COSELA®

trilaciclib for injection 300 mg

DOSING AND ADMINISTRATION GUIDE FOR COSELA

From 1st line through subsequent lines, provide proactive multilineage myeloprotection for your extensive-stage small cell lung cancer (ES-SCLC) patients by prescribing COSELA® (trilaciclib):

1st Line

- With a platinum/etoposide-containing regimen (including carboplatin or cisplatin)

Subsequent Lines

- With a topotecan-containing regimen
- With platinum/etoposide-containing regimen rechallenges

WATCH A VIDEO ABOUT DOSING AND ADMINISTRATION

Jennifer S. Webster, MN, MPH, RN, AOCNS, NPD-BC shares her expertise.

Please see inside pages for specific dosing and administration instructions.

INDICATION

COSELA® (trilaciclib) is indicated to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage small cell lung cancer (ES-SCLC).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

- COSELA is contraindicated in patients with a history of serious hypersensitivity reactions to trilaciclib.

Please see additional Important Safety Information on the back panel and accompanying full Prescribing Information.

COSELA: DOSED FIRST TIME, EVERY TIME WITH CHEMOTHERAPY

PROACTIVELY HELP PROTECT AGAINST MULTIPLE MYELOSUPPRESSIVE CONSEQUENCES WITH THE FIRST AND ONLY MYELOPROTECTION THERAPY

COSELA® (trilaciclib) is indicated to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage small cell lung cancer (ES-SCLC).

The recommended dose of COSELA is 240 mg/m^2 as a 30-minute intravenous infusion completed within 4 hours prior to the start of chemotherapy on each day chemotherapy is administered.

Reduce dose in patients with moderate or severe hepatic impairment.

- **Dosage Forms and Strengths.** For injection: 300 mg of COSELA as a lyophilized cake in a single-dose vial for reconstitution and further dilution

DOSING FOR A PLATINUM/ETOPOSIDE CONTAINING REGIMEN (WITH OR WITHOUT AN IMMUNE CHECKPOINT INHIBITOR)

DAY 1	DAY 2	DAY 3		21-DAY CYCLE
COSELA Prior to Platinum & Etoposide	COSELA Prior to Etoposide	COSELA Prior to Etoposide		

DOSING FOR TOPOTECAN-CONTAINING REGIMEN

DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	21-DAY CYCLE
COSELA Prior to Topotecan	COSELA Prior to Topotecan	COSELA Prior to Topotecan	COSELA Prior to Topotecan	COSELA Prior to Topotecan	

COSELA must be given on the same day as chemotherapy, prior to chemotherapy on each day chemotherapy is administered.

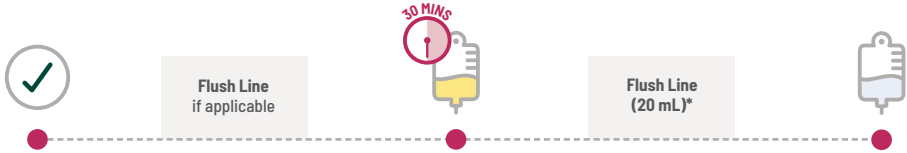
MYELOPROTECTION STRATEGY: When given prior to chemotherapy, COSELA transiently arrests hematopoietic stem and progenitor cells (HSPCs) in the G1 phase of the cell cycle.

Administering COSELA® (trilaciclib):

- Diluted COSELA solution **MUST** be administered with an infusion set, including an in-line filter (0.2 or 0.22 micron). Compatible in-line filters include polyethylene sulfone (PES), polyvinylidene fluoride (PVDF), and cellulose acetate (CA)

- **DO NOT** administer diluted COSELA solution with a polytetrafluorethylene (PTFE) in-line filter. PTFE in-line filters are not compatible with diluted COSELA solution
- **DO NOT** co-administer other drugs through the same infusion line
- **DO NOT** co-administer other drugs through a central access device unless the device supports co-administration of incompatible drugs

SAMPLE INFUSION SCHEDULE



Deliver Premeds
as appropriate

Administer COSELA
as a 30-minute infusion†

Proceed Directly to Chemo

Subsequent COSELA doses ***must be started no later than 28 hours*** after the previous COSELA dose

*Upon completion of infusion of diluted COSELA solution, the infusion line/cannula MUST be flushed with at least 20 mL sterile 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP.
†COSELA can be given within 4 hours before chemotherapy.

Missed Treatment Session(s)

- If the COSELA dose is missed, discontinue chemotherapy on the day the COSELA dose was missed. Consider resuming both COSELA and chemotherapy on the next scheduled day for chemotherapy.

Discontinuation of Treatment

- If COSELA is discontinued, wait 96 hours from the last dose of COSELA before resumption of chemotherapy only.

PREPARING AND ADMINISTERING COSELA®

COSELA® (trilaciclib) must be reconstituted and then diluted further prior to IV infusion. Aseptic technique must be used for reconstitution and dilution.

As with all parenteral drug products, visually inspect COSELA for particulate matter and discoloration prior to administration.

Reconstituting COSELA:

- Calculate the COSELA dose based on the patient's body surface area (BSA), the total volume of reconstituted COSELA solution required, and the number of COSELA vials needed.
- Reconstitute each 300 mg vial with 19.5 mL of 0.9% Sodium Chloride Injection or 5% Dextrose Injection, USP using a sterile syringe to obtain a concentration of 15 mg/mL of COSELA.

NOTE:

The dose of COSELA is determined by body surface area

The typical patient will require 2 vials of COSELA

- Gently swirl the vial for up to 3 minutes until the sterile lyophilized cake is completely dissolved. Do not shake.
- Inspect the reconstituted solution for discoloration and particulate matter. Reconstituted COSELA solution should be a clear, yellow solution. Do not use if the reconstituted solution is discolored, cloudy, or contains visible particulates.
- If needed, the unused reconstituted solution in the vial can be stored at 20°C to 25°C (68°F to 77°F) for up to 4 hours prior to transfer to the infusion bag. Do not refrigerate or freeze.
- Discard any unused portion after use.

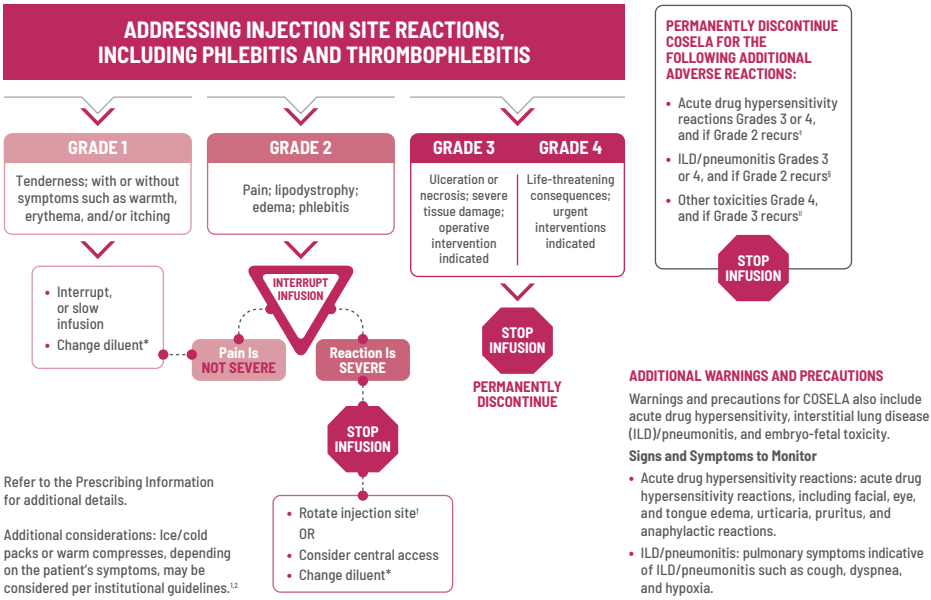
Diluting reconstituted COSELA solution:

- Withdraw the required volume from the vial(s) of reconstituted COSELA solution and dilute into an intravenous infusion bag containing 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP. The final concentration of the diluted COSELA solution should be between 0.5 mg/mL and 3 mg/mL.
- Mix diluted solution by gentle inversion. Do not shake.
- The diluted COSELA solution for infusion is a **clear, yellow solution.**

RECOMMENDED ACTIONS FOR ADVERSE REACTIONS

- Upon completion of infusion, flush line/cannula with at least 20 mL sterile 0.9% Sodium Chloride Injection, USP, or 5% Dextrose Injection, USP.
  - If 0.9% Sodium Chloride Injection, USP is being used as a diluent/flush, consider changing to 5% Dextrose Injection, USP as appropriate for subsequent infusions.

Note that COSELA® (trilaciclib) is not a vesicant.



Refer to the Prescribing Information for additional details.

Additional considerations: Ice/cold packs or warm compresses, depending on the patient's symptoms, may be considered per institutional guidelines.[1,2]

ADDITIONAL WARNINGS AND PRECAUTIONS

Warnings and precautions for COSELA also include acute drug hypersensitivity, interstitial lung disease (ILD)/pneumonitis, and embryo-fetal toxicity.

Signs and Symptoms to Monitor

- Acute drug hypersensitivity reactions: acute drug hypersensitivity reactions, including facial, eye, and tongue edema, urticaria, pruritus, and anaphylactic reactions.
- ILD/pneumonitis: pulmonary symptoms indicative of ILD/pneumonitis such as cough, dyspnea, and hypoxia.

INJECTION-SITE REACTION INCIDENCE

Injection-site reactions, including phlebitis and thrombophlebitis, occurred in 56 (21%) of the 272 patients receiving COSELA in clinical trials. Occurrence of Grade 2 adverse reactions was 10% and Grade 3 adverse reactions was 0.4%.

- Injection-site reactions, including phlebitis and thrombophlebitis, resolved in 49 (88%) of the 56 patients and led to discontinuation of treatment in 3 (1%) of the 272 patients.

*If 0.9% Sodium Chloride Injection, USP is being used as a diluent/flush, consider changing to 5% Dextrose Injection, USP as appropriate for subsequent infusions.
†Stop infusion in extremity and rotate site of infusion to site in alternative extremity.
‡Defined as: Grade 2=Moderate; minimal, local, or noninvasive intervention indicated; limiting Activities of Daily Living (ADL). Grade 3=Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL. Grade 4=Life-threatening consequences; urgent intervention indicated.
§Defined as: Grade 2=Symptomatic. Grade 3=Severe symptoms; limiting self-care ADL; oxygen indicated. Grade 4=Life-threatening respiratory compromise; urgent intervention indicated (e.g., tracheotomy or intubation).
‖Defined as: Grade 3=Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL. Grade 4=Life-threatening consequences; urgent intervention indicated.

References: 1. Injection Site Reactions. Chemocare.com. https://chemocare.com/sideeffect/injection-site-reactions. Accessed August 31, 2023. **2.** Gorski L, Hadaway L, Hagle M, *et al.* Infusion therapy standards of practice. *J Infus Nurs*. 2006;29:S1-92.

IV BAG MATERIALS, DILUENTS, AND STORAGE DURATIONS AT ROOM TEMPERATURE

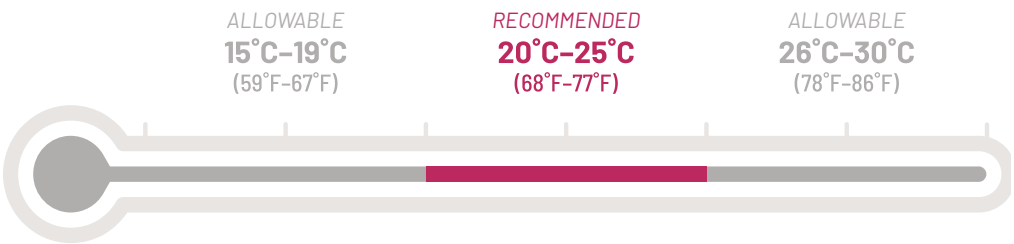
IV INFUSION BAG MATERIAL	DILUENT	DILUTED COSELA STORAGE DURATION
Polyvinyl chloride (PVC), Ethylene vinyl acetate (EVA), Polyolefin (PO), or Polyolefin/ Polyamide (PO/PA)	5% Dextrose for Injection, USP	Up to 12 hours at 20°C to 25°C (68°F to 77°F)
PVC, EVA, or PO	0.9% Sodium Chloride Injection, USP	Up to 8 hours at 20°C to 25°C (68°F to 77°F)
PO/PA	0.9% Sodium Chloride Injection, USP	Up to 4 hours at 20°C to 25°C (68°F to 77°F)

To ensure COSELA® (trilaciclib) stability, do not exceed specified storage durations. If not used immediately, store the diluted COSELA solution in the IV bag as specified here. Discard if the storage time exceeds these limits. Do not refrigerate or freeze.

STORING COSELA

Store COSELA vials at **20°C to 25°C (68°F to 77°F)**; short-term temperature variations are permitted from **15°C to 30°C (59°F to 86°F)**.

The vial stopper is not made with natural rubber latex.



If you would like additional information or have questions, you may request a Clinical Nurse Educator at www.COSELA.com/request-information

IMPORTANT SAFETY INFORMATION, CONTINUED

WARNINGS AND PRECAUTIONS

Injection-Site Reactions, Including Phlebitis and Thrombophlebitis

- COSELA administration can cause injection-site reactions, including phlebitis and thrombophlebitis, which occurred in 56 (21%) of 272 patients receiving COSELA in clinical trials, including Grade 2 (10%) and Grade 3 (0.4%) adverse reactions. Monitor patients for signs and symptoms of injection-site reactions, including infusion-site pain and erythema during infusion. For mild (Grade 1) to moderate (Grade 2) injection-site reactions, flush line/cannula with at least 20 mL of sterile 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP after end of infusion. For severe (Grade 3) or life-threatening (Grade 4) injection-site reactions, stop infusion and permanently discontinue COSELA. Injection-site reactions led to discontinuation of treatment in 3 (1%) of the 272 patients.

Acute Drug Hypersensitivity Reactions

- COSELA administration can cause acute drug hypersensitivity reactions, which occurred in 16 (6%) of 272 patients receiving COSELA in clinical trials, including Grade 2 reactions (2%). Monitor patients for signs and symptoms of acute drug hypersensitivity reactions. For moderate (Grade 2) acute drug hypersensitivity reactions, stop infusion and hold COSELA until the adverse reaction recovers to Grade ≤1. For severe (Grade 3) or life-threatening (Grade 4) acute drug hypersensitivity reactions, stop infusion and permanently discontinue COSELA.

Interstitial Lung Disease/Pneumonitis

- Severe, life-threatening, or fatal interstitial lung disease (ILD) and/or pneumonitis can occur in patients treated with cyclin-dependent kinases (CDK)4/6 inhibitors, including COSELA, with which it occurred in 1 (0.4%) of 272 patients receiving COSELA in clinical trials. Monitor patients for pulmonary symptoms of ILD/pneumonitis. For recurrent moderate (Grade 2) ILD/pneumonitis, and severe (Grade 3) or life-threatening (Grade 4) ILD/pneumonitis, permanently discontinue COSELA.

Embryo-Fetal Toxicity

- Based on its mechanism of action, COSELA can cause fetal harm when administered to a pregnant woman. Females of reproductive potential should use an effective method of contraception during treatment with COSELA and for at least 3 weeks after the final dose.

ADVERSE REACTIONS

- Serious adverse reactions occurred in 30% of patients receiving COSELA. Serious adverse reactions reported in >3% of patients who received COSELA included respiratory failure, hemorrhage, and thrombosis.
- Fatal adverse reactions were observed in 5% of patients receiving COSELA. Fatal adverse reactions for patients receiving COSELA included pneumonia (2%), respiratory failure (2%), acute respiratory failure (<1%), hemoptysis (<1%), and cerebrovascular accident (<1%).
- Permanent discontinuation due to an adverse reaction occurred in 9% of patients who received COSELA. Adverse reactions leading to permanent discontinuation of any study treatment for patients receiving COSELA included pneumonia (2%), asthenia (2%), injection-site reaction, thrombocytopenia, cerebrovascular accident, ischemic stroke, infusion-related reaction, respiratory failure, and myositis (<1% each).
- Infusion interruptions due to an adverse reaction occurred in 4.1% of patients who received COSELA.
- The most common adverse reactions (≥10%) were fatigue, hypocalcemia, hypokalemia, hypophosphatemia, aspartate aminotransferase increased, headache, and pneumonia.

DRUG INTERACTIONS

- COSELA is an inhibitor of OCT2, MATE1, and MATE-2K. Co-administration of COSELA may increase the concentration or net accumulation of OCT2, MATE1, and MATE-2K substrates in the kidney (e.g., dofetilide, dalfampridine, and cisplatin).

To report suspected adverse reactions, contact Pharmacosmos Therapeutics at 1-800-790-4189 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

This information is not comprehensive. Please see the full Prescribing Information.

Reference: COSELA (trilaciclib). Prescribing Information. Pharmacosmos Therapeutics Inc.; 2023.

PHARMACOSMOS THERAPEUTICS