Efgartigimod alfa and hyaluronidase-qvfc (VYVGART HYTRULO) in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
National Drug Mini-Monograph
January 2025

VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL INFORMATION[1]		
	Description / MOA	Neonatal Fc receptor blocker
	Indication Under Review	Chronic inflammatory demyelinating polyneuropathy (CIDP)
	Dosage Regimen	1,008mg/11,200 units once weekly via slow subcutaneous injection. **Must be administered by a healthcare professional**
	Dosage Forms Under Review	1,008 mg efgartigimod alfa and 11,200 units hyaluronidase in a single-dose vial

EFFICACY CONSIDERATIONS		
	Trial	**ADHERE, phase II trial[2]**
	Design	Multistage trial **Run-in stage:** participants on steroids or immunoglobulins were discontinued and observed for clinical deterioration to move on to Stage A. Patients off therapy for CIDP were assessed for clinical deterioration in the 3 months before screening. This run-in stage attempts to include people with active disease. **Stage A:** maximum 12-week open label period where all participants received efgartigimod and hyaluronidase once weekly until evidence of clinical improvement (ECI). ECI was defined as adjusted Inflammatory Neuropathy Cause and Treatment (aINCAT) decrease of ≥1 point (or for patients who had been on CIDP treatment and only worsened in grip strength or Inflammatory Rasch-built Overall Disability Scale (I-RODS), there needed to be improvement on these scales by ≥8 k-Pa or ≥4 points respectively) from Stage A baseline. Primary endpoint was percent of participants with confirmed ECI. Only patients with ECI could advance to Stage B. **Stage B:** randomly assigned 1:1 efgartigimod and hyaluronidase or placebo for 48 weeks or until a total of 88 relapses occurred. If Stage A assessed efficacy of efgartigimod; Stage B may allow assessment of degree of bias from the open label design of Stage A. Primary endpoint was time to first relapse (aINCAT increase of ≥1 point) from Stage B baseline.
	Population	**Key inclusion criteria:** definite or probable CIDP, CIDP Disease Activity Status (CDAS) ≥ 2, Inflammatory Neuropathy Cause and Treatment (INCAT) score ≥ 2. **Key exclusion criteria:** pure sensory CIDP, total IgG concentration < 6 g/L About half of the patients were on immunoglobulin therapy prior to enrollment.
	Results	**Stage A:** 214 out of 322 (66% (95% CI: 61-71.6)) had confirmed ECI. Subgroup ECI by CIDP treatment at enrollment: - Steroids: 78% - Immunoglobulin: 59% - Off treatment: 72% **Stage B:** Median time to first relapse not calculated for the efgartigimod and hyaluronidase group because less than half of the participants relapsed (31 of 110). Hazard ratio for aINCAT deterioration (i.e., score increase of ≥1 point) of efgartigimod versus placebo was 0.39 (95% CI 0.25–0.61; p<0.0001). The treatment difference for relapse rate was greater for people who had been on steroids and immunoglobulin (44% and 29% respectively) than people who were off treatment (10%).

SAFETY CONSIDERATIONS[1]		
	Boxed Warnings	none
	Contraindications	None other than hypersensitivity to efgartigimod, hyaluronidase, or other excipients included in the injection
	Other Warnings	**Infections** – the most common in ADHERE was COVID-19. Infections were mild to moderate in severity. **Vaccinations** – live or live-attenuated vaccinations should be avoided while a patient is treated with efgartigimod. **Hypersensitivity and infusion-related reactions** – severe anaphylaxis and hypotension leading to syncope have been reported. More common mild infusion-related reactions include hypertension, chills, and pain. Patients should be monitored for 30 minutes after administration. For mild to moderate infusion-related reactions, rechallenge can be considered with close observation, slower infusion rate, and as applicable, pre-medication.
	Top 3 AEs	Infection, injection site reaction, headache
	Drug Interactions	Efgartigimod can lower the effectiveness of other medications that bind to neonatal Fc receptor for effectiveness including immunoglobulin products and monoclonal antibodies。
	Pregnancy/Lactation	As efgartigimod reduces circulating IgG levels, this may reduce maternal passive immunity to the fetus or infant. Efgartigimod may also be transmitted from the mother to the developing fetus, which may inhibit the fetus' own immunoglobulin production.

PLACE IN THERAPY

DRUG/THERAPY	VANF	CFU	European Academy of Neurology (EAN) guideline[3]	Administration Considerations
Intravenous immunoglobulin (IVIg)	Formulary	N/A	Strong recommendation for induction and maintenance therapy	Healthcare provider must administer. Maintenance doses every 2 to 6 weeks.
Subcutaneous Immunoglobulin	Formulary, PA-F (w/ hyaluronidase: nonformulary)	Yes	Strong recommendation for maintenance therapy	Can be self-administered. Maintenance dose frequency can vary depending on product from every week to every 4 weeks.
Corticosteroids	Formulary	N/A	Strong recommendation for induction and maintenance therapy	Oral steroids can be self-administered. Several taper strategies.
Plasma exchange	N/A, not a pharmacy provided product		Strong recommendation for induction and maintenance therapy	Healthcare provider must administer. Requires good venous access and more specialized equipment than IV infusion.
Efgartigimod alfa and hyaluronidase	**Nonformulary**	**Yes**	**Not present (FDA approval after guideline publication)**	**Healthcare provider must administer. Maintenance dose every week.**

VHA PLACE IN THERAPY

1. Estimated prevalence of chronic inflammatory demyelinating polyneuropathy (CIDP) is 2.81 per 100,000 people.[4]
2. CIDP can have a relapsing/remitting course or a slow progressive course. Typical CIDP, the most common form of CIDP, is characterized by proximal and distal muscle weakness, decreased reflexes, and sensory loss.
3. The 2021 European Academy of Neurology (EAN) guideline on diagnosis and treatment of CIDP recommends corticosteroids, IVIg, or plasma exchange for induction therapy; and corticosteroids, immunoglobulin (IV or subcutaneous), or plasma exchange as maintenance therapy.[3] Other immunosuppressant and immunomodulating therapies (e.g., azathioprine, rituximab, etc.) may be alternatives in refractory disease or for patients who cannot tolerate the recommended therapies.[3,5]
4. The ADHERE trial demonstrated efgartigimod and hyaluronidase had a significantly decreased risk for relapse (defined as aINCAT increases of 1 or more points) versus placebo.[2] These Stage B results do help control for the potential bias seen in the open label Stage A outcome; however, Stage B outcomes may be impacted by selection bias as participants were only able to move on to Stage B if they were already reporting efficacy with efgartigimod and hyaluronidase in Stage A.
5. ADHERE's study design utilized efgartigimod and hyaluronidase as maintenance therapy, not induction. The average time since diagnosis in stage A was 4.9 years. In stage A, 40% of participants experienced clinical improvement by week 4.
6. The intravenous formulation of efgartigimod has not been studied in CIDP. The addition of hyaluronidase allows for subcutaneous administration. Hyaluronidase alone does not have a clinical effect on CIDP (the placebo group of ADHERE received placebo containing 2000 U/mL of hyaluronidase).
7. There is insufficient evidence to evaluate the comparative efficacy of efgartigimod to corticosteroids, immunoglobulins, or plasma exchange as there were no active comparators in ADHERE.
8. Efgartigimod and hyaluronidase may be considered as an alternative to established maintenance therapies for CIDP.

References

1. Efgartigimod alfa and hyaluronidase-qvfc (VYVGART HYTRULO) [prescribing information online] Boston, MA. Argenx. June 2024
2. Allen JA, Lin J, Basta I, et al. Safety, tolerability, and efficacy of subcutaneous efgartigimod in patients with chronic inflammatory demyelinating polyradiculoneuropathy (ADHERE): a multicentre, randomized-withdrawal, double-blind, placebo-controlled, phase 2 trial. Lancet Neurol. 2024; 23:1013-24
3. Van den Bergh PYK, van Doorn PA, Hadden RDM, et al. European academy of neurology/peripheral nerve society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculopathy: report of a joint task force – second revision. Eur J Neurol. 2021;28:3556–3583
4. Broers MC, Bunschoten C, Nieboer D, et al. Incidence and prevalence of chronic inflammatory demyelinating polyradiculoneuropathy: a systematic review and meta-analysis. Neuroepidemiology. 2019;52:161-172
5. Chaganti S, Hannaford A, Vucic S. Rituximab in chronic immune mediated neuropathies: a systematic review. Neuromuscular Disorders. 2022;32 (8):621–627.

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