MTF Formulary Management for Multiple Sclerosis Drugs

Defense Health Agency Pharmacy Operations Division

February 2015

Bottom-line:

- **The designated BCF agent is Betaseron (interferon Beta-1b SC). Avonex (interferon Beta-1a IM) was removed from the Extended Core Formulary (ECF) and designated Uniform Formulary (UF).**
- **There are no non-formulary Multiple Sclerosis (MS) Agents.**
- **Prior Authorization for Gilenya (fingolimod) was updated to reflect that patients with a significant cardiac history are not candidates for the drug.**

Uniform Formulary Decision: The Director, DHA approved the recommendations from the November 2014 DoD P&T Committee meeting in February 2015, with an implementation date of March 5, 2015.

Uniform Formulary (UF) drugs		**Non-Formulary (NF) drugs**
BCF drugs - MTFs <u>must</u> have on formulary	**MTFs <u>may</u> have on formulary**	**MTFs <u>must not</u> have on formulary**
<u>Injectable agent:</u> • Betaseron (Interferon Beta-1b)	**<u>Injectable agents:</u>** Rebif (Interferon Beta-1a SQ) Rebidose (Interferon Beta-1a SQ) Avonex (Interferon Beta-1a IM) Betaseron (Interferon Beta-1b) Extavia (Interferon Beta-1b) Copaxone (Glatiramer Acetate) **<u>Oral agents:</u>** Ampyra (Dalfampridine) Aubagio (Teriflunomide) **Gilenya (Fingolimod) **Tecfidera (Dimethyl Fumarate) Ampyra is not a disease modifying drug; it improves walking distance	**N/A** No MS drugs are designated non-formulary
**Prior authorization criteria apply to Gilenya (fingolimod) and Tecfidera (dimethyl fumarate); see below.		

Clinical Summary

- In the absence of head-to-head studies, no injectable drug is considered preferred over another in terms of efficacy and safety. There is conflicting evidence from two systematic reviews regarding the efficacy of Interferon beta-1a IM (Avonex) in terms of relapse related outcomes compared to the other interferons.
- The Canadian Agency for Drugs in Technology and Health (CADTH 2013) recommends Copaxone (glatiramer), or Interferon Beta 1b as initial choice of treatment for patients with MS.
- The oral disease modifying drugs for MS (MS-DMDs) have all shown superiority over placebo for all relevant outcomes. No head-to-head studies have been conducted comparing the oral formulations.
- Indirect comparisons of the MS-DMDs and their effect on relative annualized relapse rates (ARR) showed Gilenya (fingolimod) and Tecfidera (dimethyl fumarate) had the lowest ARR, while Avonex had the highest rate of relapse.
- Copaxone is now available in a three times a week formulation. Generics to the 20 mg formulation have yet to be approved by the FDA.

Updated: February 2015
Date of Original: May 2009

Safety

- With regard to safety, the MS-DMDs have distinct adverse reaction profiles. The interferons are associated with more flu like symptoms than Copaxone while Copaxone has more injection site reactions attributed to its use. Copaxone is pregnancy Category B.
- Gilenya is associated with cardiac abnormalities, including bradycardia and AV block. The first dose must be administered in the physician's office with the patient monitored for 6 hours following administration.
- Aubagio (Teriflunomide) is pregnancy Category X and associated with hepatotoxicity and hair loss.
- Tecfidera is associated with flushing, GI effects and lymphopenia. The association between Tecfidera and the long term risk of progressive multifocal leukoencephalopathy (PML) is unknown.
- None of the MS agents have indications in the pediatric population.

Prior Authorization Criteria:

Gilenya:

- Documented diagnosis of relapsing form of MS.
- Not approved for use with any other form of disease modifying therapy.
- Avoid use in patients with significant cardiac history within the past 6 months such as:
  i. Patients with class III/IV heart failure, myocardial infarction, unstable angina, stroke, transient ischemic attack, or decompensated heart failure requiring hospitalization
  ii. Those with a history or presence of Mobitz type II second-degree or third-degree atrioventricular (AV) block or sick sinus syndrome, unless they have a functioning pacemaker
  iii. Patients with a baseline QTc interval ≥500 ms
  iv. Those receiving treatment with class Ia or class III antiarrhythmic drugs

Tecfidera:

- Documented diagnosis of relapsing form of MS, CBC is required.
- Not approved for use with any other form of disease modifying therapy.

References

- DoD P&T Committee minutes: http://pec.ha.osd.mil/pt_minutes.php?submenuheader=5
- Current/future drug classes under review by the DoD P&T Committee: http://pec.ha.osd.mil/PT_Committee.php?submenuheader=4
- TRICARE formulary search tool: http://pec.ha.osd.mil/formulary_search.php?submenuheader=1
- Prior Authorization/Medical Necessity forms:
- http://pec.ha.osd.mil/forms_criteria.php?submenuheader=1
- Point of contact for additional information: usarmy.jbsa.medcom-ameddcs.list.pecuf2@mail.mil

Multiple Sclerosis Drugs Price Comparison at MTF	
Drug & Dosage Form	**MTF cost/month (November 2014)**
Basic Core Formulary	
Betaseron (Interferon Beta-1b)	**$ Most Cost-Effective**
Uniform Formulary	
Extavia (Interferon Beta-1b)	**$$ Cost-Effective**
Rebif (Interferon Beta-1a)	**$$ Cost-Effective**
Aubagio (Teriflunomide)	**$$ Cost-Effective**
Gilenya (Fingolimod)	**$$$ Less Cost-Effective**
Avonex (Interferon Beta-1a)	**$$$ Less Cost-Effective**
Copaxone (Glatiramer Acetate)	**$$$ Less Cost-Effective**
Rebif Rebidose (Interferon Beta-1a)	**$$$ Less Cost-Effective**
Tecfidera (Dimethyl Fumarate)	**$$$ Less Cost-Effective**

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