BlueCross BlueShield of Kansas City

An Independent Licensee of the Blue Cross and Blue Shield Association

Gilenya (fingolimod) Step Therapy Program

Policy Number:
Origination: 10/2014

Last Review: 11/2014
Next Review: 11/2015

Policy

BCBSKC will provide coverage for Gilenya when the following criteria are met.

When Policy Topic is covered:

Coverage of Gilenya is recommended in those who meet the following criteria.

Food and Drug Administration (FDA)-Approved Indications

1. **Relapsing Forms of Multiple Sclerosis (MS) in Patients Who Are Not Currently Receiving Gilenya.** Approve for patients who meet the following criteria (a, b, and c):
   - **a)** The patient has a relapsing form of MS, (relapsing forms of MS include relapsing-remitting multiple sclerosis [RRMS], secondary-progressive multiple sclerosis [SPMS] with relapses, and progressive-relapsing multiple sclerosis [PRMS]); AND
   - **b)** The agent is prescribed by, or in consultation with, a neurologist or a physician who specializes in the treatment of MS; AND
   - **c)** The patient meets ONE of the following conditions (i or ii):
     - **i.** The patient is unable to administer injections due to dexterity issues or visual impairment; OR
     - **ii.** The patient has tried one of the following: Avonex, Rebif, Betaseron, Extavia, or Copaxone.

Gilenya is indicated for the treatment of patients with relapsing forms of MS to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability. MS can be a devastating neurological disease and requires extensive follow-up and monitoring of disease activity (e.g., magnetic resonance imaging [MRI] studies to determine axonal damage). Patients are usually followed by a neurologist or a physician who specializes in the treatment of MS, or after consultation with such a specialist if access is limited, to determine the most appropriate care. The interferon beta products and Copaxone have been available in the US since the mid-1990s and have established efficacy and long-term safety. In general, Copaxone is at least as effective as interferon beta products.[7-8] Experience with Gilenya is limited and long-term safety data are not available. Guidelines by the National MS Society, updated in 2008, recommend the interferon beta products and Copaxone therapy as first-line as soon as possible after a definite diagnosis of MS with active, relapsing disease, or in those who have experienced a first attack who are at high risk for MS. There are no extensive, evidence-based, nationally recognized updated guidelines that currently address use of Gilenya.[5] A recent review, published in 2012, states that Gilenya should be reserved as a second-line agent for MS until further long-term safety investigations have established its risk versus benefit.[6] There are limitations in comparing more recently performed pivotal trials with Gilenya with the pivotal trials involving interferon beta products and Copaxone (e.g., heterogenous patient populations, use of different MS diagnostic criteria, varying standards of care, different annualized relapse rates at baseline). The TRANSFORMS trial was a direct comparison between Gilenya and Avonex, which did demonstrate superiority of Gilenya over the 1-year treatment period.[1,3] However, it should be noted that among the interferon beta products, data suggest that Avonex is less effective compared with other products (i.e., Rebif).[9] In the professional opinion of specialized physicians, these criteria have been adopted.

2. **Relapsing Forms of Multiple Sclerosis (MS) in Patients Who Are Currently Receiving Gilenya or Who Have Received Gilenya in the Past.** Approve if the patient meets the following criteria (a and b):
   a) Patient has a relapsing form of MS, (relapsing forms of MS include RRMS, SPMS with relapses, and PRMS); AND
   b) The agent is prescribed by, or in consultation with, a neurologist or a physician who specializes in the treatment of MS.

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When Policy Topic is not covered:

Coverage of Gilenya is recommended in circumstances that are listed in the Recommended Authorization Criteria (FDA-Approved Indications and Other Uses with Supportive Evidence). The following provides rationale for specific Exclusions. This is not an exhaustive list of Exclusions.

1. **Patient has a Non-Relapsing Form of Multiple Sclerosis (MS)** [e.g., primary progressive MS]. The efficacy of Gilenya have not been established in patients with MS with non-relapsing forms of MS.[1]

2. **Concurrent use of Gilenya with Other Disease-Modifying Agents Used for Multiple Sclerosis (MS) [i.e., Avonex, Rebif, Betaseron, Extavia, Copaxone, Tysabri, Aubagio® {teriflunomide tablets}, Tecfidera™ {dimethyl fumarate delayed-release capsules}].** These agents are not indicated for use in combination. Studies regarding combination use of Gilenya with other disease-modifying agents used for MS have not been done.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Considerations

Gilenya requires prior authorization through the Clinical Pharmacy Department.

This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Hayes Medical Technology Directory, Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.

Description of Procedure or Service

Gilenya, a sphingosine 1-phosphate receptor modulator, is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS) to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.[1] The recommended dose of Gilenya is 0.5 mg orally once daily (QD). The initiation of Gilenya leads to decreases in heart rate. After the first dose of Gilenya, the heart rate decreases are noted within an hour and generally are greatest at 6 hours, although the effects can be observed 24 hours after the first dose in some patients. The first dose of Gilenya should be given in a setting with resources to appropriately manage symptomatic bradycardia. Observe patients for 6 hours after the first Gilenya dose for signs and symptoms of bradycardia. Patients with prolonged QTc interval at baseline or during the observation period, or taking medications with known risks of torsades de pointes, should be observed overnight with continuous electrocardiographic (ECG) monitoring. The most common adverse events (AEs) with Gilenya include headache, influenza,

diarrhea, back pain, liver transaminase elevations, and cough. Gilenya is associated with serious toxicities such as decreased heart rate and/or atrioventricular condition after the first dose; an increased risk of infections; macular edema; pulmonary toxicity; elevated liver enzymes; and fetal risk. Gilenya is rated in Pregnancy Category C.

Rationale

Clinical Data

The efficacy of Gilenya was demonstrated in two pivotal trials that assessed Gilenya 0.5 mg QD and Gilenya 1.25 mg QD in patients with relapsing-remitting MS.[1-3] The FREEDOMS (FTY720 Research Evaluation Effects of Daily Oral therapy in Multiple Sclerosis) trial (n = 1,272) found that after 24 months, the annualized relapse rate was lower for patients randomized to Gilenya 0.5 mg QD (0.18) compared with placebo (0.40) [P < 0.001].[1-2] The percentage of patients who did not experience a relapse was higher for patients given Gilenya 0.5 mg (70%) compared with placebo (46%) [P < 0.001].[1-2] The TRANSFORMS (TRial Assessing injectable interferoN versuS FTY720 Oral in Relapsing-remitting Multiple Sclerosis) study (n = 1,292) found that after 1 year, the annualized relapse rate was lower in patients given Gilenya 0.5 mg QD (0.16) compared with patients given Avonex® (interferon beta-1a [intramuscular {IM}]) 30 mcg by IM injection (0.33) [P < 0.001].[1,3] The percentage of patients without a relapse were 83% for those given Gilenya 0.5 mg QD compared with 70% for patients given Avonex (P < 0.001).

Disease Course

Four different clinical courses in MS have been described.[4] Relapsing-remitting MS is characterized by acute worsening of neurologic function, usually followed by almost-complete recovery with limited progression. Approximately 85% of patients are initially diagnosed with relapsing-remitting MS. Disability progression is usually minimal. However, many patients will experience secondary progression of disability in time and will have a different form of MS. Secondary progressive MS follows an initial relapsing-remitting course and the disease transitions to a steadily progressive form with increased loss of function. Of the 85% of patients who initially have relapsing-remitting MS, more than 50% will develop secondary progressive MS within 10 years and 90% within 25 years. Primary progressive MS is noted as a continued worsening of disease from onset, without distinct relapses. Approximately 10% of patients are diagnosed with primary progressive MS. Progressive-relapsing MS starts with disease progression at onset with occasional acute relapses and continuing disease progression. Around 5% of patients appear to have progressive-relapsing MS at diagnosis. Around 10% of people with MS have a benign disease course, which is usually determined retrospectively. Relapses or exacerbations of MS can vary in severity, duration, and frequency, as well as in the symptomatology.

GUIDELINES

Evidence-based guidelines that extensively review the clinical literature regarding therapies for MS have not been updated recently.[5] In 2008 the National Clinical Advisory Board of the National MS Society published an expert opinion paper regarding treatment recommendations for physicians. Initiation of therapy with an interferon beta medication (i.e., Avonex, Rebif® [interferon beta-1a subcutaneous {SC}], Betaseron®/Extavia® [interferon beta-1b SC]), or Copaxone® (glatiramer acetate injection SC) should be considered as soon as possible after a definite diagnosis of MS with active, relapsing disease, and it may be considered for selected patients with a first attack who are at high risk for MS. Therapy should be continued indefinitely unless it is not tolerated or benefit is not obtained. The oral disease-modifying agents approved for relapsing forms of MS have not been incorporated into the expert opinion paper. Tysabri® (natalizumab injection) is generally recommended for those who have had an inadequate response to, or are unable to tolerate, other MS therapies. Treatment with mitoxantrone injection may be considered for selected relapsing patients with worsening disease or patients with secondary progressive MS who are worsening, whether or not relapses are occurring.[5] A review article published in 2012 notes that Gilenya should be reserved as a second-line agent for MS until further long-term safety data have evaluated the risks of infectious complications and secondary cancers.[6] Most patients with MS have a satisfactory response to first-line agents with minimal AEs and

such agents should be used as initial treatment for MS. The review also notes that there are no established clinical guidelines in the US addressing use of Gilenya in MS.

References:

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Billing Coding/Physician Documentation Information

N/A Gilenya is considered a pharmacy benefit.

Additional Policy Key Words

Policy Number**:**

Related Topics

N/A

Policy Implementation/Update Information

10/2014 New Policy titled Gilenya (fingolimod) Step Therapy Program