09-J2000-64

Original Effective Date: 09/15/16

Reviewed: 07/11/18

Revised: 08/15/19

Subject: Venetoclax (Venclexta®) Tablet

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DESCRIPTION:

Venetoclax (Venclexta) is a selective inhibitor of B-cell lymphoma-2 (BCL-2) protein, an anti-apoptotic protein. The overexpression of BCL-2 in chronic lymphocytic leukemia (CLL) tumor cells enhances cell survival and is associated with resistance to chemotherapy. Venetoclax was approved by the FDA in April 2016 for the treatment of patients with chronic lymphocytic leukemia (CLL) with 17p deletion, as detected by an FDA approved test, who have received at least one prior therapy. The indication was approved under accelerated approval based on overall response rate (ORR), with continued approval contingent upon verification of clinical benefit in a confirmatory trial. In June 2018, confirmatory data was submitted to the FDA and venetoclax was granted full approval. In addition, based on the results of the MURANO phase 3 randomized controlled trial, the FDA-approved indication was expanded to be “the treatment of patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL), with or without 17p deletion, who have received at least one prior therapy”. In May 2019, the indication for CLL/SLL was expanded to include first-line treatment (i.e., no prior therapy requirement) based on the positive results of the CLL14 clinical trial comparing venetoclax + obinutuzumab vs. obinutuzumab + chlorambucil. Venetoclax was previously granted orphan drug designation by the FDA for the treatment of CLL in September 2012. In November 2018, the FDA approved the new indication of “In combination with azacitidine or decitabine or low-dose cytarabine for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy”. Venetoclax was previously granted orphan drug designation for the treatment of AML in February 2016. Venetoclax, as sponsored by the innovator drug company, also has orphan drug designations for the treatment of multiple myeloma (August 2016) and mantle cell lymphoma (August 2017). In March 2019, the FDA issued an alert on the risks associated with the off-label use of venetoclax for the treatment of patients with multiple myeloma (MM) based on data from the BELLINI clinical trial (NCT02755597). The interim trial results demonstrated a 2-fold increased risk of death for

patients receiving venetoclax combined with bortezomib and dexamethasone as compared to the control group (21.1% vs. 11.5% patients had died at a median follow-up of 17.9 months). The FDA has required that no new patients be enrolled on the Bellini trial.

Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is a mature B-cell lymphoma that comprises approximately 7% of newly diagnosed cases of Non-Hodgkin's Lymphoma (NHL). CLL and SLL are different manifestation of the same disease and are managed in much the same way. The main difference is that in CLL the abnormal lymphocytes are found in bone marrow and blood, while in SLL they are predominately found in the lymph nodes and bone marrow. The diagnosis of CLL requires the presence of at least 5,000 clonal B-cells/mcL in the peripheral blood as determined by flow cytometry quantification. Cytogenic abnormalities that can be detected by fluorescence in situ hybridization (FISH) testing are present in over 80% of previously untreated CLL patients. The 17p chromosome deletion, del(17p) mutation, which reflects the loss of the TP53 gene, is associated with the worst outcomes and poor response to chemotherapy. About 7% of newly diagnosed patients have a del(17p) mutation. The treatment options for CLL have changed drastically in the last several decades. The introduction of monoclonal antibodies targeting cell surface antigens (e.g., CD20, CD52), immunomodulating agents, and, most recently, novel small molecules inhibiting tyrosine kinases and other proteins, have led to new and more effective regimens. Recommended treatments are based on newly diagnosed vs. refractory disease, and the patient's mutation status, age, and other comorbidities.

The safety and efficacy of venetoclax leading to initial FDA approval was established in an open-label, single-arm, multicenter clinical trial of 106 patients with CLL with del(17p) who had received at least one prior therapy. The primary endpoint was overall response rate (ORR). The median time on treatment at the time of evaluation was 12.1 months (range: 0 to 21.5 months). An ORR was observed in 80.2% (95% CI 71.3 to 87.3%, n=85) of patients, with the majority achieving partial remission (69.8%, n=74). Other responses were as follows: CR – 5.7% (n=6), CRi – 1.9% (n=2), and nPR – 2.38% (n=3). Confirmation of clinical benefit was determined in the randomized MURANO trial of adults with CLL who had received at least one line of prior therapy. The combination of venetoclax and rituximab compared with bendamustine and rituximab significantly improved PFS (not reached vs 17 months) and 2-year PFS rate (84.9% vs. 36.3%). The ORR was significantly improved in the venetoclax arm (92.3% vs 72.3%), but the rate of CR plus CRi (8.2% vs 3.6%) was not. Adverse events were as expected with the following Grade 3 or 4 adverse events in the venetoclax and bendamustine arms, respectively; neutropenia (57.7% vs 38.8%), febrile neutropenia (3.6% vs 9.6), tumor lysis syndrome (3.1% vs 1.5%), and infusion-related reaction (1.5% vs 5.3%).

The National Comprehensive Cancer Network (NCCN) Guidelines for CLL/SLL (Version 5.2019) list venetoclax + obinutuzumab (Gazyva) under "Preferred regimens" as a category 2A recommendation for first-line therapy of CLL/SLL in patients with a del(17p) mutation, and certain patients without a del(17p) mutation (i.e., frail patients with significant comorbidity (not able to tolerate purine analogs), or patients ≥65 years and younger patients with significant comorbidities). This first-line combo regimen is listed under "Other recommended regimens" as a category 2B recommendation for patients less than 65 years without significant comorbidities. The guidelines also list venetoclax in combination with rituximab (Rituxan) under "Preferred regimens" for patients with relapsed or refractory disease with or without del(17p) mutation (category 1 recommendations). For patients without a del(17p) mutation, venetoclax monotherapy is listed under "Other recommended regimens" as a category 2A recommendation. For patients with a del(17p) mutation, venetoclax monotherapy is listed under "Preferred regimens" as a category 2A recommendation. The NCCN also includes recommendations for tumor lysis syndrome (TLS) prophylaxis and monitoring based on tumor burden when initiating venetoclax treatment. The NCCN Guidelines for B-cell Lymphomas (Version 4.2019) list venetoclax monotherapy under "Preferred

regimen" as a category 2A option for the second-line treatment of mantle cell lymphoma when there is a short response duration to prior chemoimmunotherapy (shorter expected median PFS). The NCCN Guidelines for AML (Version 3.2019) list venetoclax in combination with decitabine, azacitidine, or low-dose cytarabine as category 2A recommendations for patients 60 years of age or older in the following scenarios: (1) treatment induction in candidates for intensive remission induction therapy with unfavorable cytogenetics (exclusive of AML with myelodysplasia-related changes), (2) treatment induction in patients who have AML without actionable mutations and are not a candidate for intensive remission induction therapy or declines intensive therapy, and (3) post-remission therapy following response to previous lower intensity therapy with the same regimen.

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of venetoclax (Venclexta) **meets the definition of medical necessity** for members meeting **BOTH** of the following criteria ("1" and "2"):

1. Venetoclax is administered for an indication listed in Table 1, and **ALL** of the indication-specific and maximum-allowable dose criteria are met
2. The member's tumor burden [i.e., absolute lymphocyte count (ALC) and lymph node sizes via CT scan] and other risk factors for tumor lysis syndrome (TLS) have been assessed, and the member will receive appropriate prophylaxis as necessary

Table 1

Indications and Specific Criteria		
Indication	**Specific Criteria**	**Maximum Allowable Dose**
Acute myeloid leukemia (AML)	**EITHER** of the following ("1" or "2"): 1. **ALL** of the following ("a", "b", and "c"): a. Member is 60 years of age or older b. Venetoclax is being used in combination with decitabine, azacitidine, or low-dose cytarabine c. **ANY** of the following ("i", "ii", or "iii"): i. Member is a candidate for intensive remission induction therapy, **AND** has unfavorable cytogenetics (exclusive of AML with myelodysplasia-related changes) ii. Use is for treatment induction in a member who has AML **without** actionable	For post-remission therapy or induction therapy in members 60 years of age or older: • 400 mg daily (if used in combination with azacitidine or decitabine) • 600 mg daily (if used in combination with

	mutations, **AND** is **NOT** a candidate for intensive remission induction therapy or declines intensive therapy iii. Use is for post-remission therapy following response to previous lower intensity therapy with the same regimen 2. **BOTH** of the following ("a" and "b'): a. The member has relapsed or refractory disease b. The member has received prior treatment for their AML with **TWO** or more different lines of therapy*	low-dose cytarabine) For relapsed or refractory disease: • 400 mg daily Dose must be achieved using the fewest number of tablets possible
Chronic lymphocytic leukemia (CLL)/ small lymphocytic lymphoma (SLL)	**EITHER** of the following ("1" or "2"): 1. **BOTH** of the following ("a" and "b"): a. Member is receiving as first-line therapy for previously untreated disease b. Venetoclax will be used in combination with obinutuzumab (Gazyva) 2. **ALL** of the following ("a" to "c"): a. The member has relapsed or refractory disease b. The member has received at least one prior therapy for treatment of their disease c. Venetoclax will be used as either single-agent treatment or in combination with rituximab	400 mg orally once daily achieved using the fewest number of tablets possible
Mantle cell lymphoma (MCL)	**BOTH** of the following ("1" and "2"): 1. **EITHER** of the following ("a" or "b"): a. Venetoclax is being used as second-line or later therapy for relapsed or refractory disease b. Member had a partial response to induction therapy and venetoclax is being used to achieve a complete response 2. Venetoclax will be used as single-agent treatment	400 mg orally once daily achieved using the fewest number of tablets possible
Other FDA-approved or NCCN supported diagnosis (not previously listed above)	**EITHER** of the following is met ("1" or "2"): 1. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert) 2. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A	The dosage does not exceed the maximum recommended in the FDA-approved prescribing information or the maximum recommended by the applicable NCCN

	recommendation	guidelines for the diagnosis
Duration of approval: 6 months *Investigational drug treatment as part of a registered clinical trial qualifies as an eligible line of therapy. The National Comprehensive Cancer Network (NCCN) Guidelines for AML, list enrollment in a clinical trial as the strongly preferred option for patients with relapsed/refractory AML.		

Venetoclax is **does not meet the definition of medical necessity** for the treatment of the orphan indication of multiple myeloma due to clinical trial data showing an increased risk of death as compared to an alternative FDA-approved treatment regimen.

Continuation of venetoclax meets the definition of medical necessity for members meeting **ALL** of the following criteria (”1” to “4”):

1. Authorization or reauthorization for venetoclax has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of a condition listed in Table 1 or multiple myeloma, or other FDA-approved or NCCN-supported diagnosis; **OR** the member previously met **ALL** indication-specific initiation criteria.
2. The member has not had disease progression during treatment with venetoclax
3. **ONE** of the following based on the disease being treated:
    a. For AML
        - For released or refractory AML - venetoclax will be used as a single agent or in a combination regimen
        - For post-remission therapy or induction therapy in members 60 years of age or older - venetoclax will be used in combination with decitabine, azacitidine, or low-dose cytarabine

    b. For CLL/SLL
        - For first-line use in previously untreated disease – venetoclax will be used in combination with obinutuzumab
        - For relapsed or refractory disease - venetoclax will be used as either a single agent or in combination with rituximab

    c. For MCL - venetoclax will be used as a single agent

    d. For MM - venetoclax will be used as a single-agent, in combination with dexamethasone, or in combination with both dexamethasone and bortezomib

    e. Other FDA-approved or NCCN-supported diagnosis (not previously listed above) - venetoclax is used in a treatment regimen in accordance with the FDA-approved prescribing information or NCCN guideline recommendation
4. The dosage does not exceed the following based on the indication for use - the dose must be achieved using the fewest number of tablets possible:
    a. AML
        - For released or refractory disease – 400 mg daily

- For post-remission therapy or induction therapy in members 60 years of age or older
    - 400 mg daily (if used in combination with azacitidine or decitabine)
    - 600 mg daily (if used in combination with low-dose cytarabine)

b. CLL/SLL – 400 mg daily.
- If using in combination with rituximab, venetoclax will not be used for longer than 24 months from cycle 1 day 1 of rituximab initiation.
- If using in combination with obinutuzumab, venetoclax will not be used for longer than 12 months.

c. MCL – 400 mg daily

d. MM – 800 mg daily

e. Other FDA-approved or NCCN-supported diagnosis (not previously listed above) - the maximum recommended in the FDA-approved prescribing information or the maximum recommended by the applicable NCCN guidelines for the diagnosis

Duration of approval: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- The treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)
    - Initiate therapy at 20 mg once daily for 7 days, followed by a weekly ramp-up dosing schedule to the recommended daily dose of 400 mg. If being used in combination with rituximab, rituximab is started after the patient has completed the 5-week dose ramp-up and has received the 400 mg venetoclax dose for 7 days. Rituximab is given on day 1 of each 28-day cycle for 6 cycles at a dose of 375 mg/m^2 IV for Cycle 1 and then 500 mg/m^2 IV for Cycles 2 to 6. Patients continue venetoclax once daily for 24 months total from cycle 1 day 1 of rituximab. If being used in combination with obinutuzumab, start obinutuzumab administration at 100 mg on Cycle 1 Day 1, followed by 900 mg on Cycle 1 Day 2. Administer 1,000 mg on Days 8 and 15 of Cycle 1 and on Day 1 of each subsequent 28-day cycle, for a total of 6 cycles. On Cycle 1 Day 22, start venetoclax according to the 5-week ramp-up schedule. After completing the ramp-up schedule on Cycle 2 Day 28, patients should continue at 400 mg once daily from Cycle 3 Day 1 until the last day of Cycle 12. If given as monotherapy, the product labeling recommends that venetoclax be taken until disease progression or unacceptable toxicity is observed
    - Tablets should be taken orally once daily with a meal and water. Do not chew, crush, or break tablets.
        - Week 1 – 20 mg
        - Week 2 – 50 mg
        - Week 3 – 100 mg
        - Week 4 – 200 mg

        - Week 5 and beyond – 400 mg
    - Treatment can cause rapid reduction in tumor and thus poses a risk for tumor lysis syndrome (TLS) in the initial 5-week ramp-up phase. Perform prophylaxis for TLS and monitoring as recommend in the product labeling.
- In combination with azacitidine, or decitabine, or low-dose cytarabine for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy. This indication is approved under accelerated approval based on response rates, and continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.
    - Initiate therapy at 100 mg on Day 1, 200 mg on Day 2, 400 mg on Day 3, and then, for Days 4 and beyond, 400 mg once daily (when dosing in combination with azacitidine or decitabine) or 600 mg once daily (when dosing in combination with low-dose cytarabine). The product labeling recommends that venetoclax, in combination with azacitidine or decitabine or low-dose cytarabine, be taken until disease progression or unacceptable toxicity is observed.
    - Patients treated with venetoclax may develop TLS. All AML patients should have a white blood cell count less than 25×10^9/L prior to initiation of venetoclax. Cytoreduction prior to treatment may be required. Perform prophylaxis for TLS and monitoring as recommend in the product labeling.

Dose Adjustments

- Interrupt dosing or reduce dose of venetoclax for toxicities. The specific recommendations depend on the indication for use, the type and severity of the adverse event, and number of occurrences. Refer to the product labeling for specific recommendations.
- Dosage modifications or avoidance of venetoclax are recommended for concomitant use with strong or moderate CYP3A inhibitors or P-gp inhibitors. The specific recommendations depend on the indication for use and the interacting drug. Refer to the product labeling for specific recommendations.
- Hepatic Impairment
    - No dose adjustment is recommended in patients with mild or moderate hepatic impairment
    - A recommended dose has not been determined for patients with severe hepatic impairment.
- Renal Impairment:
    - Patients with reduced renal function (CrCl <80 mL/min) are at increased risk of TLS. These patients may require more intensive prophylaxis and monitoring.
    - No dose adjustment is needed for patients with mild or moderate renal impairment (CrCl ≥30 mL/min)
    - A recommended dose has not been determined for patients with severe renal impairment (CrCl <30 mL/min) or patients on dialysis.

Drug Availability

- 10 mg, 50 mg, and 100 mg film-coated tablets as described below:

Packaging Presentation	Number of Tablets	National Drug Code (NDC)
CLL/SLL Starting Pack	Each pack contains four weekly wallet blister packs: o Week 1 (14 x 10 mg tablets) o Week 2 (7 x 50 mg tablets) o Week 3 (7 x 100 mg tablets) o Week 4 (14 x 100 mg tablets)	00074-0579-28

10 mg Wallet	14 x 10 mg tablets	00074-0561-14
50 mg Wallet	7 x 50 mg tablets	00074-0566-07
10 mg Unit Dose	2 x 10 mg tablets	00074-0561-11
50 mg Unit Dose	1 x 50 mg tablet	00074-0566-11
100 mg Unit Dose	1 x 100 mg tablet	00074-0576-11
100 mg Bottle	120 x 100 mg tablets	00074-0576-22
	180 x 100 mg tablets	00074-0576-34

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Concomitant use of venetoclax with strong inhibitors of CYP3A at initiation and during ramp-up phase in patients with CLL/SLL due to the potential for increased risk of tumor lysis syndrome

Precautions/Warnings

- **Tumor Lysis Syndrome (TLS):** TLS, including fatal events and renal failure requiring dialysis, has occurred in previously treated CLL patients with high tumor burden when treated with venetoclax. Anticipate TLS; assess risk in all patients. Premedicate with anti-hyperuricemics and ensure adequate hydration. Employ more intensive measures (intravenous hydration, frequent monitoring, hospitalization) as overall risk increases. See the product labeling for specific recommendations.
- **Neutropenia:** In patients with CLL, Grade 3 or 4 neutropenia developed in 64% of patients and Grade 4 neutropenia developed in 31% of patients treated with venetoclax in combination with rituximab. Grade 3 or 4 neutropenia developed in 63% of patients and Grade 4 neutropenia developed in 33% of patients treated with venetoclax monotherapy. Febrile neutropenia occurred in 4% of patients treated with venetoclax in combination with rituximab and in 6% of patients treated with venetoclax monotherapy. Baseline neutrophil counts worsened in 97% to 100% of patients treated with venetoclax in combination with azacitidine or decitabine or low-dose cytarabine. Neutropenia can recur with subsequent cycles of therapy. Monitor blood counts and for signs of infection; manage as medically appropriate.
- **Infections**: Fatal and serious infections such as pneumonia and sepsis have occurred. Monitor patients closely for signs and symptoms of infection and treat promptly. Withhold treatment for Grade 3 and higher infection.
- **Immunization:** Do not administer live attenuated vaccines prior to, during, or after venetoclax treatment.
- **Embryo-Fetal Toxicity:** May cause embryo-fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment.
- **Lactation:** Discontinue breastfeeding.
- **Drug Interactions:** If possible, avoid concomitant use of venetoclax with moderate CYP3A inhibitors, strong or moderate CYP3A inducers, P-gp inhibitors, or narrow therapeutic index P-gp substrates.
- **Adverse Reactions:** The most common adverse reactions (≥20%) were neutropenia, diarrhea, nausea, anemia, upper respiratory tract infection, thrombocytopenia, and fatigue.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

C9399	Unclassified drugs or biologicals (Hospital Outpatient Use ONLY)
J8999	Prescription drug, oral, chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnosis Codes That Support Medical Necessity

C83.00 - C83.09	Small cell B-cell lymphoma
C83.10 - C83.19	Mantle cell lymphoma
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse
C90.10	Plasma cell leukemia not having achieved remission
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having achieved remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission
C90.32	Solitary plasmacytoma in relapse
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse
C92.00	Acute myeloblastic leukemia, not having achieved remission
C92.01	Acute myeloblastic leukemia, in remission
C92.02	Acute myeloblastic leukemia, in relapse
C92.50	Acute myelomonocytic leukemia, not having achieved remission
C92.51	Acute myelomonocytic leukemia, in remission
C92.52	Acute myelomonocytic leukemia, in relapse
C92.60	Acute myeloid leukemia with 11q23-abnormality, not having achieved remission
C92.61	Acute myeloid leukemia with 11q23-abnormality, in remission
C92.62	Acute myeloid leukemia with 11q23-abnormality, in relapse
C92.A0	Acute myeloid leukemia with multilineage dysplasia, not having achieved remission
C92.A1	Acute myeloid leukemia with multilineage dysplasia, in remission
C92.A2	Acute myeloid leukemia with multilineage dysplasia, in relapse

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of guideline creation.

DEFINITIONS:

None

RELATED GUIDELINES:

Allogeneic Bone Marrow and Stem Cell Transplantation, 02-38240-01

Autologous Bone Marrow and Stem Cell Transplantation, 02-38241-01

Bendamustine HCl (Bendeka, Treanda) Injection

Ibrutinib (Imbruvica), 09-J2000-09

Idelalisib (Zydelig) Oral Tablet, 09-J2000-23

Obinutuzumab (Gazyva) Injection, 09-J2000-07

Rituximab (Rituxan), 09-J0000-59

OTHER:

None

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26. Venclexta (venetoclax) [package insert]. AbbVie Inc. North Chicago, IL, May 2019.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 07/10/19.

GUIDELINE UPDATE INFORMATION:

09/15/16	New Medical Coverage Guideline.
12/15/16	Revision to guideline consisting of updating the description section, position statement, and references based on updated NCCN guidelines for CLL/SLL.
02/15/17	Revision to guideline consisting of updating the description section, position statement, billing/coding, and references based on updated NCCN guidelines for B-cell lymphomas.
06/15/17	Revision to guideline consisting of updating the description section, position statement, and references based on updated NCCN guideline for CLL/SLL
08/15/17	Review and revision to guideline consisting of updating the description section and references.
03/15/18	Revision to guideline consisting of updating the description section and references based on updated NCCN Guidelines for CLL/SLL.
08/15/18	Review and revision to guideline consisting of updating the description section, position statement, dosage/administration, billing/coding, and references.
01/15/19	Revision to guideline consisting of updating the description, position statement, dosage/administration, warnings/precautions, billing/coding information, and references based on a new FDA-approved indication for AML and NCCN Guidelines update.
05/15/19	Revision to guideline consisting of updating the description, position statement, and references based on an FDA warning regarding off-label use in multiple myeloma.
08/15/19	Review and revision to guideline consisting of updating the description section, position statement, dosage/administration, precautions/warnings, related guidelines, and references.