Mepolizumab (NUCALA)

National Drug Monograph

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The purpose of VA PBM Services drug monographs is to provide a comprehensive drug review for making formulary decisions. Updates will be made when new clinical data warrant additional formulary discussion. Documents will be placed in the Archive section when the information is deemed to be no longer current.

FDA Approval Information	
Indication(s) Under Review	Mepolizumab is an interleukin-5 antagonist monoclonal antibody indicated for add-on maintenance treatment of patients with severe asthma aged 12 years and older, **and with an eosinophilic phenotype.** Mepolizumab is not indicated for treatment of other eosinophilic conditions or for the relief of acute bronchospasm or status asthmaticus.
Dosage Form(s) Under Review	For subcutaneous injection: 100mg of lyophilized powder in a single-dose vial for reconstitution
REMS	☐ REMS ☒ No REMS *See Other Considerations for additional REMS information*
Pregnancy Rating	Data on pregnancy exposure are insufficient to inform on drug-associated risks. Patients or providers can enroll patients in a registry that monitors pregnancy outcomes in women exposed to mepolizumab during pregnancy

Executive Summary	
Efficacy	• Mepolizumab was FDA approved for add-on maintenance treatment of patients with severe asthma with an eosinophilic phenotype the based upon three pivotal phase III trials • Mepolizumab vs. placebo as add-on to high-dose inhaled corticosteroids plus additional controller drug ± oral corticosteroids was shown to reduce the risk of exacerbations by about half. • Improvement in symptoms, quality of life, and improvement in pulmonary function and significance compared to placebo varied among trials. • A small study in oral steroid dependent patients found that 53% vs. 34 % of patients randomized to mepolizumab and placebo respectively reduced their oral steroid dose by at least 50%
Safety	• In clinical trials, the most commonly reported adverse effects of mepolizumab included injection-site reactions, headache, back pain, and fatigue. Hypersensitivity reactions have occurred, generally within hours of administration, but sometimes within days. • Herpes zoster infections have occurred rarely. Two serious cases of herpes zoster occurred in patients treated with mepolizumab compared with none in the placebo group. Consider varicella vaccination, if medically appropriate, prior to starting therapy with mepolizumab.
Other Considerations	• There has been a relatively small number of patients and a short duration of follow-up of studies; durability of treatment is uncertain and whether relatively uncommon adverse events, such as opportunistic infections or anaphylaxis, will emerge with greater patient exposure • Mepolizumab is administered as 100mg once every 4 weeks by subcutaneous injection into upper arm, thigh, or abdomen. Mepolizumab should be

	reconstituted and administered by a healthcare professional.
Projected Place in Therapy	Severe asthma that is not controlled on high-dose ICS + at least one controller drug ± oral corticosteroids with evidence of eosinophilic inflammation

Background

Purpose for Review

The purpose of this monograph is to evaluate the available evidence of safety, tolerability, efficacy, cost, and other pharmaceutical issues that would be relevant to evaluating mepolizumab for possible addition to the VA National Formulary

Other Therapeutic Options

Formulary Alternatives	Other Considerations
N/A	
Non-formulary Alternatives	**Other Considerations**
Omalizumab	For those who meet eligibility criteria for mepolizumab AND omalizumab, either SINGLE agent could be selected

Efficacy (FDA Approved Indications)

Literature Search Summary

A literature search was performed on PubMed/Medline (1966 to, March 29, 2016) using the search term mepolizumab. The search was limited to studies performed in humans and published in the English language.

Review of Efficacy

This review will discuss the three primary efficacy trials (**Table 1**). There are six other randomized controlled trials; most of these trials were small, or utilized dosing or included asthma phenotypes that are outside the product labeling. These six studies will not be discussed further in the efficacy section, but were included in integrated safety data.

The trial by Pavord was a dose-ranging study comparing mepolizumab 75mg, 250mg, 750mg, and placebo administered intravenously (IV). Ortega compared mepolizumab 75mg IV, mepolizumab 100mg subcutaneously (SC), and placebo. Bel compared mepolizumab 100mg SC and placebo. All treatments were administered every 4 weeks. The dose-ranging study found similar efficacy with all 3 doses; therefore, the lowest dose, 75mg IV was chosen for subsequent trials. Efficacy results for the 250mg and 750mg doses are not discussed further in this review.

Table 1: Primary Clinical Trials

Study	Duration (weeks)	Treatment arms	n
Pavord 2012	52	MPLZ 75mg IV	153
		PBO	155
Ortega 2014	32	MPLZ 75mg IV	191
		MPLZ 100mg SC	194
		PBO	191
Bel 2014	24	MPLZ 100mg SC	69
		PBO	66

Abbreviations: MPLZ=mepolizumab; PBO=placebo

Bioavailability data show that mepolizumab administered SC into the upper arm is approximately 75% of that administered IV. Clinical results show that the 75mg IV and 100mg SC doses are comparable; therefore, the data for 75mg IV are included in this review to broaden the evidence base. In practice, the SC route of administration is generally preferred by providers and patients and is the approved method of administration. Mepolizumab should NOT be administered IV.

General inclusion criteria were diagnosis of asthma and age ≥ 12; additional inclusion criteria specific to each trial are shown in **Table 2**. General exclusions were current smokers or former smokers with a smoking history of ≥10pack years, concurrent respiratory disease, current malignancy or previous history of cancer in remission for less than 12 months prior screening (excluding localized basal or squamous cell carcinoma that was resected), advanced

liver disease (Childs Class B or C), severe or clinically significant CV disease uncontrolled with standard treatment (see original publications for a list of complete inclusion/exclusion criteria).

Table 2: Inclusion Criteria for Primary Trials

Study	Baseline medications	Exacerbation history	Eosinophilic inflammation criteria
Pavord 2012	High-dose ICS + controller meds ± oral steroids	≥2 exacerbations in previous year	At least one of the following in the previous 12 months: blood eosinophil count ≥ 300 cells/mcL, sputum eosinophil count ≥ 3%, exhaled nitric oxide concentration ≥ 50ppb, or deterioration of asthma control after ≤ 25% reduction in regular maintenance ICS or oral steroids
Ortega 2014	High-dose ICS + controller meds ± oral steroids	≥2 exacerbations in previous year	Blood eosinophil count ≥ 150 cells/mcL within 6 weeks of dosing OR ≥ 300cells/mcL within 12 months of enrollment
Bel 2014	Oral steroids (≥ 6 months 5-35mg) + high-dose ICS + controller meds	Exacerbation in prior year not required	Blood eosinophil count ≥ 150 cells/mcL within 6 weeks of dosing OR ≥ 300cells/mcL within 12 months of enrollment

Abbreviations: ICS=inhaled corticosteroid

Baseline Characteristics

The mean age was approximately 50 years, 59% were female, 85% were white, mean duration of asthma was approximately 19 years, 27% were former smokers, and mean FEV1 % predicted was approximately 60%. The mean blood eosinophil count at baseline in the mepolizumab groups ranged from 240-290 across the three trials. The mean number of severe exacerbations per patient in the previous year ranged from 2.9 to 3.8 episodes across the three trials.

Exacerbations

The primary endpoint of the Pavord and Ortega trials was exacerbations. Exacerbation was defined as worsening of asthma that required systemic steroids for ≥ 3 days, an ED visit, or hospitalization. The trial by Pavord showed that mepolizumab 75mg IV reduced the risk of all exacerbations and those requiring hospitalization/ED visits compared to placebo. There was no difference between the 2 groups for hospitalization only. In the trial by Ortega, both formulations decreased the rate of all exacerbations relative to placebo; however, only the 100mg SC formulation reduced the risk of hospitalization/ED visits and hospitalization alone compared to placebo.

In Bel et al, exacerbation was not a primary outcome, but was evaluated as a prespecified outcome. The same definition of exacerbation was used as in the previously mentioned trials. There were significantly fewer exacerbations with mepolizumab 100mg SC than placebo. This is in light of a significant reduction in oral steroid dose in the mepolizumab arm (see glucocorticoid sparing section).

Table 3: Exacerbations

Study	Duration (weeks)	Treatment arms	n	Exacerbations in previous year	Exacerbation Rate(per patient-year)		
					All	Hospitalization/ ED visit	Hospitalization
Pavord 2012	52	MPLZ 75mg IV	153	3.1	1.24*	0.17*	0.11
		PBO	155	3.8	2.40	0.43	0.18
Ortega 2014	32	MPLZ 75mg IV	191	3.5	0.93*	0.14	0.06
		MPLZ 100mg SC	194	3.8	0.83*	0.08*	0.03*
		PBO	191	3.6	1.74	0.20	0.10
Bel 2014	24	MPLZ 100mg SC	69	3.3	1.44*	-	-
		PBO	66	2.9	2.12		

*significant vs. placebo

Symptom control/Quality of Life

The Asthma Control Questionnaire-5 (ACQ-5) consists of five questions regarding frequency and severity of symptoms over the past week. Each response is graded on a 0-6 scale with higher scores indicating poorer control. The minimal clinically important difference for the mean score is 0.5 points.

St. George's Respiratory Questionnaire is a disease-specific instrument designed to measure impact on overall health, daily life, and perceived well-being in patients with obstructive airways disease. The range of scores is 0-100; with lower scores indicate better functioning. A change of 4 units is considered to be clinically meaningful.

There was a statistically significant improvement in the ACQ-5 with mepolizumab relative to placebo in the trials by Ortega and Bel; however, the treatment difference vs. placebo was borderline clinically significant. Both trials showed statistically significant and clinically meaningful improvement in SGRQ (**Table 4**).

In Pavord et al, the improvement in ACQ and quality of life as measured by the Asthma Quality of Life Questionnaire (AQLQ) was not statistically or clinically different than placebo. The minimal clinically important difference for the AQLQ for the mean score is 0.5 points.

Table4: Asthma Symptoms and Quality of Life

Study	Duration (weeks)	Treatment arms	n	Baseline ACQ-5	ACQ-5	ACQ-5 tx diff [95%CI]	Baseline SGRQ/AQLQ	SGRQ/ AQLQ	SGRQ/AQLQ tx diff [95%CI]
Pavord 2012	52	MPLZ 75mg IV	153	2.2	-0.75	-0.16 [-0.39, 0.07]	4.2	0.80	0.08[-0.16, 0.32]
		PBO	155	2.5	-0.59		4.1	0.71	
Ortega 2014	32	MPLZ 75mg IV	191	2.12	-0.92*	-0.42 [-0.61, -0.23]*	44.4	-15.4*	-6.4 [-9.7, -3.2]*
		MPLZ 100mg SC	194	2.26	-0.94*	-0.44[-0.63, -0.25]*	47.9	-16.0*	-7 [-10.2 -3.8]*
		PBO	191	2.28	-0.50	-	46.9	-9.0	-
Bel 2014	24	MPLZ 100mg SC	69	2.2	-0.61*	-0.52 [-0.87, -0.17]*	50	-8.8*	-5.8 [-10.1 -1.0]*
		PBO	66	2.0	-0.09		45	-3.1	

*significant vs. placebo
AQLQ used in Pavord; SGRQ used in Ortega and Bel

Oral glucocorticoid sparing effect

The trial by Bel examined whether mepolizumab has an oral glucocorticoid-sparing effect in those who require chronic daily use. This study had four phases. The optimization phase was to establish the lowest oral steroid dose. During this phase, the oral steroid dose was reduced weekly until there was an exacerbation in asthma symptoms or an increase in the ACQ-5 score of at least 0.5 points from the visit 1 score. During the induction phase, patients received mepolizumab 100mg SC or placebo for 4 weeks. During the reduction phase, the dose of oral steroids was reduced according to protocol over a 16 week period based on asthma control and symptoms of adrenal insufficiency. Lastly, during the 4 week maintenance phase, patients remained on study drug and no further changes were made to the steroid dose.

The primary outcome was the percent reduction in oral steroid dose during the maintenance phase compared to the dose during the optimization phase. The percent reduction in dose was grouped according to categories as shown in **Table 5**. During the optimization phase the median dose of oral steroid was 12.5mg (MPLZ) and 10mg (PBO) daily. The odds ratio for reduction in oral steroid dose for all categories was 2.39 [95%CI 1.25, 4.56; p=0.008]. Significantly more patients in the mepolizumab group than placebo were able to reduce the oral steroid dose to ≤ 5mg.

Table 5: Reduction in Oral Steroid Dose

Categories for % reduction	MPLZ (%pts) N=69	Placebo (%pts) N=66
90-100%	23	11
75-<90%	17	8
50-<75%	13	15
>0- <50%	10	11
No decrease in dose, lack of asthma control, or withdrew tx	36	56
Reduction of oral steroid dose to ≤ 5mg/d	54	32

Pulmonary Function
The primary clinical trials evaluated FEV1 as a secondary or other outcome. Improvement in FEV1 with mepolizumab compared to placebo was only significant in the trial by Ortega (**Table 6**).

Table 6: Change from Baseline in FEV1 (mL)

Study	Duration (weeks)	Treatment arms	n	Change in FEV1 (mL)	Diff from PBO mL (95%CI)	p-value
Pavord 2012	52	MPLZ 75mg IV PBO	153 155	121 60	61 (-39, 161)	0.22
Ortega 2014	32	**MPLZ 100mg SC** PBO	194 191	183 86	98 (11, 184)	0.03
Bel 2014	24	MPLZ 100mg SC PBO	69 66	111 -4	114 (-42, 271)	0.15

Predictor of Efficacy According to Blood Eosinophils
A *post-hoc* analysis of data from the trial by Pavord showed that a single peripheral blood eosinophil count at screening of ≥150 cells/mcL AND clinical characteristics such as frequent exacerbations was useful in identifying patients who are more likely to benefit from treatment with mepolizumab in severe asthma. Neither FeNO nor sputum eosinophil count was found to be as accurate a biomarker of treatment response.

The FDA's analysis of the data from the Ortega study showed a trend of greater reduction in exacerbations for patients whose enrollment was based on an eosinophil count ≥ 150cells/mcL at screening than for those with values ≥300cells/mcL in the prior 12 months. However, the trend was not statistically significant due to issues concerning loss of power (**Table 7**).

Table 7: Annual Rate of Exacerbations by Blood Eosinophil Values (Ortega trial)

		MPLZ 100 SC	MPLZ 75IV	Placebo
≥150 cell/mcL at screening	N	48	59	69
	Rate/year	0.51	0.54	1.92
≥300 cells/mcL in prior 12 months	N	39	34	23
	Rate/year	1.25	1.62	1.52
Both ≥150 cell/mcL at screening AND ≥300 cells/mcL in prior 12 months	N	107	96	98
	Rate/year	0.74	0.98	1.62

Data obtained from FDA review

The FDA did not define specific blood eosinophil thresholds as part of the labeled indication for use of mepolizumab until more information is available on defining such thresholds for this asthma phenotype. In lieu, they chose to provide the data on blood eosinophil and effect on exacerbations to assist providers in making appropriate decisions for the individual patient. Therefore, the Clinical Studies section of the product label discusses that a baseline blood eosinophil count of ≥150 cells/mcL was a potential indicator of treatment benefit (Pavord trial). In a second trial (Ortega) blood eosinophil of ≥150cell/mcL obtained within 6 weeks of initiation of dosing was also a potential predictor of efficacy and showed a trend of greater exacerbation benefit with increasing eosinophil count. Those enrolled solely on the basis of a historical blood eosinophil count of ≥300cells/mcL in the past 12 months, but who had a baseline blood eosinophil count of <150cells/mcL did not have an exacerbation benefit.

Prior use of omalizumab
A subgroup analysis of patients with a history of omalizumab use from the Ortega and Bel trials found that the reduction of exacerbations with mepolizumab was similar to those who had no prior use of omalizumab.

Table 8: Exacerbation Risk in Those with and Without Prior Omalizumab Use

	Ortega		Bel	
	Prior Omalizumab	No prior omalizumab	Prior Omalizumab	No prior omalizumab
n	75	501	45	90
Rate ratio	0.43 [0.21, 0.88]	0.53 [0.40, 0.69]	0.67[0.36, 1.23]	0.71 [0.45, 1.14]

(exacerbation/years)

Mepolizumab vs. Omalizumab
Mepolizumab and omalizumab have different indications for use and the two drugs are not interchangeable. However, there may be patients who meet eligibility criteria for both drugs. In the trial by Ortega et al., approximately 30% of patients who were eligible for treatment with mepolizumab were also eligible for treatment with omalizumab. Head-to-head trials of mepolizumab and omalizumab have not been conducted; therefore, the comparative efficacy and safety are unknown at this time. There are no data supporting concurrent use of mepolizumab and omalizumab; therefore, such use cannot be recommended.

Long-term Studies
There are two ongoing long-term open-label extensions studies. One study enrolled patient from the studies by Ortega and Bel (Study 61) and the other enrolled patients from the study by Pavord.

Potential Off-Label Use

This section is not intended to promote any off-label uses. Off-label use should be evidence-based. See VA PBM-MAP and Center for Medication Safety's Guidance on "Off-label" Prescribing (available on the VA PBM Intranet site only).

Hypereosinophilic syndrome, eosinophilic esophagitis, nasal polyposis, Churg Strauss Syndrome, COPD

Safety

(for more detailed information refer to the product package insert)

	Comments
Boxed Warning	None
Contraindications	History of hypersensitivity to mepolizumab or excipients in the formulation
Warnings/ Precautions	• Hypersensitivity reactions: Hypersensitivity reactions such as angioedema, bronchospasm, hypotension, urticaria, and rash have occurred following administration of mepolizumab. Generally, reactions occur within hours of administration, but in some instances can have a delayed onset of days. Discontinue mepolizumab in the event of a hypersensitivity reaction. • Acute asthma symptoms or deteriorating disease: Do not use mepolizumab to treat acute asthma symptoms or acute asthma exacerbations • Herpes zoster: Two serious cases of herpes zoster occurred in patients treated with mepolizumab compared with none in the placebo group. Consider varicella vaccination, if medically appropriate, prior to starting therapy with mepolizumab. • Reduction of corticosteroid dosage: Do not abruptly discontinue systemic or inhaled steroids upon initiation of mepolizumab. If appropriate, reduction should be done gradually and under the care of a physician. • Parasitic (helminth) infection: It is unknown if mepolizumab will influence a patient's response against parasitic infections (patients with known parasitic infections were excluded from the clinical trials). Pre-existing infection should be treated prior to initiating therapy with mepolizumab. If an infection occurs while being treated with mepolizumab and does not respond to anti-helminth therapy, discontinue mepolizumab until infection resolves.
Safety Considerations	*Hypersensitivity Reactions* Systemic hypersensitivity reactions were few in number. The incidence was 1% and 2% mepolizumab 100mgSC (marketed product) and placebo respectively (**Table 9**). None of the systemic hypersensitivity reactions were considered to be anaphylaxis based on the National Institute of Allergy and Infectious Disease and Food Allergy and Anaphylaxis Network criteria for anaphylaxis. Local site reactions were reported more often with mepolizumab 100mg SC; the incidence was 8% compared to 3% with placebo. Events were reported as non-serious, mild to moderate in intensity and the majority resolved within a few days. One patient withdrew from the study because of an

injection site reaction. Commonly reported symptoms included pain, erythema, swelling, itching, and burning sensation (**Table 9**)

Herpes Zoster
There was an imbalance in the number of herpes zoster infections between the mepolizumab and placebo arms (**Table 9**). In the ongoing open-label extension trials, there were five additional reports of herpes zoster through October 27, 2014 (safety cutoff date) in patients treated with mepolizumab 100mg SC.

Table 9: Hypersensitivity and Infection from Primary Trials

N (%)	MPLZ 100SC (n=263)	MPLZ 75IV (n=344)	MPLZ 250IV (n=152)	MPLZ 750IV (n=156)	PBO (n=412)
Systemic hypersensitivity reactions	3 (1)	4 (1)	3 (2)	2 (1)	7 (2)
Local site reactions	21 (8)	11 (3)	0	0	14 (3)
Any infection	3 (1)	4 (1)	0	2 (1)	4 (2)
Herpes zoster	2 (<1)	4 (1)	0	0	2 (<1)
Ophthalmic herpes zoster	0	0	0	0	1 (<1)

Data from FDA review

Parasitic Infections
There was one report of parasitic infection (gastroenteritis) in a patient treated with MPLZ 100mg SC. There were no additional reports from the open-label extension trials

Malignancies
Patients with current malignancy or previous history of cancer in remission for less than 12 months prior screening (excluding localized basal or squamous cell carcinoma that was resected were excluded from the clinical trials.

In the three primary trials, there were two malignancies reported with mepolizumab (basal cell MPLZ 75IV, uterine MPLZ 250 IV) and three with the placebo group (basosquamous, prostate, and squamous cell).

In the ongoing open-label extension trials, there were nine reports of malignancies through October 27, 2014 (safety cutoff date) in patients treated with mepolizumab 100mg SC (2 prostate, 2 breast, 1 basal cell, 1 endometrial, 1 gastric, 1 skin, 1 squamous cell). The FDA review states that the reported malignancies are not uncommon in the general population and recommends continued routine pharmacovigilance for malignancies.

Adverse Reactions

Common adverse reactions

Adverse reactions with mepolizumab with incidence ≥3%, and occurring more often than placebo, are shown below.

Table 10: Adverse Reactions from Primary Trials

	MPLZ 100SC (%) (n=263)	Placebo (%) (n=257)
Headache	19	18
Injection site reaction	8	3
Back pain	5	4
Fatigue	5	4
Influenza	3	2
Urinary tract infection	3	2
Upper abdominal pain	3	2
Pruritus	3	2
Eczema	3	<1

	Muscle spasms	3	<1

Data from product package insert

Death/Serious adverse reactions (SAE)	**Deaths**: in the three primary trials, there were five deaths reported: 1 (100 SC); 2 (250 IV); 1 (750 IV); 2 (placebo) An additional three deaths were reported in the open label extension study. Three deaths in the mepolizumab group were asthma-related. **Non-fatal SAE (exposure adjusted rate per 1000 patient-years)**: 189.9 (100 SC); 204.5 (75 IV); 232.1 (250 IV); 188.1 (750 IV); 348.6 (placebo) The majority of events were asthma-related.

Discontinuations due to adverse reactions

	MPLZ 100SC	MPLZ 75IV	MPLZ 250IV	MPLZ 750IV	PBO
n(%)	3 (1)	4 (1)	8 (5)	8 (5)	12 (3)
E/1000 PYE	147	254	142	144	284

Drug Interactions

Drug-drug interactions	Formal drug interaction trials have not been conducted
Drug-food interactions	None
Drug-lab interactions	None
Pharmacogenomics	None

Risk Evaluation

As of April 2016

Sentinel event advisories	Sources: ISMP, FDA, TJC
Look-alike/sound-alike error potentials	Sources: Based on clinical judgment and an evaluation of LASA information from three data sources (Lexi-Comp, First Databank, and ISMP Confused Drug Name List)

NME Drug Name	Lexi-Comp	First DataBank	ISMP	Clinical Judgment
Mepolizumab	None	None	None	Mipomersen Omalizumab
Nucala	None	None	None	Neulasta Nucynta

Other Considerations

- If the reconstituted mepolizumab is not used immediately, store below 30ºC (86ºF). Do not freeze. Discard mepolizumab if not used within 8 hours of reconstitution.

- The California Technology Assessment Forum (CTAF), a core program of The Institute for Clinical and Economic Review (ICER), conducted a cost-effective analysis of mepolizumab in severe eosinophilic asthma.

  They concluded that addition of mepolizumab to inhaled steroids and other controller medications resulted in reduced rates of exacerbation and improved quality of life. However, based on current wholesale drug acquisition cost, the estimated cost-effectiveness of mepolizumab exceeded commonly used cost-effectiveness ratio thresholds of $100,000-$150,000 per QALY and that discounts of two-thirds to three-quarters off the current wholesale price of mepolizumab would be needed to approach these thresholds.

Dosing and Administration

100mg once every 4 weeks by subcutaneous injection into upper arm, thigh, or abdomen.
Mepolizumab should be reconstituted and administered by a healthcare professional

Special Populations (Adults)

	Comments
Elderly	There is insufficient information available to determine if there is a difference in response between older and younger patients. There were 38 patients enrolled in the clinical trials who were ≥ 65 years old that received mepolizumab. Other reported clinical experience did not identify differences in response between younger and older patients. No dosage adjustment is required, but greater sensitivity in some patients cannot be ruled out.
Pregnancy	Data on pregnancy exposure are insufficient to inform on drug-associated risks. Transfer of monoclonal antibodies across the placenta increases in a linear fashion as pregnancy progresses (greater during 2nd and 3rd trimesters). There was no evidence of adverse effects on fetal/neonatal growth (including immune function) in monkeys at maternal doses up to 30 times the exposure at the maximum recommended human dose. Patients or providers can enroll patients in a registry that monitors pregnancy outcomes in women exposed to mepolizumab during pregnancy (call 1-877-311-8972 or visit www.mothertobaby.org/asthma)
Lactation	There is no information in humans. However, mepolizumab is a humanized monoclonal antibody (IgG1 kappa), and IgG is present in human milk in small amounts. In monkeys, levels of mepolizumab in milk were ≤ 0.5% of serum concentration. The benefits of breastfeeding and mother's clinical need for mepolizumab versus any potential adverse effects should be considered.
Renal Impairment	None
Hepatic Impairment	None
Pharmacogenetics/genomics	None

Projected Place in Therapy

Patients with severe asthma that is not controlled on high-dose ICS + at least one controller drug ± oral corticosteroids with evidence of eosinophilic inflammation.

References:

Pavord ID, Korn S, Howarth P, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicenter, double-blind, placebo-controlled trial. Lancet 2012; 380: 651-59.

Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. N Engl J Med 2014; 371: 1198-1207.

Bel EH, Wenzel SE, Thompson PJ, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. N Engl J Med 2014; 371: 1189-1197.

Product package insert for NUCALA (mepolizumab). 11/2015

FDA Briefing Document for Mepolizumab (NUCALA)
http://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/125526Orig1s000MedR.pdf

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Albers FC, Bourdin A, Price R, et al. Effect of mepolizumab in severe eosinophilic asthma patients with history of omalizumab treatment; (Abstract #L7). Presented at the annual meeting of the American Academy of Allergy, Asthma & Immunology, February 20-24, 2015, Houston, TX

Institute for Clinical and Economic Review/The California Technology Assessment Forum
Mepolizumab (Nucala®, GlaxoSmithKline plc.) for the Treatment of Severe Asthma with Eosinophilia: Effectiveness, Value, and Value-Based Price Benchmarks . Published December 21, 2015
http://icer-review.org/wp-content/uploads/2016/03/CTAF_Mepolizumab_Final_Report_031416.pdf

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