



5.60.009

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	April 1, 2026
<b>Subsection:</b>	Central Nervous System Drugs	<b>Original Policy Date:</b>	April 1, 2013
<b>Subject:</b>	Aubagio	<b>Page:</b>	1 of 9

---

**Last Review Date:** March 6, 2026

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## Aubagio

### Description

#### Aubagio (teriflunomide)

#### Background

Aubagio (teriflunomide) is indicated for relapsing multiple sclerosis. It is an anti-inflammatory immunomodulatory agent, which inhibits dihydroorotate dehydrogenase, a mitochondrial enzyme involved in de novo pyrimidine synthesis. The exact mechanism by which teriflunomide exerts its therapeutic effect in multiple sclerosis is unknown but may involve a reduction in the number of activated lymphocytes in the CNS (1).

#### Regulatory Status

FDA-approved indication: Aubagio is a pyrimidine synthesis inhibitor indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease (1).

The Aubagio label includes a boxed warning citing the risk of hepatotoxicity. Aubagio is contraindicated in patients with severe hepatic impairment. Severe liver injury, including fatal liver failure, has been reported in patients treated with leflunomide, which is indicated for rheumatoid arthritis. A similar risk would be expected for teriflunomide because recommended doses of teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. Concomitant use of Aubagio with other potentially hepatotoxic drugs may increase the risk of severe liver injury. Obtain transaminase and bilirubin levels within 6 months before initiation of Aubagio and monitor ALT levels at least monthly for six months after starting Aubagio. If drug induced liver injury is suspected, discontinue Aubagio and start an accelerated

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	April 1, 2026
<b>Subsection:</b>	Central Nervous System Drugs	<b>Original Policy Date:</b>	April 1, 2013
<b>Subject:</b>	Aubagio	<b>Page:</b>	2 of 9

---

elimination procedure. Elimination of Aubagio can be accelerated by administration of cholestyramine or activated charcoal for 11 days (1).

Aubagio also carries a boxed warning on the risk of teratogenicity. Aubagio is contraindicated in pregnant women or women of childbearing potential who are not using reliable contraception. Pregnancy must be avoided during Aubagio treatment or prior to the completion of an accelerated elimination procedure after Aubagio treatment has ended. If pregnancy does occur during treatment, the drug should be immediately discontinued, and an accelerated elimination procedure should be initiated. It is possible that rapidly lowering the plasma concentration of teriflunomide by instituting an accelerated elimination procedure may decrease the risk to the fetus from Aubagio. Under these conditions, the patient should be referred to an obstetrician/gynecologist, preferably experienced in reproductive toxicity, for further evaluation and counseling. Men wishing to father a child should discontinue use of Aubagio and undergo an accelerated elimination procedure to decrease the plasma concentration of teriflunomide to less than 0.02 mg/L (1).

Teriflunomide is the principal active metabolite of leflunomide. Co-administration of teriflunomide with leflunomide is contraindicated (1).

Aubagio may decrease WBC. Do not start Aubagio in patients with active infections. Patients with active acute or chronic infections should not start treatment until the infection(s) is resolved. Monitor for signs and symptoms of infection. If a patient develops a serious infection, consider suspending treatment with Aubagio and using an accelerated elimination procedure. Aubagio is not recommended for patients with severe immunodeficiency, bone marrow disease, or severe, uncontrolled infections. Medications like teriflunomide that have immunosuppression potential may cause patients to be more susceptible to infection, including opportunistic infection. Obtain a complete blood cell count (CBC) within 6 months before the initiation of treatment with Aubagio (1).

In clinical studies with Aubagio, cases of tuberculosis have been observed. Prior to initiating Aubagio, screen patients for latent tuberculosis infection with a tuberculin skin test. Aubagio has not been studied in patients with a positive tuberculosis screen, and the safety of Aubagio in individuals with latent tuberculosis infection is unknown. For patients testing positive to tuberculosis screening, treat by standard medical practice prior to therapy with Aubagio (1).

In placebo-controlled studies, peripheral neuropathy, including both polyneuropathy and mononeuropathy, was reported more frequently in patients taking Aubagio than in patients taking placebo. If a patient develops symptoms consistent with peripheral neuropathy, evaluate the patient and consider discontinuing Aubagio and using accelerated elimination procedure (1).

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	April 1, 2026
<b>Subsection:</b>	Central Nervous System Drugs	<b>Original Policy Date:</b>	April 1, 2013
<b>Subject:</b>	Aubagio	<b>Page:</b>	3 of 9

---

Serum potassium level and renal function should be checked in Aubagio-treated patients with symptoms of hyperkalemia or with acute renal failure (1).

Rare cases of Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in patients with rheumatoid arthritis receiving leflunomide. A similar risk would be expected for teriflunomide. If a patient taking Aubagio develops any of these conditions, stop Aubagio therapy and perform an accelerated elimination procedure (1).

Blood pressure should be checked before the start of Aubagio treatment and periodically thereafter. Elevated blood pressure should be appropriately managed during treatment with Aubagio (1).

Interstitial lung disease and worsening of pre-existing interstitial lung disease have been reported during treatment with leflunomide. A similar risk would be expected for teriflunomide. If discontinuation of the drug is necessary, consider initiation of an accelerated elimination procedure (1).

Live, attenuated vaccines are generally not recommended for a person with MS because their ability to cause disease has been weakened but not totally inactivated (2).

The safety and effectiveness of Aubagio in pediatric patients have not been established (1).

### **Related policies**

Acthar Gel, Ampyra, Gilenya, Kesimpta, Lemtrada, Mavenclad, Mayzent, MS Injectables, Ocrevus, Ponvory, Tecfidera, Tysabri, Zeposia

### **Policy**

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Aubagio may be considered **medically necessary** if the conditions indicated below are met.

Aubagio may be considered **investigational** for all other indications.

## **Prior-Approval Requirements**

### **Teriflunomide only**

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	April 1, 2026
<b>Subsection:</b>	Central Nervous System Drugs	<b>Original Policy Date:</b>	April 1, 2013
<b>Subject:</b>	Aubagio	<b>Page:</b>	4 of 9

---

**Age** 18 years of age or older

## **Diagnosis**

Patient must have the following:

Relapsing Multiple Sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease

**AND ALL** of the following:

1. Recent (within the past 6 months) transaminase and bilirubin levels
2. Result for latent TB infection is negative **OR** result was positive for latent TB and patient completed treatment for latent TB
3. **NO** severe hepatic impairment
4. **NO** active infection
5. **NO** concomitant therapy with Arava (leflunomide)
6. Females of reproductive potential **only**: pregnancy has been excluded and reliable contraception will be used during treatment
7. **NOT** used in combination with another MS disease modifying agent
8. **NOT** given concurrently with live vaccines

## **Aubagio only**

**Age** 18 years of age or older

## **Diagnosis**

Patient must have the following:

Relapsing Multiple Sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease

**AND ALL** of the following with provided documentation (e.g., medical records, laboratory reports):

1. Recent (within the past 6 months) transaminase and bilirubin levels
2. Result for latent TB infection is negative **OR** result was positive for latent TB and patient completed treatment for latent TB
3. **NO** severe hepatic impairment
4. **NO** active infection

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	April 1, 2026
<b>Subsection:</b>	Central Nervous System Drugs	<b>Original Policy Date:</b>	April 1, 2013
<b>Subject:</b>	Aubagio	<b>Page:</b>	5 of 9

---

5. **NO** concomitant therapy with Arava (leflunomide)
6. Females of reproductive potential **only**: pregnancy has been excluded and reliable contraception will be used during treatment
7. **NOT** used in combination with another MS disease modifying agent
8. **NOT** given concurrently with live vaccines
9. Patient **MUST** have tried the preferred product(s) (see Appendix 1) unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

## **Prior – Approval *Renewal* Requirements**

### **Teriflunomide only**

**Age** 18 years of age or older

### **Diagnosis**

Patient must have the following:

Relapsing Multiple Sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease

**AND ALL** of the following:

1. **NO** severe hepatic impairment
2. **NO** active infection (including tuberculosis)
3. **NO** concomitant therapy with Arava (leflunomide)
4. Females of reproductive potential **only**: pregnancy has been excluded and reliable contraception will be used during treatment
5. **NOT** used in combination with another MS disease modifying agent
6. **NOT** given concurrently with live vaccines

### **Aubagio only**

**Age** 18 years of age or older

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	April 1, 2026
<b>Subsection:</b>	Central Nervous System Drugs	<b>Original Policy Date:</b>	April 1, 2013
<b>Subject:</b>	Aubagio	<b>Page:</b>	6 of 9

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## Diagnosis

Patient must have the following:

Relapsing Multiple Sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease

**AND ALL** of the following with provided documentation (e.g., medical records, laboratory reports):

1. **NO** severe hepatic impairment
2. **NO** active infection (including tuberculosis)
3. **NO** concomitant therapy with Arava (leflunomide)
4. Females of reproductive potential **only**: pregnancy has been excluded and reliable contraception will be used during treatment
5. **NOT** used in combination with another MS disease modifying agent
6. **NOT** given concurrently with live vaccines
7. Patient **MUST** have tried the preferred product(s) (see Appendix 1) unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

## Policy Guidelines

### Pre - PA Allowance

None

### Prior - Approval Limits

<b>Quantity</b>	7 mg	90 tablets per 90 days <b>OR</b>
	14 mg	90 tablets per 90 days

**Duration** 12 months

### Prior – Approval *Renewal* Limits

Same as above

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	April 1, 2026
<b>Subsection:</b>	Central Nervous System Drugs	<b>Original Policy Date:</b>	April 1, 2013
<b>Subject:</b>	Aubagio	<b>Page:</b>	7 of 9

## Rationale

### Summary

Aubagio is an immunomodulatory agent with anti-inflammatory properties and is indicated for the treatment of patients with relapsing forms of multiple sclerosis. Aubagio carries a boxed warning for an increased risk for liver injury and teratogenicity. Patients with active acute or chronic infections should not start treatment until the infection(s) is resolved. Co-administration of Aubagio with Arava (leflunomide) is contraindicated. Aubagio has not been studied in patients with a positive tuberculosis screen, and the safety of Aubagio in individuals with latent tuberculosis infection is unknown. Elimination of Aubagio can be accelerated by administration of cholestyramine or activated charcoal for 11 days. The safety and efficacy of Aubagio in pediatric patients have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Aubagio while maintaining optimal therapeutic outcomes.

### References

1. Aubagio [package insert] Cambridge, MA: Genzyme Corporation; June 2024.
2. Cahill JF, Izzo A, Garg N. Immunization in patients with multiple sclerosis. *Neurological Bulletin*. 2010;2(1):17-21.

## Policy History

Date	Action
March 2013	Addition to PA
July 2013	Correction to quantity based on a 28-day blister pack
September 2013	Annual editorial review and reference update.
December 2014	Annual editorial review Removal of requirement ALT levels 2 times less than ULN, agreement to monitor transaminase and bilirubin levels at least once a month for first six months of therapy, and recent (within the past 6 months) complete blood count (CBC).
March 2015	Annual editorial review and reference update
September 2016	Annual editorial review and reference update. Addition of these medications should not be used in combination with other MS disease modifying agents. Policy code changed from 5.07.09 to 5.60.09

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	April 1, 2026
<b>Subsection:</b>	Central Nervous System Drugs	<b>Original Policy Date:</b>	April 1, 2013
<b>Subject:</b>	Aubagio	<b>Page:</b>	8 of 9

---

December 2016	Annual editorial review Clarification on the TB requirement and addition of not given concurrently with live vaccines
March 2017	Annual review
June 2017	Annual review
November 2018	Annual editorial review and reference update
July 2019	Revised quantity limits to match new packaging
September 2019	Annual review
December 2019	Revised relapsing MS indication to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease
March 2020	Annual review
April 2020	Added statement that Aubagio is a preferred product
June 2020	Annual review and reference update
September 2020	Annual review
December 2020	Annual review and reference update
March 2021	Annual review and reference update
June 2021	Annual review
March 2022	Annual review and reference update
December 2022	Annual review and reference update. Changed policy number to 5.60.009. Per SME, revised initiation requirement so patient has to be TB negative or complete treatment for TB before starting Aubagio
March 2023	Annual review
April 2023	Added Medex requirement for brand Aubagio and added Appendix 1. Revised contraception requirement for consistency
June 2023	Annual review
December 2023	Annual review
March 2024	Annual review
December 2024	Annual review and reference update
March 2025	Annual review
December 2025	Annual review. Removed list of injectable MS medications from Appendix and removed that patient must t/f teriflunomide. Added documentation requirement for non-preferred medication
March 2026	Annual review

### Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.**

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	April 1, 2026
<b>Subsection:</b>	Central Nervous System Drugs	<b>Original Policy Date:</b>	April 1, 2013
<b>Subject:</b>	Aubagio	<b>Page:</b>	9 of 9

---

### **Appendix 1 - List of Preferred Products**

List of preferred products:

[https://info.caremark.com/content/dam/enterprise/caremark/microsites/dig/pdfs/pa-fep/fep-misc/FEP\\_ProductMedChx.pdf](https://info.caremark.com/content/dam/enterprise/caremark/microsites/dig/pdfs/pa-fep/fep-misc/FEP_ProductMedChx.pdf)

Refer to formulary documents for confirmation of coverage:

<https://www.fepblue.org/pharmacy/prescriptions#drug-lists>