comparator. ● Represents the primary outcome reported in the study; ● Represents the secondary outcome reported in the study*

Conclusions

- While improvements in QoL, NP and nasal obstruction were the most frequently considered clinical decision drivers, the range of outcome measures highlights that **HTA bodies value interventions in CRSwNP differently**, with certain clinical decision drivers being more important to some than others
- The importance of clinical efficacy outcomes such as NP score and nasal obstruction reduction, as well as PROs, underscores the need to emphasise these factors for new biologic therapies for patients with CRSwNP
  - Dupilumab and mepolizumab had more HTA decisions than omalizumab, which correlated with statistically significant differences in the most frequently considered clinical decision drivers for these biologics
- The limitation of this study was that the variables and analyses were dependent on the data available in the regulatory label and/or HTA decision, which are not primarily intended for the purpose of analysing clinical decision drivers
- These findings may help **guide evidence-generation strategies** and data collection on clinical decision drivers which are of most clinical importance to HTA bodies, aiding reimbursement and optimising biologic treatment outcomes for patients with CRSwNP

Abbreviations

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-Neuordnungsgesetz; CADTH, Canadian Agency for Drugs and Technologies in Health; CRSwNP, chronic rhinosinusitis with nasal polyps; CHUIKYO, Central Social Insurance Medical Council; EQ-5D, European Quality of Life-5 Dimension; EMA, European Medicines Agency; 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; IQWiG, Institute for Quality and Efficiency in Health Care; MFDS, Ministry of Food and Drug Safety; MHRA, Medicines and Healthcare products Regulatory Agency; NHSA, National Healthcare Security Administration; NICE, National Institute for Health and Care Excellence; NMPA, National Medical Products Administration; NP, nasal polyp; PBAC, Pharmaceutical Benefits Advisory Committee; PMDA, Pharmaceuticals and Medical Devices Agency; PRO, patient-reported outcome; QoL, quality of life; SF-36, Short-Form 36; SMC, Scottish Medicine Consortium; SNOT-22, Sino-Nasal Outcome Test-22; TGA, Therapeutic Goods Administration; TLV, *Tandvårds-OCH & läkemedelsförmånsverket* (Dental and Pharmaceutical Benefits Agency); UPSIT, The University of Pennsylvania Smell Identification Test.

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Disclosures

WA, RA-C 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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