Cosela (trilaciclib)
Policy Number: CXXXXX-X

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DUE BY OR BEFORE
04/28/2021	04/2021	04/26/2022
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
J3490 C9399	RxPA	Q2 2021 20210428

PRODUCTS AFFECTED:
Cosela (trilaciclib)

DRUG CLASS:
Antineoplastics and Adjunctive Therapies- Kinase Inhibitor

ROUTE OF ADMINISTRATION:
Intravenous

PLACE OF SERVICE:
Buy and Bill
The recommendation is that medications in this policy will be for medical benefit coverage and the IV infusion products administered in a place of service that is a non-hospital facility-based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center).

AVAILABLE DOSAGE FORMS:
300 mg single-dose vial for injection, NDC 73462-101-01

FDA-APPROVED USES:
Indicated to decrease the incidence of chemotherapy-induced myelosuppression in adult members when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage small cell lung cancer

COMPENDIAL APPROVED OFF-LABELED USES:
None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS: Small Cell Lung Cancer

REQUIRED MEDICAL INFORMATION:
A. SMALL CELL LUNG CANCER
   1. Documentation that the member has a diagnosis of extensive stage small cell lung cancer.

NOTE: Extensive stage is defined as Stage IV (T any, N any, M 1a/b/c) or T3-4 due to multiple lung nodules that are too extensive or have tumor/nodal volume that is too largeto be encompassed in a tolerable radiation plan).
AND

2. Documentation of members chemotherapy treatment plan indicating that member will be treated with a platinum/etoposide-containing regimen or a topotecan-containing regimen AND that trilaciclib will be administered within 28 hours on sequential days when chemotherapy is administered [DOCUMENTATION REQUIRED].
AND
3. For female members of childbearing potential, provider attests that member has had a negative pregnancy screening and has been counseled to use effective contraception during treatment with trilaciclib, and for 3 weeks following final dose. Note: Based on its mechanism of action, trilaciclib can cause fetal harm if administered to a pregnant woman.
AND
4. Documentation that member has a Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 to 2.
AND
5. Prescriber attests that use of trilaciclib is medically necessary and more appropriate forthe member than the use of granulocyte colony stimulating factors (GCSF) and other supportive measures (example: erythropoiesis-stimulating agents (ESAs), transfusions) due to member-specific risk factors for chemotherapy induced neutropenia or chemotherapy induced anemia (see Appendix).

DURATION OF APPROVAL:
Initial authorization: 3 months
Continuation of Therapy: 6 months or maximum duration of planned chemotherapy, whichever is shorter

QUANTITY:
240 mg/m^2 per dose, up to 3 doses for a platinum/etoposide-containing regimen per cycle OR up to 5 doses for a topotecan-containing regimen per cycle.

PRESCRIBER REQUIREMENTS:
Must be prescribed by, or in consultation with, an oncologist, hematologist, or other specialist treating cancer [Consultation notes must be submitted if applicable]

AGE RESTRICTIONS:
18 years of age and older

CONTINUATION OF THERAPY:
A. SMALL CELL LUNG CANCER:

1. Documentation that member is compliant with Cosela (trilaciclib) therapy as verified by theprovider and/or fill history.
AND
2. Documentation of clinical benefits to support continuation of treatment including positive response to therapy as evidenced by one of the following while treated with Cosela (trilaciclib):

(a) Member did not experience prolonged neutropenia, defined as an absolute neutrophil count (ANC) less than 0.5 x 109 lasting more than 7 days; (b) Member did not experience neutropenicinfection or febrile neutropenia; (c) Member did not experience Grade 3 thrombocytopenia (platelet count less than 50,000 cells/mm3 or have an increase in transfusions (platelet or red blood cells) during treatment period; D. Member did not require

next chemotherapy cycle to beheld due to myelosuppression or require more than one chemotherapy dose reduction due to myelosuppression.
AND

3. Documentation that member has not experienced any adverse reactions warranting discontinuation of treatment with Cosela (trilaciclib) (see Appendix).
AND
4. Documentation that members treatment plan continues to be a platinum/etoposide-containingregimen or a topotecan-containing regimen AND documentation of the number of cycles remaining [DOCUMENTATION REQUIRED].

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Cosela (trilaciclib) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Cosela (trilaciclib) include a history of hypersensitivity to trilaciclib.

OTHER SPECIAL CONSIDERATIONS:
Cosela (trilaciclib) is administered as a 30-minute intravenous infusion completed within 4 hours prior to the start of chemotherapy on each day chemotherapy is administered. The interval between doses of Cosela on sequential days should not be greater than 28 hours.

If Cosela (trilaciclib) is discontinued, the member should wait 96 hours from the last dose of Cosela before resumption of chemotherapy only.

Cosela has not been studied in members with moderate to severe hepatic impairment (total bilirubin >1.5 × ULN, irrespective of AST).

BACKGROUND:
Cosela (trilaciclib) is a kinase inhibitor which transiently inhibits CDK 4 and 6. Hematopoietic stem cell and progenitor cell (HSPC) proliferation is dependent on the CDK 4 and 6 activity. By transiently (up to 32 hours) arresting HSPC in the G1 phase of the cell cycle, Cosela exerts myeloprotective effects. Approximately 32 hours after the dose, the bone marrow resumes proliferation.

Trilaciclib was studied in three randomized, double blind, placebo-controlled trials, all in patients with extensive stage- small cell lung cancer (ES-SCLC). Study 1 (G1T28-05) administered trilaciclib prior to treatment with etoposide, carboplatin, and atezolizumab in patients (n=107) with a new diagnosis of ES-SCLC. In the study arm, Trilaciclib (n=54) was administered prior to chemotherapy on days 1, 2 and 3 of a 21-day cycle. Fewer patients required dose reductions of either etoposide (6% trilaciclib, 26% placebo) or carboplatin (2% trilaciclib, 25% placebo), comparedto placebo.
Study 2 (G1T28-02) administered trilaciclib prior to treatment with etoposide and carboplatinin patients (n=77) with a new diagnosis of ES-SCLC who had not been previously treated with chemotherapy. In the study arm, Trilaciclib (n=39) was administered prior to chemotherapy on days 1, 2 and 3 of a 21-day cycle. The rate of red blood cell transfusions was 0.5/100 weeks in the trilaciclib arm, compared to 1.9/100 weeks in the placebo arm (n=38).

Study 3 (G1T28-03) administered trilaciclib prior to treatment with topotecan in patients (n=61) with ES-SCLC who had been previously treated with chemotherapy. In the study arm, trilaciclib (n=32) was administered prior to topotecan on days 1 through 5 of a 21-day cycle, with treatment continued until disease progression. The mean duration of severe neutropenia was lower

in the trilaciclib arm (mean 2 days, standard deviation 3.9 days) compared to placebo (mean 7 days, standard deviation 6.2 days). Additionally, the number and percentage of patients with severe neutropenia was lower in the trilaciclib arm (13, 40.6%) compared to placebo (22, 75.9%).

NCCN guidelines[3] state that trilaciclib may be used as a prophylactic option to decrease the incidence of chemotherapy induced myelosuppresion when administered before platinum/etoposide with or without a checkpoint inhibitor or a topotecan containing regimen for ES-SCLC, or that granulocyte colony stimulating factors (G-CSF) may be administered after chemotherapy (category 2A, SCL-D). In the studies, trilaciclib was studied against placebo, not compared to alternative treatment. Additionally, patients who were treated with trilaciclib still required G-CSFs, but at a rate lower compared to placebo (35% trilaciclib, 67% placebo).

APPENDIX:

Adverse Reactions requiring permanent discontinuation of Cosela:

- Grade 3 Injection Site Reactions: Ulceration or necrosis; severe tissue damage; operative intervention indicated
- Grade 4 Injection Site Reactions: Life-threatening consequences; urgent interventions indicated
- Grade 3 Acute Drug Hypersensitivity reactions: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL
- Grade 4 Acute Drug Hypersensitivity reactions: Life-threatening consequences; urgent interventions indicated
- Grade 3 Interstitial lung disease/pneumonitis: Severe symptoms; limiting self-care ADL; oxygen indicated.
- Grade 4 Interstitial lung disease/pneumonitis: Life-threatening respiratory compromise; urgent intervention indicated (e.g., tracheotomy or intubation)

Member risk factors for consideration of use of Granulocyte Colony Stimulating Factors[2] (MGF 2, 3, category 2A):

- Prior chemotherapy or radiation therapy
- Persistent neutropenia
- Bone marrow involvement by tumor
- Recent surgery and/or open wounds
- Liver Dysfunction (bilirubin >2.0)
- Renal Dysfunction (creatinine clearance <50)
- Age >65 years receiving full chemotherapy dose intensity
- Febrile neutropenia or dose-limiting neutropenic event

Member risk factors for chemotherapy induced anemia[2] (ANEM-2, category 2A):

- Progressive decline in hemoglobin with recent intensive chemotherapy or radiation
- Comorbid cardiac disease, chronic pulmonary disease, or cerebral vascular disease

Molina Healthcare, Inc. covers injectable/infused treatment in a hospital outpatient setting or at a hospital-affiliated infusion suite* when the level of care is determined to be medically necessary. Considerations used to determine if an alternative level of care is not suitable may include the following findings:

1. The patient is clinically unstable based on documented medical history and susceptible to complication with drug administration (e.g., cardiopulmonary or renal dysfunction, risk for fluid overload)
2. The requested medication is administered as part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent,

anti-emetic) for treatment of cancer or with dialysis
3. The patient exhibits physical or cognitive impairment and a capable caregiver is not available to assist with safe administration of prescribed medication in the home
4. It is the patient's first dose of the medication or it is being re-initiated after at least 12 months*
5. The patient has experienced adverse events with past administration of the drug and cannot be managed by premedication or resources available at a non-hospital facility-based location (NHFBL)
6. Documented history of difficulty establishing and maintaining patent vascular access, or is not a candidate for a mode of long-term vascular access during the duration of prescribed treatment

Note: a hospital outpatient setting, or a hospital-affiliated infusion suite is expected to have immediate access to specific services of a medical center/hospital setting, including having emergency resuscitation equipment and personnel (ACLS protocol), emergency services, and inpatient admission or intensive care, if necessary

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

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