Clinical Policy Title:	Mepolizumab
Policy Number:	RxA.600
Drug(s) Applied:	Nucala®
Original Policy Date:	03/06/2020
Last Review Date:	3/1/2024
Line of Business Policy Applies to:	All lines of business

Criteria

I. Initial Approval Criteria

A. Severe Asthma with eosinophilic phenotype (must meet all)**:**

1. Diagnosis of severe asthma;
2. Patient has a baseline blood eosinophil count ≥ 150 cells/mcL within the past 3 months or blood eosinophil count ≥ 300 cells/mcL within the past 12 months;
3. Patient has experienced ≥ 2 exacerbations within the last 12 months, requiring one of the following (a or b):
    a. Systemic corticosteroid treatment;
    b. Asthma related hospital admission;
4. Patient is currently being treated with the following medication, unless there is a contraindication or intolerance (a or b):
    a. High dose inhaled corticosteroid (ICS); and an additional controller medication (e.g., long-acting beta-2 agonist (LABA) or leukotriene modifier (LTRA));
    b. One maximally-dosed combination ICS/LABA product [e.g., Advair (fluticasone propionate/salmeterol), Breo Ellipta (fluticasone/vilanterol)]
5. Prescribed by or in consultation with an allergist/immunologist, or a pulmonologist;

Initial Approval Duration
All Lines of Business (except Medicare): 12 months

B. Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss) (must meet all)**:**

1. Prescribed by or in consultation with a pulmonologist, rheumatologist, immunologist, or nephrologist;
2. Relapsed or is refractory to standard of care therapy (i.e., corticosteroid treatment with or without immunosuppressive therapy)
3. Concurrently prescribed with corticosteroid therapy (e.g. prednisone or prednisolone)

Initial Approval DurationAll Lines of Business (except Medicare): 12 months

C. Chronic rhinosinusitis with nasal polyps (must meet all)**:**

1. Diagnosis of recurrent and symptomatic CRSwNP;
2. Prescribed by or in consultation with an otolaryngologist, pulmonologist, or immunologist;
3. Patient had an inadequate response to at least 8 weeks of nasal corticosteroid therapy, unless contraindicated or clinically significant adverse events are experienced;
4. Nucala® is prescribed concurrently with another agent for CRSwNP, unless contraindicated or clinically

significant adverse events are experienced;

Initial Approval Duration

All Lines of Business (except Medicare): 12 months

D. Hypereosinophilic Syndrome (must meet all)**:**

1. Diagnosis of Hypereosinophilic Syndrome (HES);
2. Prescribed by or in consultation with a pulmonologist, allergist, or immunologist;
3. Other non-hematologic secondary HES are ruled out (e.g., drug hypersensitivity, parasitic helminth infection, HIV infection, non-hematologic malignancy)
4. Patient is FIP1L1-PDGFRα kinase-negative HES;
5. Patient has experienced at least 2 HES flares within the past 12 months;
6. Pre-treatment blood eosinophil count ≥ 1,000 cells/mcL within the past 12 months;
7. Trial and failure, contraindication, or intolerance to corticosteroid therapy (e.g., prednisone) or cytotoxic/immunosuppressive therapy (e.g., hydroxyurea, cyclosporine, imatinib);

Initial Approval Duration

All Lines of Business (except Medicare): 12 months

II. Continued Therapy Approval

A. Severe Asthma (must meet all)**:**

1. Patient is currently receiving or has been treated with this medication within the past 90 days, excluding manufacturer samples;
2. Demonstrated adherence to asthma controller therapy that includes an ICS plus a controller medication, unless there is a contraindication or intolerance;

Approval Duration

All Lines of Business (except Medicare): 12 months

B. Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss); **Chronic rhinosinusitis with nasal polyps**(must meet all):

1. Patient is currently receiving or has been treated with this medication within the past 90 days, excluding manufacturer samples.

Approval Duration

All Lines of Business (except Medicare): 12 months

C. Hypereosinophilic Syndrome (must meet all):

1. Patient is currently receiving or has been treated with this medication within the past 90 days, excluding manufacturer samples;
2. Nucala® is prescribed concurrently with baseline HES therapy (e.g., oral corticosteroids, immunosuppressive therapy).

Approval Duration

All Lines of Business (except Medicare): 12 months

References

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2. Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. N Engl J Med 2014; 371:1198-207. Available at: https://www.nejm.org/doi/full/10.1056/nejmoa1403290. Accessed January 23, 2023.
3. Bel EH, Wenzel SE, Thompson PH, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. New Engl J Med 2014; 371:1189-1197. Available at: https://www.nejm.org/doi/full/10.1056/nejmoa1403291. Accessed January 23, 2023.
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6. Groh M, Pagnoux C, Baldini C, et al. Eosinophilic granulomatosis with polyangiitis (Churg- Strauss) (EGPA) Consensus Task Force recommendations for evaluation and management. Eur J Intern Med. 2015 Sep;26(7):545-53. Available at: https://pubmed.ncbi.nlm.nih.gov/25971154/. Accessed January 24, 2023.
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11. Butt NM, Lambert J, Ali S, et al. Guideline for the investigation and management of eosinophilia. *Br J Haematol*. 2017;176(4):553-572. Available at: https://onlinelibrary.wiley.com/doi/10.1111/bjh.14488. Accessed January 24, 2023.
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13. GlaxoSmithKline. Study 200622: A Randomized, Double-Blind, Placebo-Controlled Study to Investigate the Efficacy and Safety of Mepolizumab in the Treatment of Adolescent and Adult Subjects with Severe Hypereosinophilic Syndrome. Clinicaltrials.gov; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT02836496. Accessed January 24, 2023.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	02/2020	03/06/2020
Policy was reviewed: 1. Clinical policy title was updated 2. Line of business policy applies to was updated to All lines of business	09/23/2020	12/07/2020

3. For Severe Asthma: Dose criteria updated based on age for Initial & continued therapy approval criteria 4. Concurrent therapy criteria added for all indication under both Initial therapy approval & Continued therapy approval criteria 5. Currently receiving medication that has been authorized by RxAdvance..." 6. Appendix B was reviewed and updated 7. Reference reviewed and updated.		
Policy was reviewed: 1. Background was updated to include new indication "CRSwNP", and "HES". 2. Dosing information was updated to new indication (CRSwNP, HES), dosing regimen and max dose information. 3. Dosing information was updated to include Max. dose for indication Severe asthma. 4. Initial Approval Criteria I.A.2 was updated from “Patient has an absolute blood eosinophil count…” to “Patient has a baseline blood eosinophil count…” 5. Initial Approval Criteria I.A.5 was updated from “Patient has experienced ≥ 2 exacerbations with in the last 12 months…” to “Nucala® is prescribed concomitantly…a long-acting beta-2 agonist (LABA) or leukotriene modifier (LTRA)” 6. Initial Approval Criteria I.A.6 was updated from “Nucala® is prescribed concomitantly with an ICS plus either a LABA or LTRA” to “Documentation that Patient has been adherent…for at least 3 months”	10/12/2021	12/07/2021

7. Initial Approval Criteria I.A.7 “Patient has experienced ≥ 2 exacerbations with in the last 12 months..” was inserted. 8. Initial Approval Criteria I.C.7 and I.C.8 “inadequate response..” and “prescribed concurrently…” were added. 9. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 10. Initial and continued approval criteria were updated to include approval criteria for CRSwNP, and HES. 11. Continued Therapy Criteria II.A.1, and II.B.1 were rephrased to "Patient is currently receiving medication that has been authorized by RxAdvance...". 12. Continued Therapy Approval II.B.4 was updated to change dose limit for EGPA from 100 mg every 4 weeks to 300 mg every 4 weeks. 13. Appendix A was updated to include abbreviations for “CRSwNP, HES, NPS, VAS and EULAR”. 14. Appendix B was updated to remove "ciclesonide, fluticasone furoate, salmeterol, mometasone/ formoterol, and fluticasone/ vilanterol" generics as these were not available in US. 15. Appendix B was updated to change dosing regimen for zyflo from 1200 mg orally twice daily to 600 mg orally four times daily. 16. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is		

available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 17. Appendix C was updated to rephrase contraindication as "History of hypersensitivity to mepolizumab or excipients in the formulation." 18. References were reviewed and updated.		
Policy was reviewed: 1. Dosage Forms: Updated to include new dosage form, single-dose prefilled syringe: 40 mg/0.4 mL. 2. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C. 3. References were reviewed and updated.	2/28/2022	4/18/2022
Policy was reviewed: 1. Initial Approval Criteria, I.B.1 Updated diagnosis criteria From Diagnosis of EGPA (Churg-Strauss) to Diagnosis of EGPA (Churg-Strauss) defined as presence of all of the following (a, b, and c): a. Asthma; b. At least 2 of the following characteristics of EGPA: histopathological evidence of eosinophilic vasculitis, perivascular eosinophilic infiltration, or eosinophil-rich granulomatous inflammation; neuropathy; pulmonary infiltrates; sino-nasal abnormality; cardiomyopathy; glomerulonephritis; alveolar	01/24/2023	04/13/2023

hemorrhage; palpable purpura; or antineutrophil cytoplasmic antibody (ANCA) positivity; c. Patient has an absolute blood eosinophil count ≥ 150 cells/mcL within the last 3 months; 2. Initial Approval Criteria, I.B.4: Updated to include new diagnostic criteria Patient meets one of the following (a or b): a. Patient has experienced at least 1 relapse in the past 2 years while receiving a glucocorticoid, which required an increase in glucocorticoid dose, initiation or increase in other immunosuppressive therapy, or hospitalization; b. Patient has refractory disease in the past 6 months, defined as either (i or ii): i. Failure to achieve remission following ≥ 3 month trial of a standard induction regimen (e.g., glucocorticoids, cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil); ii. Recurrence of EGPA symptoms during glucocorticoid dose taper; 3. Initial Approval Criteria, I.D.8: Updated to include new concurrent therapy criteria Nucala is prescribed concurrently with baseline HES therapy (e.g., oral corticosteroids, immunosuppressive therapy); 4. Continued Therapy Criteria, II.D.3: Updated to include new concurrent therapy criteria Nucala is prescribed concurrently		

with baseline HES therapy (e.g., oral corticosteroids, immunosuppressive therapy); 5. Appendix B, Dosing Regimen, methylprednisolone (Medrol): Updated dosing information from 6.0 mg/day to 0.8 mg/kg/day to 4 to 48 mg/day orally, administered in 4 divided doses for indication EGPA. 6. Appendix B, Dosing Regimen, prednisone: Updated dosing information from 7.5 mg/day to 1 mg/kg/day to 5 to 60 mg/day orally in 1 to 4 divided doses for indication EGPA. 7. References were reviewed and updated.		
Policy was reviewed.	10/19/2023	10/19/2023
Policy was reviewed. 1. Updated Severe Asthma indication to specify with eosinophilic phenotype. 2. Updated embedded SSE to add LABA, LTRA, ICS/LABA as step-thru options. 3. Added requirements of concurrent use of CS for Churg-Strauss disease.	3/1/2024	3/1/2024