1. Is the drug being used to treat an OHP funded condition
   AND is the requested treatment funded by OHP for that condition?
   Note that mitoxantrone is the only FDA approved treatment for secondary progressive MS
   a. Yes – Go to question 2
   b. No – Deny as follows
      Cat 1 if diagnosis is not a funded condition
      Cat 5 if prescribed treatment is not a covered benefit for member diagnosis

2. Is the member an adult (over the age of 18) with relapsing-remitting multiple sclerosis?
   a. Yes- Go to question 4
   b. No- Go to question 3

3. Is the request for ocrelizumab in an adult member with relapsing/remitting or primary progressive multiple sclerosis?
   a. Yes – Go to ocrelizumab criteria
   b. No- Deny- Cat 3: *Medication is being used outside of FDA approved indications*

4. Is the prescriber a neurologist who regularly treats multiple sclerosis patients?
   a. Yes- Go to question 5
   b. No – Deny Cat 5 - *All persons with a current condition of multiple sclerosis requiring disease modifying drug therapy should be linked to a provider able to provide comprehensive management to reduce risk of adverse outcomes.*

5. Is the request for a preferred agent glatiramer acetate, interferon beta or rituximab?
   a. Yes- Go to question 13
   b. No – Go to question 6

6. Is the request for Tecfidera (dimethyl fumarate) or Aubagio (teriflunomide)?
   a. Yes – Go to question 7
   b. No- Go to question 8

7. Has the member tried and failed treatment with at least 2 preferred agents with at least 6 months of therapy and 80% or better compliance to therapy?
   Failure of therapy documented with demonstrated clinical relapses, CNS lesion progression on MRI and/or worsening disability.
   a. Yes – Go to question 12
   b. No – Deny Cat 5 – *Member has not demonstrated use of preferred agents as treatment or failure of preferred treatments to slow disease progression*.

8. Is the request for Gilenya (fingolimod) or Tysabri (natalizumab)?
   a. Yes- Go to question 10
   b. No- Go to question 9

9. Is the request for alemtuzumab (Lemtrada)?
    a. Yes- Go to question 11
    b. No- Forward to pharmacist / medical director for appropriateness evaluation of request

10. Does the member have severe, highly active, rapidly evolving MS (Defined as at least two disabling relapses within one year and at least one gadolinium-enhancing lesion or a significant increase in T2 lesion load in comparison with a previous MRI and /or disease progression with an observable increase in disability over a six- month period)
    AND
    Has tried and failed at least 2 preferred agents with at least 6 months of therapy and 80% or better compliance to therapy?
    AND
    Has tried and failed either dimethyl fumarate (Tecfidera) or teriflunomide (Aubagio) with at least 6 months of therapy and 80% or better compliance to therapy?

a. Yes- Go to question 12
b. No- Deny Cat 5- Not medically appropriate- *these agents have serious safety risks associated with their use and should be reserved for use in patients whose MS symptoms are severe and inadequately controlled on preferred agents with more favorable long term safety records.*

11. Does the member have severe, highly active, rapidly evolving MS (Defined as at least two disabling relapses within one year and at least one gadolinium-enhancing lesion or a significant increase in T2 lesion load in comparison with a previous MRI and /or disease progression with an observable increase in disability over a six- month period)
    AND
    Has tried and failed **ALL** preferred treatments (interferon beta, glatiramer acetate & rituximab) with at least 6 months of therapy and 80% or better compliance with treatment.
    AND
    Has tried and failed at least 3 of the following agents: Tecfidera (dimethyl fumarate), Aubagio (teriflunomide), Gilenya (fingolimod) and/or Tysabri (natalizumab) with at least 6 months of therapy and 80% or better compliance with treatment.

a. Yes- Go to question 12
b. No-Deny Cat 5- Not medically appropriate- *these agents have serious safety risks (including death) associated with their use and should be reserved for use in patients whose MS symptoms are severe and inadequately controlled on other agents with more favorable long term safety records.*

12. Does the member have risk factors for an adverse outcome with the use of the medication as listed below?
    - Hepatic disease or impairment (ALT /AST $\geq$ 2 times the upper limit of normal (**Teriflunomide, Dimethyl fumarate, Fingolimod)**
    - Using any antineoplastic, immunosuppressant, or immunomodulating medications, a history of progressive multifocal leukoencephalopathy (PML) and/or a compromised immune system. (**Natalizumab, Dimethyl Fumarate, Alemtuzumab**)
    - Recent (within 6 to 12 months) myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), or heart failure, a history of second or third degree atrioventricular block or sick sinus syndrome (unless treated with a pacemaker), a prolonged QT interval at baseline, and/or treatment with anti-arrhythmic drug, calcium channel blocker or beta - blocker. **(Fingolimod)**
    - Macular edema **(Fingolimod)**
    - Previous grade 3 or 4 infusion reaction, active infection, pre-existing or ongoing malignancy **(Alemtuzumab, Rituximab)**
    - Possible pregnancy -member must have negative pregnancy test and documented reliable contraception **(Teriflunomide)**

    a. Yes –Deny Cat 5- not medically appropriate -*member at high risk of adverse outcome with use of this medication due to pre-existing conditions.*
    b. No – Go to question 13.

13. Is the medication being used within FDA approved dosing guidelines?

Preferred agents

Glatiramer Acetate (Copaxone, Glatopa) --- 20 mg SQ daily OR 40 mg SQ three times weekly

Interferon beta 1a –(Avonex)– 30 mcg IM once weekly OR Rebif -22 mcg or 44 mcg three times weekly

Interferon beta 1b – (Betaseron, Extavia) – 250 mcg SQ every other day

Peginterferon beta 1a – (Plegridy)-125 mcg SQ every 14 days

Rituximab – Rituxan - 500 to 1000 mg IV every 6 months

Non- preferred agents

Dimethyl Fumarate (Tecfidera) – 240 mg orally BID

Fingolimod (Gilenya) -0.5 mg orally QD

Teriflunomide (Aubagio) - 7 mg or 14 mg orally QD

Alemtuzumab (Lemtrada) – 12 mg IV QD for 5 days, then 12 mg IV QD for 3 days beginning 12 months later- **NOT APPROVED FOR USE BEYOND 8 infusions / 2 years**

Natalizumab (Tysabri) – 300 mg IV every 4 weeks

a. Yes – May approve for 6 month trial
b. No – Deny Cat 3 – *Medication is being used outside of FDA approved dosing*

Renewal Criteria

1. Has the member's condition improved (fewer relapses, slowed progression of disability, slower rate of lesion formation on MRI)
   AND
   Has member been compliant with therapy (using 80% of the time or more)
   a. Yes – Go to question 2
   b. No - May approve for up to additional 3 months to continue assessment of efficacy and adherence IF member is tolerating medication or Deny Cat 5 if not medically appropriate.

2. Has member tolerated medication without significant side effects AND is the member being monitored (CBC, LFTs, screening for infection/malignancy)?
   a. Yes- May approve up to 12 months
   b. No- May approve up additional 3 months to allow screening to be completed OR Deny Cat 5.

Ocrevus (ocrelizumab)

1. Does the member have relapsing remitting multiple sclerosis?
   a. Yes – Go to question 3
   b. No – Go to question 2

2. Does the member have primary progressive multiple sclerosis?
   a. Yes – Go to question 3
   b. No- Deny Cat 3 – Ocrevus is only FDA approved for the treatment of RRMS and PPMS

3. Is the member under the care of a neurologist who regularly treats MS patients?
   a. Yes – Go to question 4
   b. No- Deny Cat 5 - *All persons with a current condition of multiple sclerosis requiring disease modifying drug therapy should be linked to a provider able to provide comprehensive management to reduce risk of adverse outcomes.*

4. Deny Ocrevus and offer rituximab (Rituxan) J9310-
   Rituxan is nearly identical to Ocrevus and has many years of efficacy and safety data available.

Ampyra (dalfampridine)

1. Is the member and adult aged 18 to 70 years with a diagnosis of multiple sclerosis?
   a. Yes- Go to question 2
   b. No- Deny Cat 3 – This medication is only FDA approved for adult patients with multiple sclerosis under the age of 70.

2. Is the member under the care of a neurologist?
   a. Yes- Go to question 3
   b. No - Deny Cat 5 - *All persons with a current condition of multiple sclerosis requiring drug therapy should be linked to a provider able to provide comprehensive management to reduce risk of adverse outcomes.*

3. Does the member have a history of seizures OR moderate to severe renal impairment (eGFR less than 50 ml/min)
   a. Yes – Deny Cat 5 – *Seizure disorders and renal impairment represent contraindications to treatment with this medication*.
   b. No – Go to question 6

4. Is the patient ambulatory with a walking disability requiring use of a walking aid
   OR;
   have moderate ambulatory dysfunction and does not require a walking aid
   AND
   able to complete the baseline timed 25-foot walk test between 8 and 45 seconds?
   AND
   Is the use of dalfampridine necessary for the treatment of member's MS and expected to improve the health of the member?
   a. Yes – Approve for up to 4 weeks for trial – 10 mg orally every 12 hours
   b. No – Deny Cat 3 – Medication is being prescribed outside of FDA prescribing OR
      Deny Cat 10 – Services for convenience that are not necessary for the treatment and expected to improve the basic health status of the member are not a covered benefit.

Renewal Criteria

1. Has the patient been taking dalfampridine for at least 4 weeks and has demonstrated that walking speed has improved while on dalfampridine (documentation of ≥20% improvement from baseline in timed 25 foot walk).
   AND
   Has the use of the medication demonstrated an improvement in the basic health of the member?

a. Yes – May approve for up to 6 months
b. No – Deny Cat 5 – *Fewer than 50% of MS patients will respond to therapy. Objective improvements do not justify continued therapy.*