MEPOLIZUMAB (Nucala®) PROTOCOL FOR THE TREATMENT OF SEVERE REFRACTORY EOSINOPHILIC ASTHMA

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INDICATION FOR USE: [1, 2]

TREATMENT	HSE APPROVED INDICATION	ICD10	Protocol Code
Mepolizumab (Nucala®)	Mepolizumab (Nucala®) is indicated as an add-on treatment for severe refractory eosinophilic asthma in adults over 18 years of age.	J82.83	**RESP001**

TREATMENT: [1]

DRUG	DOSE	ROUTE	CYCLE	DURATION OF THERAPY
Mepolizumab	100 mg	Subcutaneous Injection	Every 4 weeks	Long-term treatment
The need for continued therapy should be considered at least on an annual basis as determined by physician assessment of the patient's disease severity and level of control of exacerbations. Treatment is initiated within hospital, however patients should be transferred to self-administration when their supervising consultant deems it appropriate.				

ELIGIBILITY: [2]

- Confirmed diagnosis of Severe Refractory Eosinophilic Asthma by a respiratory physician, specialising in severe asthma.
- Patient has been fully adherent to maintenance therapy assessed using the following criteria:
  - Adherence to maintenance therapy
  - Inhaler technique assessed AND has the patient been educated on inhaler use.
  - Compliance assessed by 3 consecutive monthly visits to clinical specialist nurse with adherence advice, PEFR diary and reported asthma outcomes.
    OR if performed
  - Patient is adherent with prescribed therapy confirmed by INCA device over 3 months.
- Blood eosinophil count:
  - Greater or equal to 300cells/microlitre (0.3×10^9 per Litre) in the previous 12 months
    OR
  - In patients on longterm maintenance oral corticosteroids (OCS) with an eosinophil count less than 300cells/microlitre (0.3×10^9 per Litre); a pre-OCS eosinophil level should be used to confirm eosinophilic phenotype. (*Concensus recommendation of Severe Asthma Advisory Group)*
- If exacerbation rate:
  - 2 or more exacerbations requiring systemic corticosteroids in the previous 12months
    OR
  - Continuous OCS (greater or equal to 5mg prednisolone daily or equivalent) over the previous 6 months
- The company provides mepolizumab at the commercial in confidence price agreed with the HSE.

NOTE: *In clinical studies for anti-IL5 therapies the extent to which exacerbation rates were reduced increased in patients with higher blood eosinophil levels and with greater exacerbation history.*

CONTRAINDICATIONS: [1]

- Hypersensitivity to mepolizumab or to any of the excipients in the formulation.

EXCLUSIONS FOR FUNDING:

- Patients less than 18 years of age
- Patients treated with omalizumab (Xolair®) within the past year
- Patients who do not meet the eligibility criteria above

STOPPING CRITERIA: [2]

Response to therapy should be reviewed by the treating physician at 3 monthly intervals. A definitive decision to continue therapy should be made at 12 months of treatment based on disease severity and level of exacerbation control:

- Stop anti-IL5 therapy if asthma has not responded adequately to treatment.
- An adequate response is defined as:
    - A clinically meaningful reduction in the number of asthma exacerbations requiring systemic corticosteroids or hospitalisation.
      OR
    - A clinically significant reduction in continuous OCS use while maintaining improved asthma control.

USE WITH CAUTION:

Refer to SmPC for up to date information

TESTS:

Baseline measurements / tests:

- Inhaler technique and compliance
- Blood eosinophil count
- Number of exacerbations in previous 12 months
- Continuous OCS use in previous 6 months
- Smoking status
- IgE

Regular measurements / tests:

- Inhaler technique and compliance
- Smoking status
- Number of GP visits
- Number of exacerbations requiring hospitalisation
- Number of exacerbations requiring hospital visit but not admission

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS: [1]

Dose adjustments are not recommended

Renal and Hepatic Impairment:

No dose adjustment is required for patients with renal or hepatic impairment

SUPPORTIVE CARE: [1]

Pre-medications: None

Take home medications: None

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS: [1]

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details. **This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions.**

Headache: was the most common reported adverse reaction during treatment for severe eosinophilic asthma (20%)

Injection site reactions: was the second most commonly reported adverse effect (8 %)

Back pain: the third most common adverse effect (6%).

Systemic non-allergic administration related reactions: the most common manifestations of systemic non-allergic administration related reactions in the severe eosinophilic asthma studies were rash, flushing and myalgia; these manifestations were reported infrequently and in less than 1 % of patients receiving mepolizumab 100 mg subcutaneously.

OTHER INFORMATION:

- Mepolizumab should not be used to treat acute asthma exacerbations.

Outcome Monitoring & Reporting:

- The clinical trials demonstrated a reduction in clinically significant exacerbations of asthma. In order to measure this in the real world setting the collection of these outcomes is required.
- A data collection form has been provided for assessment of these outcomes at baseline and at each injection visit. HSE funding is dependent on return of these outcomes.
- For doses accessed via the High Tech Hub (HTH), there is no requirement to submit a claim form or outcome data to AHDMP.

Self-administration

- The initial doses of mepolizumab should be administered under the supervision of a trained health care professional in a hospital setting. The patient should be instructed in the subcutaneous injection technique and on how to self-administer during this time.
- After proper training in the subcutaneous injection technique patients should be considered for self-administer mepolizumab with medical follow-up as necessary.
- Where self-administration is deemed appropriate, all prescriptions for community dispensing must be issued through the High Tech Hub (HTH).

- Where self-administration is deemed inappropriate, the patient details and reason to justify continued hospital administration of mepolizumab should be e-mailed to AHDMP@hse.ie to ensure that hospital reimbursement is continued.

DRUG INTERACTIONS:

Current drug interaction databases should be consulted for more information.

ATC CODE:

Mepolizumab R03DX09

REIMBURSEMENT CATEGORY:

Hospital Reimbursement via Rosetta / Community supply reimbursed by the PCRS

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Respiratory physician, within an asthma centre who specialises in severe asthma as outlined by the *Briefing Paper: National Severe Asthma Network 2015 (Sub-group of National Clinical Programme for Respiratory Medicine).*[2]

REFERENCES:

1. Nucala 100mg solution for injection in a pre-filled pen – Summary of Product Characteristics. Available online at:https://www.medicines.ie/medicines/nucala-100-mg-solution-for-injection-in-pre-filled-pen-34929/spc. Accessed 24.02.2022.
2. *Briefing Paper: National Severe Asthma Network 2015 (Sub-group of National Clinical Programme for Respiratory Medicine).*
3. Pavord ID, Korn S, Howarth P, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial. Lancet 2012; 380: 651-9.
4. Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. N Engl J Med 2014; 371: 1198-207.
5. Bel EH, Wenzel SE, Thompson PJ, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. N Engl J Med 2014; 371: 1189-9