Revlimid

Description

Revlimid (lenalidomide)

Background
Revlimid is classed as an immunomodulator and is a chemical derivative of thalidomide. Although the exact mechanism of action is unknown, lenalidomide also has anti-inflammatory and anticancer properties. It selectively inhibits secretion of inflammatory cells, enhances the activity of immunity cells, and inhibits the growth of new blood vessels. The medication stops the growth of myeloma cells by causing cell cycle arrest and cell death. Revlimid is pregnancy category X, and may cause severe birth defects or fetal death (1-3).

Regulatory Status
FDA labeled indications: Revlimid is a thalidomide analogue indicated for the treatment of patients with: (1)

1. Multiple myeloma (MM), in combination with dexamethasone
2. Multiple myeloma (MM), as maintenance following autologous hematopoietic stem cell transplantation (auto-HSCT)
3. Transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes (MDS) associated with a deletion 5q abnormality with or without additional cytogenetic abnormalities
4. Mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included Velcade (bortezomib)
5. Previously treated follicular lymphoma (FL), in combination with a rituximab product
6. Previously treated marginal zone lymphoma (MZL), in combination with a rituximab product

Limitations of Use:
Revlimid is not indicated and is not recommended for the treatment of patients with chronic lymphocytic leukemia (CLL) outside of controlled clinical trials (1).

Off Label Uses: (2-5)
1. Myelodysplastic syndromes (MDS) – without the 5q deletion cytogenic abnormality
2. Systemic light chain amyloidosis
3. Classical Hodgkin lymphoma
4. Relapsed, refractory, or progressive non-Hodgkin lymphoma (NHL) with any of the following histologies:
   a. Mantle cell lymphoma (MCL)
   b. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
   c. Diffuse large B-cell lymphoma
   d. AIDS-related diffuse large B-cell lymphoma
   e. Primary effusion lymphoma
   f. Castleman’s disease
   g. Nongastric/Gastric mucosa associated lymphoid tissue (MALT) lymphoma
   h. Primary cutaneous B-cell lymphoma

Revlimid is a pregnancy category X medication, and includes a boxed warning citing embryo-fetal toxicity, hematologic toxicity and venous thromboembolism. If Revlimid is used during pregnancy, it may cause birth defects or embryo-fetal death. Pregnancy must be excluded before start of treatment. Pregnancy must be prevented during treatment by the use of two reliable methods of contraception (1).

Revlimid can cause significant neutropenia and thrombocytopenia. For patients with del 5q myelodysplastic syndromes, monitor complete blood counts weekly for the first 8 weeks and monthly thereafter (1).

Revlimid has a significantly increased risk of deep vein thrombosis (DVT) and pulmonary embolism (PE) in patients with multiple myeloma receiving Revlimid with dexamethasone (1).

Revlimid is available only through a restricted distribution program called the Revlimid REMS program (formerly known as the “RevAssist program”) (1).
Safety and effectiveness of Revlimid in pediatric patients below the age of 18 years have not been established (1).

**Related policies**

Pomalyst

**Policy**

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

Revlimid may be considered medically necessary in patients 18 years of age and older for the treatment of multiple myeloma, myelodysplastic syndromes (MDS), relapsed, refractory, or progressive non-Hodgkin lymphoma (NHL), and for the treatment of systemic light chain amyloidosis and classical Hodgkin lymphoma and if the conditions indicated below are met.

Revlimid is considered investigational for patients less than 18 years of age and for all other indications.

**Prior-Approval Requirements**

**Age** 18 years of age or older

**Diagnoses**

Patient must have **ONE** of the following:

1. Multiple myeloma (MM) with **ONE** of the following:
   a. Must be used in combination with dexamethasone or another corticosteroid
   b. Used as maintenance following autologous hematopoietic stem cell transplantation (auto-HSCT)

2. Myelodysplastic syndromes (MDS)
   a. Low- or intermediate-1 risk
   b. Transfusion-dependent anemia
3. Relapsed, refractory, or progressive non-Hodgkin lymphoma (NHL) with any of the following histologies:
   a. Mantle cell lymphoma (MCL)
   b. Follicular lymphoma
   c. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
   d. Diffuse large B-cell lymphoma
   e. AIDS-related diffuse large B-cell lymphoma
   f. Primary effusion lymphoma
   g. Castleman’s disease
   h. Nongastric/Gastric mucosa associated lymphoid tissue (MALT) lymphoma
   i. Primary cutaneous B-cell lymphoma
   j. Marginal zone lymphoma

4. Systemic light chain amyloidosis

5. Classical Hodgkin lymphoma

AND the following:
   a. Prescriber and patient must be enrolled with the Revlimid REMS Program
      (formerly known as the “RevAssist® Program"

Prior – Approval Renewal Requirements

Age  18 years of age or older

Diagnoses

Patient must have ONE of the following:

1. Multiple myeloma (MM)
2. Myelodysplastic syndromes (MDS)
3. Relapsed, refractory, or progressive non-Hodgkin lymphoma (NHL) with any of the following histologies:
   a. Mantle cell lymphoma (MCL)
   b. Follicular lymphoma
   c. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
d. Diffuse large B-cell lymphoma  
e. AIDS-related diffuse large B-cell lymphoma  
f. Primary effusion lymphoma  
g. Castleman’s disease  
h. Nongastric/Gastric mucosa associated lymphoid tissue (MALT) lymphoma  
i. Primary cutaneous B-cell lymphoma  
j. Marginal zone lymphoma  

4. Systemic light chain amyloidosis  
5. Classical Hodgkin lymphoma

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval Renewal Limits

Duration 12 months

Rationale

Summary

Revlimid is classed as an immunomodulator and is a chemical derivative of thalidomide. It is indicated for the treatment of patients with multiple myeloma (MM), transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes (MDS) associated with a deletion 5q abnormality with or without additional cytogenetic abnormalities, and mantle cell lymphoma (MCL), chronic lymphocytic leukemia (CLL), and diffuse large B-cell lymphoma. To avoid embryo-fetal exposure to Revlimid it is only available through a restricted distribution program. Prescribers must be certified with the Revlimid REMS Program (formerly known as the “RevAssist®” Program) (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Revlimid while maintaining optimal therapeutic outcomes.
Section: Prescription Drugs  Effective Date: October 1, 2019
Subsection: Antineoplastic Agents  Original Policy Date: August 22, 2014
Subject: Revlimid  Page: 6 of 7

References

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>August 2014</td>
<td>New addition to PA</td>
</tr>
<tr>
<td>September 2014</td>
<td>Annual review</td>
</tr>
<tr>
<td>October 2014</td>
<td>Removal of Multiple Myeloma one prior therapy requirement</td>
</tr>
<tr>
<td>November 2014</td>
<td>Removal of the requirement combination with dexamethasone or another corticosteroid in the Multiple Myeloma renewal section</td>
</tr>
<tr>
<td>December 2014</td>
<td>Rewording of the Myelodysplastic syndromes (MDS)</td>
</tr>
<tr>
<td>February 2015</td>
<td>Annual review and reference update</td>
</tr>
<tr>
<td>June 2015</td>
<td>Addition of follicular lymphoma, chronic lymphocytic leukemia (CLL), and diffuse large B-cell lymphoma. Change to mantle cell lymphoma to only require 1 prior therapy instead of 2 and removal of requirement of Velcade being tried and failed</td>
</tr>
<tr>
<td>September 2016</td>
<td>Annual review and reference update</td>
</tr>
<tr>
<td></td>
<td>Removal of laboratory confirmation of the deletion 5q cytogenetic abnormality and complete blood counts monitored weekly for the first 8 weeks of therapy and at least monthly thereafter and removal of used in combination with Rituxan (rituximab)</td>
</tr>
</tbody>
</table>
|                 | Addition of indications: relapsed, refractory, or progressive non-Hodgkin lymphoma (NHL) with any of the following histologies: mantle cell lymphoma (MCL), follicular lymphoma, chronic lymphocytic leukemia (CLL) /small lymphocytic lymphoma (SLL), diffuse large B-cell lymphoma, AIDS-related diffuse large B-cell lymphoma, primary effusion lymphoma, Castleman’s disease, non-gastric/Gastric mucosa associated lymphoid tissue (MALT) lymphoma, primary cutaneous B-cell lymphoma, or splenic...
<table>
<thead>
<tr>
<th>Subject:</th>
<th>Revlimid</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Section:</strong></td>
<td>Prescription Drugs</td>
</tr>
<tr>
<td><strong>Effective Date:</strong></td>
<td>October 1, 2019</td>
</tr>
<tr>
<td><strong>Subsection:</strong></td>
<td>Antineoplastic Agents</td>
</tr>
<tr>
<td><strong>Original Policy Date:</strong></td>
<td>August 22, 2014</td>
</tr>
<tr>
<td><strong>Page:</strong></td>
<td>7 of 7</td>
</tr>
</tbody>
</table>

marginal zone lymphoma; and for the treatment of systemic light chain amyloidosis and classical Hodgkin lymphoma
Policy number change from 5.04.47 to 5.21.47

- **March 2017**
  Addition of multiple myeloma when used as maintenance following autologous hematopoietic stem cell transplantation (auto-HSCT)

- **September 2017**
  Annual review

- **June 2018**
  Annual editorial review and reference update

- **June 2019**
  Annual review and reference update. Removed splenic from the diagnosis of marginal zone lymphoma

- **September 2019**
  Annual review

**Keywords**

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 13, 2019 and is effective on October 1, 2019.