Drug Use Research & Management Program
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New Drug Evaluation: efgartigimod alfa-fcab injection, for intravenous use

Date of Review: April 2022
Generic Name: efgartigimod alfa-fcab

End Date of Literature Search: 02/01/2022
Brand Name (Manufacturer): Vyvgart™ (Argenx)
Dossier Received: yes

Research Questions:

1. What is the evidence for efficacy and harms for efgartigimod when used as a treatment for generalized myasthenia gravis (MG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive?
2. Are there specific subpopulations that would benefit or be at increased risk of harms with the use of efgartigimod?

Conclusions:

- Efgartigimod approval was based on one placebo-controlled, phase 3, manufacturer funded, 26-week, randomized controlled trial (RCT) in 167 adult patients with generalized MG. The primary outcome was conducted in patients who were seropositive for the AChR antibody (77% of enrolled patients).[1]
- There was low quality evidence that efgartigimod infusion was found to be more effective than placebo for the primary outcome of percentage of Myasthenia Gravis-Activities of Daily Living (MG-ADL) responders at week 8 (odds ratio [OR] 4.95; 95% confidence interval [CI], 2.21 to 11.53; P<0.001; absolute risk reduction [ARR] 38% / number needed to treat [NNT] 3).[1] Responders were defined as patients with a two or more point reduction in the MG-ADL total score compared to baseline that was maintained for four consecutive weeks, with the first reduction occurring no later than one week after the last infusion of the product after 4 weeks of initial treatment. Approximately, 70% of patients experienced the minimum point reduction in the MG-ADL to be classified as a responder with a clinically significant change.
- Adverse reactions occurring in 10% or more of patients treated with efgartigimod, and more frequently than placebo, are respiratory tract infections, headache and urinary tract infections. Serious adverse reactions occurred in 5% of efgartigimod patients versus 8% in the placebo group.[1] Efgartigimod transiently reduces IgG levels and should not be given if the patient has an active infection and immunization with live-attenuated or live vaccines is not recommended during treatment.[2]
- Exploratory analysis of subgroup populations (e.g., gender, age and MG-ADL score) demonstrated no differences in results compared to general findings.
- There is insufficient evidence for the use of efgartigimod in black women, in which there is a higher prevalence of MG compared to white women.

Recommendations:

- Designate efgartigimod as non-preferred on the preferred drug list (PDL) and subject to prior authorization (PA) criteria.

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Background:

Myasthenia gravis (MG) is an autoimmune disease that is rare with an incidence of 150 to 250 per million people. Females, 40 years and younger, are more commonly affected by MG than males and males 50 years and older have a higher incidence than females.[3] The pathophysiology of MG often involves autoantibodies against skeletal muscle nicotinic acetylcholine receptors.[4] Approximately 85% of patients with MG are AChR antibody positive.[5] To a lesser extent, muscle-specific tyrosine kinase (MuSK) and low-density lipoprotein receptor-related protein-4 (LRP4) are also involved. Myasthenia gravis affects antibody formation at the postsynaptic receptors at the neuromuscular junction causing weakness and disability involving ocular, bulbar, limb and respiratory muscles. Common symptoms may include ptosis, diplopia, facial weakness, dyspnea, dysphagia, dysarthria and weakness in the extremities and neck. Symptoms of MG can worsen after activity and improve upon rest.[6] In rare cases life-threatening respiratory failure, defined as a myasthenia crisis, can occur. The diagnosis of MG and the extent of disability is classified by the Myasthenia Gravis Foundation of America (MGFA) Classification Scale. The scale classifies patients according to class ranging from Class I (stable remission) to Class V (requiring intubation). It is not uncommon for patients with MG to also have associated comorbidities such as other autoimmune disorders, thymoma or myocarditis.[6]

Treatment determinants of MG involve the age of patient, respiratory or bulbar involvement, disease severity and progression. Current treatments target the amount of acetylcholine at the neuromuscular junction or to suppress the immune system to limit the production of autoantibodies.[3] Standard of care includes symptom management (e.g., acetylcholinesterase inhibition), chronic immunosuppressive therapy (e.g., glucocorticoids and nonsteroidal immunosuppressive drugs), and short-acting immunomodulating treatments (e.g., therapeutic plasma exchange and intravenous immune globulin [IVIG]) (**Table 1**).[4] Guidelines recommend treatment with pyridostigmine first-line for most patients with MG.[7] Corticosteroids or immunosuppressant therapy should be offered to patients who continue to have symptoms while taking pyridostigmine. There is a paucity of high quality evidence to guide immunosuppressant therapy in MG; however, azathioprine is recommended as the first-line immunosuppressant treatment based on moderate evidence.[7] Other immunosuppressants that are used for MG are: cyclosporine, mycophenolate mofetil, methotrexate and tacrolimus. If conventional therapies fail to control symptoms of MG, immunomodulatory therapies such as eculizumab or rituximab may be considered.[3] Eculizumab is Food and Drug Administration (FDA) approved for the treatment of MG and is recommended for severe, refractory, AChR antibody positive patients. Rituximab is recommended off-label with low-quality evidence of efficacy in patients who are MuSK antibody positive.[3,8] Oral methotrexate also has a role in treating MG as a steroid-sparing therapy in patients that have not responded to other steroid-sparing therapies.[8] Patients that present with severe disease or disease that is progressing rapidly should be treated as if in a myasthenic crisis using rapid therapies (e.g., therapeutic plasma exchange and IVIG). Thymectomy may be considered in some cases as a surgical option for patients with thymoma and lack of symptom control with anticholinesterase inhibitors with or without immunotherapies. There is large variability in the onset and time to maximal effect of treatments. Many medications, specifically those that effect neuromuscular transmission, can exacerbate MG and symptoms should be monitored for changes any time a new drug is initiated. Patients who test positive for MuSK have more success with glucocorticoids and respond less well to anticholinesterase therapies.[4]

Table 1. Medications to Treat Myasthenia Gravis[4]

Medication	Dose	Time of effect	Notes
Initial Therapy			
Pyridostigmine†	Adults: 30 mg 3 times daily orally Max dose is 120 mg every 4 hours while awake Children and adolescents: 0.5 to 1 mg/kg every 4-6 hours with meals Max dose is 7 mg/kg per 24 hours divided in 5 to 6 doses	Onset: 15 minutes Maximal effect: 2 hours	- Indicated for mild to moderate MG - Patient response is variable

Chronic Immunotherapies for patients requiring additional symptom management			
Prednisone	20 mg daily and increase by 5 mg every 3 to 5 days to a target dose of 60 mg per day orally Max dose of 80 mg per day	Onset: 2 to 3 weeks Maximal effect: 5 to 6 months	- Titrate dose over 4 to 8 weeks
Azathioprine*	50 mg daily for 2 to 4 weeks orally Titration of 50 mg every 2 to 4 weeks to maintenance dose of 2 to 3 mg/kg	Onset: 12 months Maximal effect: 1 to 2 years	- Considered first-line as a steroid sparing therapy
Mycophenolate mofetil*	2000 mg daily orally	Onset: 6 to 12 months Maximal effect: 1 to 2 years	- Often used first-line however evidence is less robust
Cyclosporine	5 mg/kg daily divided in 2 doses orally	Onset: 6 months Maximal effect: 12 months	- Effective in prednisone naïve and prednisone-dependent - Renal toxicity and drug interactions
Tacrolimus	3 to 8 mg per day orally	Onset: 6 months Maximal effect: 12 months	- Renal toxicity and drug interactions
Eculizumab†[7]	900 mg IV weekly for the first 4 weeks 1200 mg for the 5th dose 1 week later 1200 mg every 2 weeks thereafter	Onset: Less than 1 week Maximal effect: 3 weeks	- Boxed warning for life-threatening and fatal meningococcal infection - Only available through a Risk Evaluation and Mitigation Strategy (REMS) - Not indicated for MuSK antibody positive or LRP4 antibody positive patients.
Rapid Immunotherapies			
Plasmapheresis	Not applicable	Onset: 1 to 7 days Maximal effect: 1 to 3 weeks	- Reserved for seriously ill patients in the midst of myasthenic crisis
Intravenous immune globulin	2 g/kg IV given over 2 to 5 days	Onset: 1 to 2 weeks Maximal effect: 1 to 3 weeks	- Dose should be more spread over more days in individuals who have congestive heart failure or older adults
Key: * Glucocorticoid-sparing therapy; † FDA approved for treating myasthenia gravis Abbreviations: IV = intravenous; LRP4 = low-density lipoprotein receptor-related protein-4; MuSK = muscle-specific tyrosine kinase			

The goals of treatment for patients with MG are symptom management (neurological deficits), sustained remission and full functional capacity. One outcome commonly used in clinical trials to determine efficacy is the MG-ADL total score. The MG-ADL measures the impact of MG on daily function with scores ranging from 0 (normal function) to 3 (loss of ability to perform function). Total scores range from 0 to 24. The minimally clinically important difference (MCID) is 2 or more point increase in total MG-ADL score.[10] The Quantitative Myasthenia Gravis (QMG) assessment is also used to determine muscle weakness in patients who have MG, which is based on a 13-item, 4-point scale ranging from 0 to 39.[3] The MCID for the QMG is a 3 or more point reduction.[11]

There were 44 unique patients within fee-for-service (FFS) population with a diagnosis of MG within the last year. There is no PDL class for MG and 3 claims total for drugs FDA approved for MG (e.g., pyridostigmine, eculizumab and efgartigimod).

See **Appendix 1** for **Highlights of Prescribing Information** from the manufacturer, including Boxed Warnings and Risk Evaluation Mitigation Strategies (if applicable), indications, dosage and administration, formulations, contraindications, warnings and precautions, adverse reactions, drug interactions and use in specific populations.

Clinical Efficacy:
Efgartigimod is a neonatal FC receptor blocker indicated for the treatment of gMG in adult patients who are anti-AChR antibody positive.[2] Efgartigimod reduces IgG subtypes without affecting the concentrations of other immunoglobulins or albumin.

Efgartigimod was studied in one, placebo-controlled, double-blind, phase 3 trial. One-hundred sixty seven patients who were classified as having MGFA class II to IV were randomized to efgartigimod 10 mg/kg or placebo infusion given as a 4-week treatment cycle of once weekly for 28 weeks (including a 2 week screening period). Additional cycles were administered according to clinical response which was determined when MG-ADL score was at least 5 (with >50% MG-ADL non-ocular related) and if the patient was an MG-ADL responder when they no longer had a clinically meaningful decrease compared to baseline (MG-ADL clinically meaningful improvement defined as having 2 point or greater improvement in total MG-ADL). Additional cycles were administered no sooner than 8 weeks from initiation of the previous cycle. A patient could receive a maximum of 3 cycles during the 26-week study. Patients enrolled in the study were predominately female (71%), white and MGFA Class III (suggesting moderate weakness). Fifty-seven percent of patients had undergone a thymectomy with differential rates in the efgartigimod group (70%) compared to placebo (43%). All patients were required to be on a stable dose of at least one treatment for gMG. At baseline 71% of percent of patients were on a steroid, 61% were on a non-steroidal immunosuppressant therapy and 51% were on both treatments.

The primary endpoint was the percentage of MG-ADL responders during cycle 1. Patients were considered MG-ADL responders if there was a 2 or more point reduction in the MG-ADL total score compared to baseline that was maintained for 4 consecutive weeks, with the first reduction occurring no later than 1 week after the last infusion of the product in cycle 1. The primary endpoint was assessed at 8 weeks and only included patients who were seropositive for the AChR antibody. The secondary endpoint was the percent of QMG responders during cycle 1 in the AChR antibody seropositive population. QMG responders were those who experienced a 3 or more point reduction in the total QMG score compared to baseline that was maintained for 4 consecutive weeks, with the first reduction occurring no later than 1 week after the last infusion of efgartigimod in cycle 1.

A majority of patients (66%) received 2 cycles of efgartigimod. Fifty-six percent of patients completed just one cycle and 6% completed a third cycle (results not reported).[1] At 8 weeks, the number of MG-ADL responders was higher in the efgartigimod group (68% vs. 30%; ARR 38%/NNT 3). Patients that received a second cycle had similar results, with 71% of patient treated with MG-ADL responders in the efgartigimod group compared to 26% of patients treated with placebo. Findings for MG-ADL Responders in cycle 1 for all patients, regardless of AChR-Ab positivity, was higher in the efgartigimod group compared to placebo (ARR 38% / NNT 4). The majority of patients (77.8%) experienced a minimum improvement of 2 points in the MG-ADL score, indicating the minimum value to be considered clinically significant. Similar results were reported with the QMG score, with a minimum point change of 3 points occurring in 63% of patients treated with efgartigimod compared to 14% in the placebo group. For the secondary endpoint of percent of QMG responders in cycle 1, efgartigimod was more effective than placebo (OR 10.84; 95% CI, 4.18 to 31.20; $p<0.0001$; ARR 49%/NNT 2). Improvements were demonstrated from week 1 and maximum improvement for the primary endpoint and key secondary endpoints occurred at week 4. Exploratory subgroup analyses did not find any differences in results for gender, age or MG-ADL disability at baseline.

Limitations to the evidence include efficacy conclusions based on one, small study in adults with gMG. A higher incidence of thymectomy in the efgartigimod group may offer an advantage as patients that have undergone a thymectomy experience less muscle weakness and need for immunosuppressant drugs. Most

patients (86%) were on background immunosuppressant therapy (steroids and non-steroidal immunosuppressive therapies). There were more females enrolled in the study compared to males (75% vs. 25%); however, this is representative of the population diagnosed with gMG in this age group. Most patients experienced MG-ADL and QMG score changes that met the minimum point value to be considered clinically significant.

Clinical Safety:

Most common adverse reactions occurring in 5% or more of patients treated with efgartigimod are respiratory tract infections, headache, urinary tract infections, paresthesia and myalgia (**Table 2**). Serious adverse reactions occurred in 5% of efgartigimod patients (e.g., thrombocytosis, rectal adenocarcinoma, worsening MG, and depression) versus 8% in the placebo group (e.g., myocardial ischemia, atrial fibrillation and spinal ligament ossification). There were no deaths in either group. Treatment discontinuations due to adverse reactions were the same in efgartigimod and placebo treated patients (4% in each group). Efgartigimod infusion should be delayed if the patient has an active infection and patients should be monitored for infections while undergoing treatment.

Table 2. Adverse Reactions in Patients Treated with Efgartigimod compared to Placebo at an Incidence of 5% or more[2]

Adverse Reaction	Efgartigimod (N=84)	Placebo (N=83)
Respiratory tract infection	33%	29%
Headache (migraine and procedural)	32%	29%
Urinary tract infection	10%	5%
Paresthesia (oral hypoesthesia, hypoesthesia, and hyperesthesia)	7%	5%
Myalgia	6%	1%

Comparative Endpoints:

Clinically Meaningful Endpoints:

1) Remission of MG symptoms
2) Ability to perform activities of daily living
3) Serious adverse events
4) Study withdrawal due to an adverse event

Primary Study Endpoint:

1) Magnitude of change in MG-ADL

Table 3. Pharmacology and Pharmacokinetic Properties[2]

Parameter	
Mechanism of Action	Efgartigimod is a human IgG1 antibody fragment that binds to the neonatal Fc receptor (FcRn), causing reductions of circulating IgG.
Oral Bioavailability	NA
Distribution and Protein Binding	Volume of distribution 15 to 20 L Protein binding not described
Elimination	Less than 0.1% recovered in the urine
Half-Life	80 to 120 hours
Metabolism	Degraded by proteolytic enzymes into small peptides and amino acids

Abbreviations: L – liter; NA – not applicable

Table 4. Comparative Evidence Table

Ref./ Study Design	Drug Regimens/ Duration	Patient Population	N∞	Efficacy Endpoints	ARR/ NNT	Safety Outcomes	ARR/ NNH	Risk of Bias/ Applicability
1. Howard, et al[1] DB, PC, Phase 3, RCT	1. Efgartigimod 10 mg/kg (given as 4 infusions per cycle, 1 infusion per week)* 2. Placebo 26 week study	Demographics: Female: 71% Age: 47 years White: 85% Asian: 10% Time since MG diagnosis: 9 years MGFA class II: 39% MGFA class III: 58% MGFA class IV: 4% MG-ADL total mean score: 9.0 Previous thymectomy: 57% Acetylcholine receptor antibody-positive: 77% MG therapy at baseline - Steroid: 76% Any NSIST: 61% Steroid and NSIST: 52% Key Inclusion Criteria: - Ages 18 years and older with generalized MG - MG-ADL score of at least 5 (>50% non-ocular) - Stable dose of at least one treatment for MG Key Exclusion Criteria: - Rituximab or eculizumab in the previous 6 months before screening - Thymectomy in the previous 3 months - Intravenous immunoglobulin or plasma exchange within 1 month of screening - Active hepatitis B - Seropositive for hepatitis C - seropositive for HIV with low CD4 count - Serum IgG levels less than 6 g/L at screening - Pregnant	mITT: 1. 84 2. 83 PP: 1. 79 2. 73 Attrition: 1. 5 (6%) 2. 10 (12%)	Primary Endpoint: MG-ADL Responders in Cycle 1 for patients who are seropositive for the AChR antibody‡: 1. 44 (68%) 2. 19 (30%) OR 4.95 (95% CI, 2.21 to 11.53) P<0.001 Secondary Endpoint: Quantitative Myasthenia Gravis responders in cycle 1†: 1. 41 (63%) 2. 9 (14%) OR 10.84 (95% CI, 4.18 to 31.20) P<0.0001 MG-ADL Responders in Cycle 1 (all patients): 1. 57 (68%) 2. 31 (37%) OR 3.70 (95% CI, 1.85 to 7.58) P<0.0001	ARR 38%/ NNT 3 ARR 49% / NNT 2 ARR 31% / NNT 4	Serious Adverse Events: 1. 4 (5%) 2. 7 (8%) Discontinuations due to Adverse Events: 1. 3 (4%) 2. 3 (4%) Any Infection: 1. 39 (46%) 2. 31 (37%) Headache: 1. 24 (29%) 2. 23 (28%) Nasopharyngitis: 1. 10 (12%) 2. 15 (18%)	N/A	**Risk of Bias (low/high/unclear)**: Selection Bias: (Low) Randomized via central interactive response technology via web and voice systems. Randomization stratified via acetylcholine receptor antibody, NSISTs and Japanese nationality. More patients in the efgartigimod had undergone thymectomy compared to placebo, 70% vs. 43%, respectively. Performance Bias: (Low) Matching placebo in identical containers. Participants, investigators and clinical staff blinded. Detection Bias: (Unclear) Outcome assessment not described. Attrition Bias: (Low) Attrition was low in both groups. Analysis was done on the mITT population. Handling of missing data was not described. Reporting Bias: (Low) Study followed original trial design. Other Bias: (High) Study was funded by the manufacture. Funding source had role in data collection, data interpretation and analysis. **Applicability**: Patient: The results of this trial are most applicable to patients taking immunosuppressive therapy, who were acetylcholine receptor antibody-positive and had moderate disease based on MG-ADL scores. Intervention: The dose of efgartigimod is appropriate based on phase 2 studies. Comparator: Active treatment comparison would be helpful to determine place in therapy. Outcomes: The primary outcome, although a subjective assessment of efficacy, has been used for other therapies seeking approval for use in gMG patients and is recommended by the FDA. Responders were defined based on minimum clinically important differences referenced in the literature. Setting: Fifty-six centers in 15 countries in North America, Japan and Europe.

Key: * All patients receive an initial cycle with subsequent cycles administered according to clinical response when MG-ADL score was at least 5 (with >50% MG-ADL non-ocular) and if the patient was an MG-ADL responder, no clinically meaningful decrease compared to baseline (MG-ADL clinically meaningful improvement defined as having 2 point or greater improvement in total MG-ADL); ‡‡ Patients were considered MG-ADL responders if there was a 2 or more point reduction in the MG-ADL total score compared to baseline that was maintained for 4 consecutive weeks, with the first reduction occurring no later than 1 week after the last infusion of the product in cycle 1† Quantitative Myasthenia Gravis (QMG) score is physician assessed with quantitative measures (clinically meaningful improvement defined as 3 or more point reduction); ∞ All patients, acetylcholine receptor antibody-positive and those were acetylcholine receptor antibody-negative.
Abbreviations: AchR = anti-acetylcholine receptor; ARR = absolute risk reduction; CI = confidence interval; ITT = intention to treat; MG = myasthenia gravis: MG-ADL = Myasthenia Gravis Activities of Daily Living; MGFA = Myasthenia Gravis Foundation of America; mITT = modified intention to treat; N = number of subjects; NA = not applicable; NNH = number needed to harm; NNT = number needed to treat; NR = not reported; NSIST = non-steroidal immunosuppressant therapy; NR = not reported; OR = odds ratio; PP = per protocol.

References:

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Appendix 1: Prescribing Information Highlights

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VYVGART safely and effectively. See full prescribing information for VYVGART.

VYVGART ™ (efgartigimod alfa-fcab) injection, for intravenous use
Initial U.S. Approval: 2021

----------INDICATIONS AND USAGE----------
VYVGART is a neonatal Fc receptor blocker indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive. (1)

----------DOSAGE AND ADMINISTRATION----------
- Evaluate the need to administer age-appropriate vaccines according to immunization guidelines before initiation of a new treatment cycle with VYVGART. (2.1)
- The recommended dosage is 10 mg/kg administered as an intravenous infusion over one hour once weekly for 4 weeks. In patients weighing 120 kg or more, the recommended dose is 1200 mg per infusion. (2.2)
- Administer subsequent treatment cycles based on clinical evaluation; the safety of initiating subsequent cycles sooner than 50 days from the start of the previous treatment cycle has not been established. (2.2)
- Must be diluted with 0.9% Sodium Chloride Injection, USP prior to administration. (2.3)
- Administer as an intravenous infusion over one hour via a 0.2 micron in-line filter. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
Injection: 400 mg in 20 mL (20 mg/mL) single-dose vial. (3)

----------CONTRAINDICATIONS----------
None. (4)

----------WARNINGS AND PRECAUTIONS----------
- Infections: Delay administration of VYVGART to patients with an active infection. Monitor for signs and symptoms of infection in patients treated with VYVGART. If serious infection occurs, administer appropriate treatment and consider withholding VYVGART until the infection has resolved. (5.1)
- Hypersensitivity Reactions: Angioedema, dyspnea, and rash have occurred. If a hypersensitivity reaction occurs, discontinue the infusion and institute appropriate therapy. (5.2)

----------ADVERSE REACTIONS----------
Most common adverse reactions (≥ 10%) in patients treated with gMG are respiratory tract infections, headache, and urinary tract infection. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact argenx at 1-833-argx411 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
Closely monitor for reduced effectiveness of medications that bind to the human neonatal Fc receptor. When concomitant long-term use of such medications is essential for patient care, consider discontinuing VYVGART and using alternative therapies. (7)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 12/2021

Efgartigimod (Vyvgart™)

Goal(s):

- Restrict use to OHP-funded conditions.
- Promote use that is consistent with medical evidence.

Length of Authorization:

Up to 12 months

Requires PA:

- Vyvgart™ (efgartigimod) pharmacy and physician administered claims.

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is this an FDA approved indication?	**Yes**: Go to #3	**No:** Pass to RPh. Deny; medical appropriateness
3. Is this a request for continuation of therapy?	**Yes:** Go to **Renewal Criteria**	**No:** Go to #4
4. Is the diagnosis funded by OHP?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; not funded by the OHP.
5. Is the request for efgartigimod made by, or in consultation with, a neurologist or rheumatologist?	**Yes**: Go to #6	**No:** Pass to RPh. Deny; medical appropriateness
6. Does the patient have an active infection?	**Yes:** Pass to RPh. Deny; medical appropriateness.	**No:** Go to #7

Approval Criteria		
7. Has the patient received, or have contraindications to, all routine immunizations recommended for their age? Note: Routine vaccinations for patients at least 2 years of age typically included hepatitis B, hepatitis A, diphtheria, tetanus, pertussis, pneumococcal conjugate, inactivated poliovirus, influenza, and at least 2 doses of measles, mumps, rubella, and varicella. Immunization with live-attenuated or live vaccines is not recommended during efgartigimod treatment.	**Yes:** Go to #8. Document physician attestation of immunization history	**No:** Pass to RPh. Deny; medical appropriateness. Administer vaccines before initiation of a new treatment cycle of efgartigimod
8. Does the patient have a positive serological test for anti-AChR antibodies?	**Yes:** Go to #9	**No:** Pass to RPh. Deny; medical appropriateness
9. Does the patient have a Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of class II, III or IV?	**Yes:** Go to #10	**No:** Pass to RPh. Deny; medical appropriateness
10. Does the patient have a myasthenia gravis-specific activities of daily living scale (MG-ADL) total score of 5 points or more?	**Yes:** Go to #11 Record baseline MG-ADL score	**No:** Pass to RPh. Deny; medical appropriateness
11. Has the patient received or is currently receiving two immunosuppressant therapies (as monotherapy or in combination) for at least one year without adequate symptom control or do they have contraindications to these therapies? Example immunosuppressant therapies: - Azathioprine - Cyclosporine - Mycophenolate mofetil - Tacrolimus - Methotrexate - Cyclophosphamide	**Yes:** Go to #12	**No:** Pass to RPh. Deny; medical appropriateness. Recommend trial of immunosuppressant therapy

Approval Criteria		
12. Is the request for efgartigimod dosing that corresponds to FDA labeling? • 10 mg/kg once weekly for 4 weeks • For patients weighing 120 kg or more, the recommended dose is 1200 mg per infusion	**Yes:** Approve for up to two cycles. Each cycle is 1 dose/week for 4 weeks. The second cycle should not be administered sooner than 50 days from start of previous cycle.	**No:** Pass to RPh. Deny; medical appropriateness

Renewal Criteria		
1. Has it been 50 days or more from the start of the previous efgartigimod treatment cycle?	**Yes**: Go to #2	**No:** Pass to RPh. Deny; medical appropriateness
2. Is this request for the first renewal of efgartigimod?	**Yes**: Go to #3	**No:** Go to #4
3. Has the patient experienced a reduction in symptoms of at least 2 points from MG-ADL total baseline score?	**Yes**: Approve for up to 5 cycles. Each cycle is 1 dose/week for 4 weeks. Additional cycles should not be administered sooner than 50 days from start of previous cycle. Record MG-ADL score	**No:** Pass to RPh. Deny; medical appropriateness
4. Has the patient maintained a stable MG-ADL score over the last 12 months of efgartigimod therapy?	**Yes**: Approve for up to 7 cycles. Each cycle is 1 dose/week for 4 weeks. Additional cycles should not be administered sooner than 50 days from start of previous cycle. Record MG-ADL score	**No:** Pass to RPh. Deny; medical appropriateness