

## HEALTH TECHNOLOGY BRIEFING JUNE 2019

### Benralizumab in addition to mometasone furoate for severe nasal polyposis

<b>NIHRIO ID</b>	24095	<b>NICE ID</b>	10146
<b>Developer/Company</b>	AstraZeneca UK Ltd	<b>UKPS ID</b>	Not available

<b>Licensing and market availability plans</b>	Currently in phase III clinical trial.
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### SUMMARY

Benralizumab in addition to mometasone furoate is in development for the treatment of severe nasal polyposis/polyps. Nasal polyps are painless soft growths inside the nose. The exact cause is still unknown but asthma and a bad reaction to aspirin are known to increase the risk of developing the disease. Nasal polyps contain inflammatory fluid and they can be associated with allergy and infection. Nasal polyps are characterised by the accumulation of a certain type of white blood cells called eosinophils. Eosinophils secrete inflammatory proteins including a type called interleukin-5 (IL-5) which play a role in prolonging the survival and migration of eosinophils to the specific tissue sites.

Benralizumab is a monoclonal antibody designed to attach to IL-5 receptors (targets) on the surface of eosinophils which in turn activates the body's natural defence (immune system) to kill eosinophils. Mometasone furoate is a corticosteroid with anti-inflammatory properties used to decrease the size of polyps and to help in the inhibition of eosinophil infiltration into polyp tissue. If licensed, benralizumab in addition to mometasone furoate will offer an additional treatment option for patients with severe nasal polyposis who are still symptomatic despite standard of care therapy.

*This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was unavailable to comment.*

## PROPOSED INDICATION

Adults with severe bilateral nasal polyposis who are still symptomatic despite standard of care therapy.<sup>1</sup>

## TECHNOLOGY

### DESCRIPTION

Benralizumab (Fasenra, MEDI563) is an anti-eosinophil, humanised afucosylated, monoclonal antibody (IgG1, kappa) against interleukin-5 (IL-5) receptor  $\alpha$  that induces direct, rapid, and nearly complete depletion of eosinophils through an apoptotic process involving natural killer cells.<sup>2,3</sup> The increased expression of IL-5 suggests a delay of eosinophil apoptosis and this process contribute to the eosinophilia that has an important role in the pathogenesis of nasal polyps.<sup>4,5</sup>

Benralizumab in addition to mometasone furoate is currently in clinical development for the treatment of severe nasal polyposis. In the phase III clinical trial (NCT03401229; OSTRO), participants with severe bilateral nasal polyposis who are still symptomatic despite standard of care therapy will receive subcutaneous (SC) benralizumab 30 mg in combination with mometasone furoate nasal spray 400 mcg. Benralizumab 30 mg SC will be delivered every 4 weeks for the first 3 doses and every 8 weeks thereafter, with a total of 8 doses. Mometasone furoate nasal spray will be delivered in 2 doses (1 dose = 50 mcg/actuation) in each nostril twice daily and will be used for a minimum of 4 weeks prior to randomization and will be continued throughout the study.<sup>1</sup>

### INNOVATION AND/OR ADVANTAGES

Current treatment options for nasal polyps is steroids given as nose drops or a spray to shrink the polyp. It may also be given as tablets for up to two weeks if the polyps are large and the nose drops and sprays did not work. If there's no sign of improvement after about 10 weeks, patients may have surgery to remove the polyps.<sup>6</sup> 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.<sup>7</sup> IL-5 is an important cytokine in eosinophil biology, promoting eosinophil differentiation, chemotaxis, activation, and survival.<sup>8</sup>

Post-hoc pooled analysis of two Phase III trials concluded that benralizumab demonstrated enhanced clinical efficacy for patients with severe, uncontrolled eosinophilic asthma and nasal polyps.<sup>9</sup>

Benralizumab would be the first biological therapy available for nasal polyposis.<sup>10</sup>

### DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Benralizumab in addition to mometasone furoate does not currently have Marketing Authorization in the EU for any indication.

Currently, benralizumab is licensed in the EU/UK as an add-on maintenance treatment in adult patients with severe eosinophilic asthma inadequately controlled despite high-dose inhaled corticosteroids plus long-acting  $\beta$ -agonists. The most commonly reported adverse reactions during treatment are headache (8%) and pharyngitis (3%). Anaphylactic reactions have been reported.<sup>3</sup>

## PATIENT GROUP

### DISEASE BACKGROUND

Nasal polyps are soft, painless, noncancerous growths on the lining of the nasal passages or sinuses. They hang down like teardrops or grapes.<sup>11</sup> Nasal polyps contain inflammatory fluid and, while they can be associated with allergy and infection, the exact reason why some people get them and not others is not known.<sup>12</sup>

Nasal polyps are histologically characterised by massive oedema and accumulation of eosinophils. Accumulation of eosinophils is the most characteristic feature of nasal polyposis. Eosinophils may contribute to nasal polyp formation and growth not only through inflammation but also by exerting their effects on an extracellular matrix including stimulation of collagen synthesis. Eosinophils can synthesise and secrete several important inflammatory and regulatory cytokines, in particular, TL-3, IL-5 and granulocyte/macrophage colony-stimulating factor (GM-CSF). These cytokines have been shown to prolong eosinophil survival in vitro and to enhance various metabolic functions. They are also involved in the migration of eosinophils toward specific tissue sites.<sup>13</sup>

Certain things can increase the risk of nasal polyps, like asthma and a bad reaction to taking aspirin.<sup>6</sup> Small nasal polyps may not cause symptoms, however, larger nasal polyps or groups of nasal polyps can block the nasal passages and sinuses or lead to breathing problems, a lost sense of smell and frequent infections.<sup>11</sup> Symptoms of nasal polyps include blocked nose, runny nose, constant need to swallow (post-nasal drip), nosebleeds, and snoring.<sup>6</sup>

### CLINICAL NEED AND BURDEN OF DISEASE

Nasal polyps commonly occur in more general diseases such as late-onset asthma in adults, aspirin intolerance or cystic fibrosis.<sup>12</sup> Nasal polyps become more common with age, and the average age of onset is around 42 years. They are more frequently found in men than women.<sup>14</sup>

Between 2017-18 in England, the Hospital Episodes Statistics recorded a total of 10,160 patients with a primary diagnosis of nasal polyp (J33).<sup>15</sup> In 2017-18 there were 5,666 admissions (of which 4,042 were day cases) for polypectomy of the internal nose (ICD-10 code E08.1) in England which resulted in 5,692 finished consultant episodes (FCE) and 1,703 FCE bed days.<sup>15</sup> The surgical revision rate at 5 years for patients with chronic rhinosinusitis with polyps has been reported as 20.6%.<sup>16</sup>

## PATIENT TREATMENT PATHWAY

### TREATMENT PATHWAY

Medical management with topical and possibly systemic corticosteroids is usually considered the initial treatment of choice, with endoscopic sinus surgery reserved for those patients who fail to improve.<sup>6,17</sup>

### 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 nose drops and sprays didn't work.<sup>6</sup>

Mometasone Furoate 50 micrograms/dose Nasal Spray, suspension is indicated for the treatment of nasal polyps in adults 18 years of age and older.<sup>18</sup>

## PLACE OF TECHNOLOGY

If licensed, benralizumab in addition to mometasone furoate will offer an additional treatment option for patients with severe bilateral nasal polyposis who are still symptomatic despite standard of care therapy.

## CLINICAL TRIAL INFORMATION

<b>Trial</b>	OSTRO, <a href="#">NCT03401229</a> , D3252C00001, <a href="#">EudraCT 2017-003675-61</a> ; aged 18-75 years; phase III
<b>Sponsor</b>	AstraZeneca
<b>Status</b>	Ongoing
<b>Source of Information</b>	Trial registry <sup>1,19</sup>
<b>Location</b>	EU countries (not including the UK), USA and Canada
<b>Design</b>	Randomised, placebo-controlled, double-blind study
<b>Participants</b>	N=400 (planned); aged 18-75 years older; Patients with bilateral sinonasal polyposis that, despite treatment with a stable dose of intranasal corticosteroids (INCS) for at least 4 weeks prior to visit 1, in addition to history of treatment with systemic (systemic corticosteroids -oral, parenteral) or prior surgery for nasal polyposis, have severity consistent with a need for surgery.
<b>Schedule</b>	<p>Participants were randomised to one of the treatment arms:</p> <ol style="list-style-type: none"> <li>1. Benralizumab 30 mg SC injection once every 4 weeks for the first 3 doses - weeks 0, 4 and 8 and every 8 weeks thereafter - weeks 16, 24, 32, 40 and 48. Total of 8 doses. Mometasone furoate nasal spray - 2 doses (1 dose = 50 micrograms/actuation) in each nostril twice daily. Total daily dose of mometasone furoate should be 400 mcg and used for a minimum of 4 weeks prior to randomization and will be continued throughout the study.</li> <li>2. SC injection matching placebo once every 4 weeks for the first 3 doses - weeks 0, 4 and 8 and every 8 weeks thereafter - weeks 16, 24, 32, 40 and 48. Total of 8 doses. Mometasone furoate nasal spray - 2 doses (1 dose = 50 micrograms/actuation) in each nostril twice daily. Total daily dose of mometasone furoate should be 400 mcg and used for a minimum of 4 weeks prior to randomization and will be continued throughout the study.</li> </ol>
<b>Follow-up</b>	<p>Treatment duration: 56 weeks</p> <p>Follow up period: 6 months without dosing.</p>
<b>Primary Outcomes</b>	<p>Time frame at 56 weeks:</p> <ul style="list-style-type: none"> <li>• Effect of benralizumab on nasal polyp burden.</li> <li>• Effect of benralizumab on patient-reported nasal blockage.</li> </ul>
<b>Secondary Outcomes</b>	<p>Time frame at 56 weeks (visit 11):</p> <ul style="list-style-type: none"> <li>• Effect of benralizumab on disease specific health-related quality of life (HRQoL).</li> <li>• Effect of benralizumab on nasal polyp surgery.</li> <li>• Proportion of NP surgery.</li> </ul>

	<ul style="list-style-type: none"> <li>• Systemic corticosteroids (SCS) use for relief of nasal symptoms. Proportion of patients with SCS use for NP.</li> <li>• SCS use for relief of nasal symptoms. Time to first SCS course for NP.</li> <li>• Symptoms associated with nasal polyps. Change from baseline in nasal symptom score(s) as captured in the daily diary. Patients report the severity of symptom related to NP at its worst using a 4-point verbal rating scale (0-None to 3-Severe).</li> <li>• Symptoms associated with nasal polyps. Sense of smell captured as change from baseline in University of Pennsylvania Smell Identification Test (UPSIT) score.</li> <li>• Sinus opacification by computed tomography (CT) scan (subset of patients). Change from baseline in Lund Mackay score</li> <li>• Patient-reported general health status.</li> <li>• SCS use for relief of nasal symptoms. Total SCS dose used.</li> <li>• SCS use for relief of nasal symptoms. Number of courses of SCS for NP.</li> <li>• SCS use for relief of nasal symptoms. Total duration of SCS use for NP.</li> <li>• Sinus opacification by computed tomography (CT) scan (subset of patients). Change from baseline in sinus severity score by Quantitative CT analysis.</li> </ul>
<b>Key Results</b>	-
<b>Adverse effects (AEs)</b>	-
<b>Expected reporting date</b>	Estimated primary completion date in September 2020.

## ESTIMATED COST

Benralizumab is already marketed in the UK for the treatment of severe eosinophilic asthma; a pre-filled disposable injection (30 mg per 1 ml) costs £1,955.00.<sup>20</sup>

## RELEVANT GUIDANCE

### NICE GUIDANCE

No relevant guidance identified.

### NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

No relevant guidance identified.

### OTHER GUIDANCE

- British Society for Allergy and Clinical Immunology (BSACI). BSACI guidelines for the management of rhinosinusitis and nasal polyposis. 2008.<sup>21</sup>
- European Academy of Allergology and Clinical Immunology. European Position Paper on Rhinosinusitis and Nasal Polyposis. 2005.<sup>14</sup>

## ADDITIONAL INFORMATION

AstraZeneca UK Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

## REFERENCES

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