Clinical Policy Title:	lenalidomide
Policy Number:	RxA.461
Drug(s) Applied:	lenalidomide, Revlimid®
Original Policy Date:	03/06/2020
Last Review Date:	08/28/2024
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

I. Initial Approval Criteria

A. Multiple Myeloma (MM) (must meet all):

1. Diagnosis of MM;
2. The requested medication is prescribed in one of the following ways (a, b, c or d):
   a. In combination with dexamethasone;
   b. As a single agent in steroid-intolerant patients with previously treated myeloma with relapse or progressive disease;
   c. As maintenance therapy as a single agent or in combination with bortezomib following autologous hematopoietic stem cell transplantation;
   d. As maintenance therapy as a single agent or in combination with bortezomib for active (symptomatic) myeloma after response to primary myeloma therapy.

Approval Duration

All Lines of Business (except Medicare): 12 months, Split-fill

B. Myelodysplastic Syndrome (MDS) (must meet all):

1. Diagnosis of 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;
2. Member meets one of the following (a, b, or c):
   a. Has symptomatic anemia;
   b. Has transfusion-dependent anemia;
   c. Has anemia that is not controlled with an erythropoiesis-stimulating agent (e.g., Epogen/Procrit [epoetin alfa injection], Aranesp [darbepoetin alfa injection]).

Approval Duration

All Lines of Business (except Medicare): 12 months, Split-fill

C. Mantle Cell Lymphoma (MCL) (must meet all):

1. Diagnosis of MCL;
2. Member meets one of the following (a or b):
   a. Has tried and failed at least two prior therapies;
   b. Used in combination with rituximab*;
   *Prior authorization may be required for rituximab.

Approval Duration

All Lines of Business (except Medicare): 12 months, Split-fill

D. Marginal Zone Lymphoma (MZL) (must meet all):
1. Diagnosis of MZL (including gastric or non-gastric mucosa-associated lymphoid tissue (MALT) lymphoma, nodal MZL, and splenic MZL);
2. Member meets one of the following (a or b):
   a. Has tried and failed at least one prior therapy;
   b. Used in combination with rituximab product;
      *Prior authorization may be required for rituximab.

Approval Duration
All Lines of Business (except Medicare): 12 months, Split-fill

E. Follicular Lymphoma (FL) (must meet all)**:**
1. Diagnosis of FL;
2. Member meets one of the following (a or b):
   a. Has tried and failed at least one prior therapy;
   b. Used in combination with rituximab product;
      *Prior authorization may be required for rituximab.

Approval Duration
All Lines of Business (except Medicare): 12 months, Split-fill

F. Other NCCN Compendium Supported Diagnoses/Indications (off-label) (must meet all):
1. Prescribed for NCCN category 1 or 2a recommended indications.

Approval Duration
All Lines of Business (except Medicare): 12 months, Split-fill

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Auto-approval based on lookback functionality within the past 120 days as a proxy for member responding positively to therapy.

Approval Duration
All Lines of Business (except Medicare): 12 months

References

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2. National Comprehensive Cancer Network. Myelodysplastic Syndromes Version 3.2024. Available at: http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed August 28, 2024.
3. National Comprehensive Cancer Network. Multiple Myeloma Version 4.2024. Available at: http://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. August 28, 2024.
4. National Comprehensive Cancer Network. B-cell Lymphomas Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed August 28, 2024.
5. National Comprehensive Cancer Network. Systemic Light Chain Amyloidosis Version 2.2024. Available at http://www.nccn.org/professionals/physician_gls/PDF/amyloidosis.pdf. Accessed August 28, 2024.
6. National Comprehensive Cancer Network. T-cell Lymphomas Version 4.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed August 28, 2024.
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8. National Comprehensive Cancer Network. Myeloproliferative Neoplasms Version 2.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed August 28, 2024.
9. National Comprehensive Cancer Network. Central Nervous System Cancers Version 2.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed August 28, 2024.
10. National Comprehensive Cancer Network. Hodgkin Lymphoma Version 3.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf. Accessed August 28, 2024.
11. Lacy MQ, Ertz MA, et.al. Long-term results of response to therapy, time to progression, and survival with lenalidomide plus dexamethasone in newly diagnosed myeloma. Mayo Clinic Proceedings. 2007 Oct; 82 (10):1179-84. Available at: https://pubmed.ncbi.nlm.nih.gov/17908524/ . Accessed August 28, 2024.
12. FDA Drug Safety Communication: Safety review update of cancer drug Revlimid® (lenalidomide) and risk of developing new types of malignancies. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-safety-review-update-cancer-drug-revlimid-lenalidomide-and-risk. August 28, 2024.
13. National Comprehensive Cancer Network. Histiocytic Neoplasms. Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/histiocytic_neoplasms.pdf. Accessed August 28, 2024.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Line of business Policy Applies to was updated to "All lines of business". 3. Initial and Continued approval criteria's approval duration for Commercial was updated from "Length of benefit" to 6 months and 12 months respectively. 4. Continued therapy approval criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 5. References were reviewed and updated.	09/04/2020	12/07/2020
Policy was reviewed: 1. Initial Approval Criteria I.F.c.iv, I.F.c.v, & I.F.c.vi was updated to include off label indication as per NCCN guidelines. 2. Initial Approval Criteria I.F.d.i, I.F.d.ii, I.F.d.iii, I.F.d.iv was updated to include off label indication as per NCCN guidelines. 3. Initial Approval Criteria I.F.g was updated to include "used in combination with prednisone taper". 4. Initial Approval Criteria I.F.h.i, I.F.h.ii, I.F.h.iii & I.F.h.iv was updated to include off label indication as per NCCN guidelines. 5. Initial Approval Criteria I.F.k was updated to include "First-line or subsequent therapy as a	9/8/2021	12/07/2021

single…" off label indication as per NCCN guidelines. 6. Initial Approval Criteria I.F.I.iii was updated to remove " AIDS related" and to include "given single agent (no HIV) or with antiretroviral therapy (ART) for people with HIV (PWH)". 7. Initial Approval Criteria I.F.I.x was updated to include "or initial palliative intent therapy". 8. Initial Approval Criteria I.F.2 was updated to include "Prescriber must be certified with the Lenalidomide REMS program". 9. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria, I.A.4, I.B.4, I.C.4, I.D.4, I.E.4, I.F.4: Updated to include new trial and failure criteria For Revlimid® requests, member must use generic lenalidomide, if available (e.g., contraindications to excipients). 2. Initial Approval Criteria, I.C.4.c: Updated to remove prior combination therapy criteria "Second line therapy as a single agent or in combination with rituximab". 3. Initial Approval Criteria, I.D.4.a: Updated to remove prior combination therapy criteria "First-line therapy in combination with rituximab". 4. Initial Approval Criteria, I.F.1.a, I.F.1.b, I.F.1.c, I.F.1.d: Updated to remove approval criteria for multiple myeloma. 5. Initial Approval Criteria, I.F.1.e: Updated to remove approval criteria for POEMS syndrome. 6. Initial Approval Criteria, I.F.1.f: Updated to remove approval criteria for MDS/MPN. 7. Initial Approval Criteria, I.F.1.a: Updated to remove prior combination therapy criteria "Used in combination with prednisone taper". 8. Initial Approval Criteria, I.F.1.b: Updated combination therapy criteria from Systemic light chain amyloidosis (i, ii, iii or iv): i. Treatment for relapsed/refractory disease in combination with dexamethasone; ii. Treatment for relapsed/refractory disease in combination with dexamethasone and cyclophosphamide; iii. Treatment for relapsed/refractory disease in combination with dexamethasone and ixazomib; iv. Treatment for newly diagnosed disease or	03/30/2022	07/18/2022

consider for relapsed/refractory disease as a repeat of initial therapy if relapse-free for several years in combination with dexamethasone and bortezomib; to Systemic light chain amyloidosis in combination with dexamethasone. 9. Initial Approval Criteria, I.F.1.c: Updated indication from Primary central nervous system (CNS) lymphoma for relapsed or refractory disease to Primary central nervous system (CNS) lymphoma as a single agent or in combination with rituximab* for relapsed or refractory disease, or if member is unsuitable or intolerant to high-dose methotrexate. 10. Initial Approval Criteria, I.F.1.d: Updated indication from Classic Hodgkin lymphoma as subsequent therapy for relapsed or refractory disease, or as palliative therapy to Classic Hodgkin lymphoma as third-line or subsequent therapy for relapsed or refractory disease. 11. Initial Approval Criteria, I.F.1.k: Updated to remove approval criteria for Langerhans Cell: First-line or subsequent therapy as a single agent for (i or ii): i. Single system multifocal skin disease (including mucosa); ii. Relapsed/refractory disease. 12. Initial Approval Criteria, I.F.1.e.iii: Updated indication from Kaposi Sarcoma as subsequent therapy for relapsed or refractory disease, given single agent (no HIV) or with antiretroviral therapy (ART) for people with HIV (PWH) to AIDS-related Kaposi sarcoma (KS), and both of the following (1 and 2): 1) Revlimid is prescribed in combination with antiretroviral therapy; 2) Failure of liposomal doxorubicin and paclitaxel, unless clinically significant adverse effects are experienced or both are contraindicated. 13. Initial Approval Criteria, I.F.1.e.x: Updated indication from Peripheral T-cell lymphoma as second-line or initial palliative intent therapy and subsequent therapy to Peripheral T-cell lymphoma as second-line and subsequent therapy. 14. Initial Approval Criteria, I.F.1.e.xi: Updated to remove prior off label indication criteria "Primary CNS lymphoma as a single agent or in		

combination with rituximab* for relapsed or refractory disease". 15. Initial Approval Criteria, I.F.2: Updated prescriber criteria from Prescribed by or in consultation with an oncologist or hematologist (Prescriber must be certified with the Lenalidomide REMS program) to Prescribed by or in consultation with an oncologist, immunologist (AIDS-related KS) or hematologist (Prescriber must be certified with the Lenalidomide REMS program). 16. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria, I.A.4, I.B.4, I.C.4, I.D.4, I.E.4 and I.F.4: Updated to remove prior generic preferred criteria "For Revlimid® requests, member must use generic lenalidomide, if available (e.g., contraindications to excipients)". 2. Initial Approval Criteria, I.A.4.d: Updated dosing criteria from As maintenance therapy as a single agent for active (symptomatic) myeloma after response to primary myeloma therapy to As maintenance therapy as a single agent or in combination with bortezomib for active (symptomatic) myeloma after response to primary myeloma therapy. 3. Updated duration for approval for all indications for all lines of business from 6 months to 12 months. 4. Initial Approval Criteria, I.B.1: Updated diagnosis criteria from to be consistent with indication language from package insert. 5. Initial Approval Criteria, I.B.4: Updated to "Member meets one of the following (a, b, or c): Has symptomatic anemia; Has transfusion-dependent anemia; Has anemia that is not controlled with an erythropoiesis-stimulating agent (e.g., Epogen/Procrit [epoetin alfa injection], Aranesp [darbepoetin alfa injection])." 6. Initial Approval Criteria, I.D.4: Updated to "Member meets one of the following (a or b): Has tried and failed at least one prior therapy; Used in combination with rituximab product;". 7. Initial Approval Criteria, I.E.4: Updated to "Meets one of the following (a or b): Has tried and failed at least one prior therapy; Used in combination with rituximab product;	06/30/2023	07/13/2023

*Prior authorization may be required for rituximab." 8. Initial Approval Criteria, I.F.1: Updated to remove all indications as they can be checked individually via NCCN guidelines. 9. Initial Approval Criteria, I.F.2: Updated prescriber criteria from Prescribed by or in consultation with an oncologist, immunologist (AIDS-related KS) or hematologist (Prescriber must be certified with the lenalidomide REMS program) to Prescribed by or in consultation with one of the following specialists (a or b): a. AIDS-related KS: an oncologist or immunologist; b. All other diagnoses: an oncologist or hematologist; 10. References were reviewed and updated.		
Policy was reviewed.	10/19/2023	10/19/2023
Policy was reviewed: 1. Added generic lenalidomide to Drug(s) Applied. 2. Removed age restrictions. 3. Removed prescriber restrictions. 4. Removed dose restrictions. 5. Add Split-fill 6. Updated Continued therapy approval with auto-approval based on lookback functionality within the past 120 days. 7. Removed reauthorization requirement for positive response to therapy. 8. Updated approval duration verbiage. 9. References were reviewed and updated.	8/28/2024	9/13/2024