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HEALTH TECHNOLOGY BRIEFING
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Mepolizumab for chronic rhinosinusitis with nasal polyposis, in addition to standard care

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Developer/Company	GlaxoSmithKline UK Ltd	**UKPS ID**	648707

Licensing and market availability plans	Currently in phase III clinical trials

SUMMARY

Mepolizumab is in development for the treatment of chronic rhinosinusitis with polyposis (polyps) (CRSwNP). Nasal polyps are characterised by oedema (swelling) and accumulation of a type of white blood cell called eosinophils. Nasal polyps cause symptoms such as nasal blockage, loss of smell and rhinorrhoea (frequent runny nose). The cause of CRSwNP is not completely understood, however, it is more common in people with other conditions including asthma. In addition, CRSwNP has been linked to having high levels of a protein called IL-5, which interacts with eosinophils and promotes their development.

Mepolizumab is an antibody that binds to IL-5 to prevent it from interacting with its receptor on the surface of eosinophils. This binding prevents their maturation, differentiation, mobilisation, activation and survival; thereby controls their activity. Mepolziumab is administered subcutaneously. If licenced, mepolizumab will offer an additional treatment option – on top of standard care – for patients with CRSwNP, who frequently suffer from uncontrolled symptoms and disease recurrence.

PROPOSED INDICATION

Treatment of severe, recurrent, bilateral nasal polyps.[1]

TECHNOLOGY

DESCRIPTION

Mepolizumab (Nucala, SB-240563) is a humanized immunoglobulin G1 (IgG1) monoclonal antibody directed against interleukin-5 (IL-5). Upon administration, mepolizumab selectively binds to IL-5, preventing it from associating with interleukin-5 receptor subunit alpha (IL5RA) on the surface of eosinophils (a type of white blood cell) and their progenitors. IL-5 plays a role in the regulation of eosinophil development from haematopoietic progenitors (white blood cell precursors) as well as eosinophil maturation, differentiation, mobilisation, activation, and survival.[2]

Mepolizumab is at phase III clinical trial development (SYNAPSE, NCT03085797) for the treatment of CRSwNP. Participants received a total of thirteen doses of 100mg of mepolizumab via subcutaneous injection every 4 weeks for 52 weeks in addition to standard care - standard care includes daily nasal spray of 400µg mometasone furoate.[1] The results from SYNAPSE met both co-primary endpoints, with mepolizumab, in addition to standard of care, demonstrating statistically significant improvements in both the size of nasal polyps at week 52 and in nasal obstruction during weeks 49-52, compared to placebo added to standard of care.[3]

INNOVATION AND/OR ADVANTAGES

Despite treatment with nasal/oral corticosteroids and endoscopic sinus surgery, many patients with CRSwNP are uncontrolled; the symptoms persist and the disease is recurrent.[4] In addition, There are risks with long-term corticosteroid use and major complications have been reported with sinus surgeries.[4,5] Prominent nasal polyp and mucosal eosinophilia with increased tissue expression of IL-5 have prompted investigators to explore the clinical utility of IL-5–blocking strategies. IL-5 is an important cytokine in eosinophil biology, promoting eosinophil differentiation, chemotaxis, activation, and survival.[6]

There are currently no biological therapies reimbursed in the UK for chronic rhinosinusitis with nasal polyposis.[7] The addition of mepolizumab to current standard therapy with corticosteroids has the potential to reduce nasal polyp size, recurrence, symptoms and the need for surgery. Mepolizumab fulfils an unmet need for patients caught in a cycle of surgeries with limited alternative treatment options.[3]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Mepolizumab is licensed in the UK as an add-on treatment for severe refractory eosinophilic asthma in adults, adolescents and children aged 6 years and older.[8] Common or very common side-effects include: upper abdominal pain; administration related reactions; eczema; fever; headache; hypersensitivity; increased risk of infection; nasal congestion. [9]

Mepolizumab is currently in phase III clinical trials, for chronic obstructive pulmonary disease (COPD) and eosinophilic granulomatosis with polyangiitis.[10-12] Mepoluzumab has received both fast track and orphan drug designations by the US Food and Drug Administration (FDA) and orphan drug designation by the European Medicines Agency (EMA) for hypereosinophilic syndrome (HES).[11,13]

PATIENT GROUP

DISEASE BACKGROUND

Chronic rhinosinusitis (CRS) is characterised by chronic inflammation within the paranasal sinuses, lasting for more than twelve weeks.[14] CRS has been clinically divided into two subgroups: CRS without nasal polyps (CRSsNP) and with nasal polyps (CRSwNP).[14] Patients with CRSwNP represent approximately 20-30% of patients with CRS, however, they have more severe disease and utilise more healthcare resources.[15]

Symptoms experienced by patients with nasal polyps include nasal blockage, loss of smell, rhinorrhoea (continuously runny nose), and symptoms derived from lower airway involvement.[16] CRSwNP is often associated with co-morbidities such as asthma, and aspirin/non-steroidal anti-inflammatory drug exacerbated respiratory disease (AERD).[17] Nasal polyps become more common with increasing age, and the average age of onset is around 42 years.[18] They are more frequently found in men than women, estimated at a 4:1 ratio, but no specific genetic or environmental factors have been strongly linked to the development of this disorder.[15,19]

CLINICAL NEED AND BURDEN OF DISEASE

CRS is one of the most common medical conditions worldwide, reported to affect almost 12% of the adult population.[20] Nasal polyposis commonly occurs as a co-morbidity with other diseases such as asthma or aspirin intolerance. Of patients with polyps, 20-40% have co-existing asthma; they are also associated with aspirin intolerance and cystic fibrosis.[19]

Between 2018 and 2019, the Hospital Episode Statistics (HES) for England recorded a total of 9,302 primary diagnosis cases of nasal polyp (J33.1 to J33.9), 9,204 hospital admissions of which 6,934 were day cases.[21] As for procedures, for the same period in England there were a total of 7,364 functional endoscopic nasal surgeries or procedures (OPCS4 code Y76.2) registered by HES.[22]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

There are no specific treatments for nasal polyps. Polyps have been shown to shrink when nasal sprays or drops containing nasal steroids are used. Stronger steroids in drop form or as a tablet can be used short-term.[19]

Polyps shrink with sprays or drops in 80% of cases. If the polyps persist for 10 weeks or over surgery can be used to help the patient breathe better.[15,19] In three out of four patients the polyps come back after an average period of four years.[19]

CURRENT TREATMENT OPTIONS

Steroid nose drops or a spray to shrink the polyps are usually considered the initial treatment of choice. Patients may receive steroid tablets for up to 2 weeks if the polyps are large, or if the nose drops or sprays did not work.[23]

Mometasone Furoate (50µg) Nasal Spray, suspension is indicated for the treatment of nasal polyps in adults 18 years of age and older.[24]

PLACE OF TECHNOLOGY

If licensed, mepolizumab will offer an add on treatment for patients with CRSwNP.

CLINICAL TRIAL SUMMARY INFORMATION

Trial	SYNAPSE; NCT03085797; EudraCT 2016-004255-70; A Phase 3 Randomised, Triple-blind, Placebo-controlled trial of Mepolizumab Versus Placebo for the Treatment of severe, recurrent, bilateral nasal polyps; Phase III Location: Europe (including the UK), US, Canada and other countries
Trial design	Randomised, Triple-blind, Placebo-controlled
Population	- Population size N=413 (actual) - Severe, bilateral nasal polyps - Adults, 18 years and older
Intervention(s)	- Subcutaneous injection of 100mg mepolizumab plus standard care - Subcutaneous injection of placebo plus standard care
Comparator(s)	Matched placebo
Outcome(s)	- Change from baseline in total endoscopic nasal polyp score at Week 52 - Change from baseline mean nasal obstruction visual analogue scale (VAS) score during the 4 weeks prior to week 52 See trial record for full list of outcomes
Results (efficacy)	See clinical trial record
Results (safety)	See clinical trial record

ESTIMATED COST

Mepolizumab (Nucala) 100mg/1mL solution for injection in vial, pre-filled pen or pre-filled syringes has an NHS indicative price of £840.[9]

RELEVANT GUIDANCE

NICE GUIDANCE

No relevant guidance identified.

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

No relevant guidance identified.

OTHER GUIDANCE

- European Academy of Allergology and Clinical Immunology. European Position Paper on Rhinosinusitis and Nasal Polyps. 2020. [18]
- NHS Tayside Department of ENT. Nasal polyps management. 2017.[25]
- British Society for Allergy and Clinical Immunology (BSACI). BSACI guidelines for the management of rhinosinusitis and nasal polyposis. 2008.[26]

ADDITIONAL INFORMATION

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