RYTARY™ (carbidopa and levodopa) extended-release oral capsule
TASMAR® (tolcapone) oral tablet
ZELAPAR (selegiline hydrochloride) orally disintegrating tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. Incomplete forms or forms without the chart notes will be returned.
Description:

Rytary (carbidopa/levodopa) extended release capsule is indicated for the treatment of Parkinson’s disease (PD), post-encephalitic parkinsonism, and parkinsonism that may follow carbon monoxide intoxication or manganese intoxication. Tasmar (tolcapone) tablet is indicated as an adjunct to carbidopa and levodopa for the treatment of signs and symptoms of idiopathic PD in patients who are experiencing symptom fluctuations and are not responding satisfactorily to or are not appropriate candidates for other adjunctive therapies. Zelapar (selegiline) oral disintegrating tablet is indicated as an adjunct in the management of patients with PD being treated with carbidopa/levodopa who exhibit deterioration in the quality of their response to this therapy.

Motor symptoms of PD are caused by a progressive degeneration of Dopamine (DA) containing neurons in the brain. Non-motor manifestations such as cognitive and psychiatric symptoms are thought to be due to degeneration of other neurotransmitter systems within the brain. Degeneration of the DA neurons leads to DA deficiency and as a result the development of the classic triad of motor symptoms of resting tremor, muscle rigidity and bradykinesia. With the development of DA deficiency, there is also a relative excess of acetylcholine activity.

Drug therapy is targeted at reducing symptoms by enhancing the effects of DA or inhibiting the effects of acetylcholine. Levodopa has been long recognized in clinical practice guidelines and texts as the standard of care for PD. It is a precursor of DA and is able to cross the blood brain barrier where it is converted to DA. Levodopa is thought to be protective against the dopaminergic neuron damage observed in PD. Levodopa is converted to DA in the periphery before it is able to cross the blood brain barrier resulting in gastrointestinal adverse effects and a lower than expected concentration of levodopa within the brain. To avoid this, levodopa is combined with carbidopa resulting in a decrease in the peripheral conversion of levodopa to DA and allowing for more levodopa to reach the brain to then be converted to DA. The combination of carbidopa/levodopa is one of the most effective treatments available for symptomatic relief of PD.

Other treatments include DA receptor agonists, catechol-O-methyl-transferase (COMT) inhibitors, selective monoamine oxidase type-B (MAOI-B) inhibitors, Amantadine, and selective use of anticholinergic agents. These agents are effective and safe in controlling motor symptoms in patients with advanced PD when used as adjunctive treatment to Levodopa. There is insufficient evidence to conclude that any one of these medications is clinically superior to another and there is insufficient evidence that shows one PD medication as superior to another in terms of improvement in functional outcomes.

Low cost generic options are available in immediate and extended-release formulations of carbidopa/levodopa as well as for each class of adjunctive therapy and are sufficient to meet the needs of most patients.
**Definitions:**

<table>
<thead>
<tr>
<th>Oral Anti-Parkinson’s disease agents</th>
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<tbody>
<tr>
<td>Carbidopa</td>
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<tr>
<td>Carbidopa generic tabs</td>
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<tr>
<td>Lodosyn tabs</td>
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<tr>
<td>Carbidopa+Levodopa</td>
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<tr>
<td>Carbidopa+Levodopa – immediate release generic tabs</td>
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<tr>
<td>Carbidopa+Levodopa ER – extended release generic tabs</td>
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<td>Carbidopa+Levodopa – ODT generic tabs</td>
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<tr>
<td>Rytary – extended release caps</td>
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<tr>
<td>Sinemet – immediate release tabs</td>
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<tr>
<td>Sinemet CR – extended release tabs</td>
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<tr>
<td>Carbidopa+Levodopa+Entacapone</td>
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<tr>
<td>Carbidopa+Levodopa+Entacapone generic tabs</td>
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<td>Stalevo tabs</td>
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<tr>
<td>COMT inhibitors</td>
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<tr>
<td>Entacapone generic tabs</td>
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<td>Comtan (entacapone) tabs</td>
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<tr>
<td>Tolcapone generic tabs</td>
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<tr>
<td>Tasmar (tolcapone) tabs</td>
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<tr>
<td>MAO-B inhibitors</td>
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<tr>
<td>Selegiline generic tabs and caps</td>
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<td>Eldedryl (selegiline) caps</td>
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<tr>
<td>Zelapar (selegiline) – ODT tab</td>
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<tr>
<td>Azilect (rasagiline) tabs</td>
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<tr>
<td>Xadago (safinamide) tabs</td>
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<tr>
<td>DA agonists</td>
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<tr>
<td>Bromocriptine generic tabs</td>
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<tr>
<td>Parlodel (bromocriptine) tabs</td>
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<tr>
<td>Pramipexole – immediate release generic tabs</td>
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<td>Pramipexole ER – extended release generic tabs</td>
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<tr>
<td>Mirapex (pramipexole) – immediate release tabs</td>
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<td>Mirapex ER (pramipexole) – extended release tabs</td>
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<tr>
<td>Ropinirole – immediate release generic tabs</td>
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<tr>
<td>Ropinirole ER – extended release generic tabs</td>
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<tr>
<td>Requip (ropinirole) – immediate release tabs</td>
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<tr>
<td>Requip XL(ropinirile) – extended release tabs</td>
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<tr>
<td>Neupro (rotigotine) – extended release patch</td>
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RYTARY™ (carbidopa and levodopa) extended-release oral capsule
TASMAR® (tolcapone) oral tablet
ZELAPAR (selegiline hydrochloride) orally disintegrating tablet (cont.)

The Child-Pugh classification system:

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<thead>
<tr>
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<th>Score: 1 point</th>
<th>Score: 2 points</th>
<th>Score: 3 points</th>
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</thead>
<tbody>
<tr>
<td><strong>Serum Albumin (g/dL)</strong></td>
<td>&gt;3.5</td>
<td>3.0 - 3.5</td>
<td>&lt;3.0</td>
</tr>
<tr>
<td><strong>Serum Bilirubin (mg/dL)</strong></td>
<td>&lt;2.0</td>
<td>2.0 - 3.0</td>
<td>&gt;3.0</td>
</tr>
<tr>
<td><strong>Prothrombin time (seconds)</strong></td>
<td>1 - 4</td>
<td>4 - 6</td>
<td>&gt;6</td>
</tr>
<tr>
<td><strong>Ascites</strong></td>
<td>none</td>
<td>moderate</td>
<td>severe</td>
</tr>
<tr>
<td><strong>Encephalopathy</strong></td>
<td>none</td>
<td>mild</td>
<td>severe</td>
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</tbody>
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The three classes and their scores are:
- **Class A** is score 5 – 6: Well compensated
- **Class B** is score 7 – 9: Significant functional compromise
- **Class C** is score >9: Decompensated disease
Rytary (carbidopa and levodopa, extended release)

Medication class:
Anti-Parkinson agent, decarboxylase inhibitor, dopamine agonist

FDA-approved indication(s):
- Treatment of Parkinson's disease
- Treatment of post-encephalitic parkinsonism
- Treatment of parkinsonism that may follow carbon monoxide intoxication or manganese intoxication

Recommended Dose:
- Starting dose is 23.75 mg / 95 mg three times daily; increase to 36.25 mg / 145 mg three times daily on the fourth day of treatment. The dose frequency may be changed from three times a day to a maximum of five times a day
- Maximum dosage
  - 612.5 mg carbidopa / 2450 mg levodopa

Available Dosage Forms:
- 23.75/95 mg, 36.25/145 mg, 48.75/195 mg, and 61.25/245 mg carbidopa/levodopa capsules

Warnings and Precautions:
- Avoid sudden discontinuation or rapid dose reductions
- Because of risk of exacerbating psychosis, patients with a major psychotic disorder should not be treated with Rytary
- Consider stopping Rytary in those who develop significant daytime sleepiness or episodes of falling asleep during activities that require active participation such as conversations eating, driving, etc.
- Consider stopping Rytary if there is development of new or increased gambling urges, sexual urges, uncontrolled spending or other urges
- The use of selective MAO-B inhibitors (such as rasagiline and selegiline) with Rytary may be associated with orthostatic hypotension
- Dopamine D2 receptor antagonists (such as phenothiazines, butyrophenones, risperidone, metoclopramide) and isoniazid may reduce the effectiveness of levodopa
- Iron salts or multivitamins containing iron salts can form chelates with levodopa and carbidopa and can cause a reduction in the bioavailability of Rytary

Criteria:

Criteria for initial therapy: Rytary is considered medically necessary and will be approved when ALL of the following criteria are met:

1. Individual is 18 years of age or older
RYTARY™ (carbidopa and levodopa) extended-release oral capsule
TASMAR® (tolcapone) oral tablet
ZELAPAR (selegiline hydrochloride) orally disintegrating tablet (cont.)

2. A confirmed diagnosis of Parkinson’s disease
3. Tried, Failed, or has Contraindication to use of generic extended-release Carbidopa/Levodopa tablets
4. There are no contraindications such as use with or within 14 days of stopping isocarboxazid, phenelzine, or tranylcypromine

Initial approval duration: 12 months

Criteria for continuation of coverage (renewal request): Rytary is considered medically necessary and will be approved with documentation of ALL of the following:

1. The condition has not worsened while on therapy
2. Individual has been adherent with the medication
3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
4. There are no significant interacting drugs

Renewal duration: 12 months
RYTARY™ (carbidopa and levodopa) extended-release oral capsule
TASMAR® (tolcapone) oral tablet
ZELAPAR (selegiline hydrochloride) orally disintegrating tablet (cont.)

Tasmar (tolcapone)

Medication class:
Anti-Parkinson agent, COMT inhibitor

FDA-approved indication(s):
- Adjunct to levodopa and carbidopa for the treatment of the signs and symptoms of idiopathic Parkinson’s disease in patients experiencing symptom fluctuations and are not responding satisfactorily or are not candidates for other adjunctive therapy

Recommended Dose:
- The initial dose is always 100 mg three times per day. It is unknown whether the risk of acute fulminant liver failure is increased at the 200 mg dose, use 200 mg only if the anticipated incremental clinical benefit is justified
- If a patient fails to show the expected incremental benefit on the 200 mg dose after a total of 3 weeks of treatment (regardless of dose), Tasmar should be discontinued

Maximum dosage
- 200 mg three times per day

Available Dosage Forms:
- 100 mg tablet

Warnings and Precautions:
- Patients should ordinarily not be treated concurrently with a non-selective MAO inhibitor such as isocarboxazid, phenelzine, or tranylcypromine
- Patients who fail to show substantial clinical benefit after 3 weeks of initiation of treatment should stop Tasmar
- It should not be initiated in patients with clinical evidence of liver disease or 2 ALT or AST values > ULN
- Patients who develop hepatocellular injury from Tasmar and are withdrawn from drug treatment should not be considered for retreatment
- Discontinue for clinical evidence of hepatotoxicity or if ALT or AST are 2x ULN
- Avoid sudden discontinuation or rapid dose reductions
- Because of risk of exacerbating psychosis, patients with a major psychotic disorder should not be treated with Tasmar
- Consider stopping Tasmar in those who develop significant daytime sleepiness or episodes of falling asleep during activities that require active participation such as conversations eating, driving, etc.
- Consider stopping Tasmar if there is development of new or increased gambling urges, sexual urges, uncontrolled spending or other urges
- Hepatotoxicity toxicity
  - Signs & symptoms may include: clay colored stools, jaundice, fatigue, loss of appetite, lethargy, nausea, lethargy, dark urine, pruritus, right upper quadrant tenderness
RYTARY™ (carbidopa and levodopa) extended-release oral capsule
TASMAR® (tolcapone) oral tablet
ZELAPAR (selegiline hydrochloride) orally disintegrating tablet (cont.)

Criteria:

- **Criteria for initial therapy:** Tasmar is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:
  1. Individual is 18 years of age or older
  2. Requires continued use of Carbidopa and Levodopa
  3. Individual experiencing symptom fluctuations
  4. Individual is not responding to or not a candidate for other adjunctive therapy for Parkinson’s disease
  5. Tried, Failed, or has Contraindication to use of generic tolcapone and entacapone (brand and generic)
  6. There are no contraindications such as liver disease, individuals who were withdrawn from Tasmar due to hepatic injury, history of non-traumatic rhabdomyolysis, or hyperpyrexia and confusion related to medication

  **Initial approval duration:** 2 months

- **Criteria for continuation of coverage (renewal request):** Tasmar is considered *medically necessary* and will be approved with documentation of **ALL** of the following:
  1. The condition has not responded while on therapy
     - Lack of response is defined as continues to have symptom fluctuation despite addition of Tasmar
  2. Individual has been adherent with the medication
  3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use, such as:
     - Any of the contraindication listed above
     - Hepatotoxicity toxicity
  4. There are no significant interacting drugs

  **Renewal duration:** 12 months
Zelapar (selegiline) ODT

Medication class:
Anti-Parkinson agent, mono-amine type B inhibitor

FDA-approved indication(s):
- An adjunct in the management of patients with Parkinson’s disease being treated with levodopa/carbidopa who exhibit deterioration in the quality of their response to this therapy

Recommended Dose:
- Initiate treatment with 1.25 mg once daily x 6 weeks; after 6 weeks, may increase to 2.5 mg once daily
  - **Maximum dosage**
  - 2.5 mg once daily

Available Dosage Forms:
- 1.25 mg orally disintegrating tablet

Warnings and Precautions:
- Dose should not exceed 2.5 mg per day due to risks associated with non-selective inhibition of MAO, selectivity of Zelapar for MAO-B may not be absolute at the recommended dose of 2.5 mg per day
- It is not recommended in patients with severe renal impairment (creatinine clearance < 30 mL/min) and end-stage renal disease
- It is not recommended in patients with severe hepatic impairment (Child-Pugh score > 9)
- Consider stopping Zelapar in those who develop significant daytime sleepiness or episodes of falling asleep during activities that require active participation such as conversations eating, driving, etc.
- Because of risk of exacerbating psychosis, patients with a major psychotic disorder should not be treated with Zelapar
- Consider stopping Zelapar if there is development of new or increased gambling urges, sexual urges, uncontrolled spending or other urges
- Avoid concurrent use with or within 14 days of stopping any antidepressant
- Avoid use within 5 weeks of stopping Fluoxetine
- Avoid use of sympathomimetics including OTC
- The possibility exists that very high tyramine containing foods could cause elevations in blood pressure, patients should avoid high tyramine containing foods
- Avoid sudden discontinuation or rapid dose reductions
- Tablets contain phenylalanine and as such there is a risk for phenylketonuria in susceptible patients
- Metabolism of Zelapar produces an \( l \)-methamphetamine & \( l \)-amphetamine metabolites that are eliminated in the urine
- Serotonin syndrome
  - Signs & symptoms may include: confusion, hypomania, hallucinations, agitation, delirium, HA, coma, syncope, shivering, sweating, high fevers, hypertension, hypotension, tachycardia, nausea, diarrhea, muscle rigidity, myoclonus, muscle twitching, hyperreflexia with clonus and tremor
- Hypertensive crisis
• Signs & symptoms may include: chest pain, severe HA accompanied with confusion and blurred vision, nausea, vomiting, severe anxiety, shortness of breath, seizure

Criteria:

➢ **Criteria for initial therapy:** Zelapar is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:

1. Individual is 18 years of age or older
2. Requires continued use of Carbidopa and Levodopa
3. Individual is experiencing deterioration in the quality of the response to therapy
4. Tried, Failed, or has Contraindication to use of generic selegiline tablets and capsules
5. There are no contraindications
   - Contraindication include:
     • Hypersensitivity to Selegiline
     • Concurrent use with cyclobenzaprine, dextromethorphan, or St. John's wort
     • Concurrent use with or within 14 days of stopping **ANY** of the following:
       - Methadone
       - Meperidine
       - Propoxyphene
       - Tramadol
       - Isocarboxazid
       - Phenelezine
       - Tranylcypromine
       - Azilect (rasagiline)
       - Other Selegiline products

**Initial approval duration:** 6 months

➢ **Criteria for continuation of coverage (renewal request):** Zelapar is considered *medically necessary* and will be approved with documentation of **ALL** of the following:

1. The condition has not responded
   - Lack of response is defined as continues to have symptom fluctuation despite addition of Zelapar
2. Individual has been adherent with the medication
3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use, such as:
   - Any of the contraindication listed above
   - Serotonin syndrome
   - Hypertensive crisis

4. There are no significant interacting drugs

**Renewal duration:** 12 months

**Resources:**


Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.

REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

<table>
<thead>
<tr>
<th>Member Information</th>
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<tbody>
<tr>
<td>Member Name (first &amp; last):</td>
<td>Date of Birth:</td>
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<tr>
<td>Address:</td>
<td>City:</td>
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</tbody>
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<tr>
<th>Prescribing Provider Information</th>
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<tbody>
<tr>
<td>Provider Name (first &amp; last):</td>
<td>Specialty:</td>
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<tr>
<td>Office Address:</td>
<td>City:</td>
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<tr>
<td>Office Contact:</td>
<td>Office Phone:</td>
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<td>Pharmacy Name:</td>
<td>Pharmacy Phone:</td>
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<tr>
<th>Requested Medication Information</th>
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<tbody>
<tr>
<td>Medication Name:</td>
<td>Strength:</td>
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<tr>
<td>Directions for Use:</td>
<td>Quantity:</td>
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☐ Check if requesting brand only  ☐ Check if requesting generic
☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

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<thead>
<tr>
<th>Turn-Around Time For Review</th>
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<tbody>
<tr>
<td>Standard</td>
<td>Urgent. Sign here: _______________________________</td>
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<tr>
<th>Clinical Information</th>
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<tbody>
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<td>1. What is the diagnosis? Please specify below.</td>
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<tr>
<td>ICD-10 Code:</td>
<td>Diagnosis Description:</td>
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<td>2. ☐ Yes ☐ No Was this medication started on a recent hospital discharge or emergency room visit?</td>
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<tr>
<td>3. ☐ Yes ☐ No There is absence of ALL contraindications.</td>
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<td>4. What medication(s) has the individual tried and failed for this diagnosis? Please specify below.</td>
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<td>Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.</td>
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<thead>
<tr>
<th>Medication Name, Strength, Frequency</th>
<th>Dates started and stopped or Approximate Duration</th>
<th>Describe response, reason for failure, or allergy</th>
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<th>5. Are there any supporting labs or test results? Please specify below.</th>
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<td>Date</td>
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Blue Cross Blue Shield of Arizona, Mail Stop A115, P.O. Box 13466, Phoenix, AZ 85002-3466  
Page 1 of 2
6. **Is there any additional information the prescribing provider feels is important to this review? Please specify below.**
   For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

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**Signature affirms that information given on this form is true and accurate and reflects office notes**

Prescribing Provider’s Signature:                      Date:  

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**Please note:** Some medications may require completion of a drug-specific request form.

**Incomplete forms or forms without the chart notes will be returned.**

Office notes, labs, and medical testing relevant to the request that show medical justification are required.