relacorilant (Lifyorli™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO346

Description

Relacorilant (Lifyorli) is an orally administered selective glucocorticoid receptor antagonist (SGRA).

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
relacorilant (Lifyorli)	Treatment of adults with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received 1-3 prior systemic treatment regimens, at least one of which included bevacizumab, indicated in combination with nab-paclitaxel	125 mg dose (blister card)	18 capsules/21 days
		150 mg dose (blister card)	27 capsules/21 days

Initial Evaluation

I. **Relacorilant (Lifyorli)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an oncologist; **AND**
   C. Treatment will be used in combination with nab-paclitaxel* (Abraxane); **AND**
   D. A diagnosis of **recurrent or persistent high-grade (grade 3) serous, epithelial ovarian, fallopian tube, or primary peritoneal cancer** when the following are met:
      1. Documentation of platinum-resistant disease, defined as progression within 6 months of prior platinum-based therapy (e.g., cisplatin, carboplatin, oxaliplatin); **AND**
      2. Member has received at least one prior bevacizumab*-containing treatment regimen; **AND**
         i. Member has <u>not</u> received more than three prior systemic therapies (e.g., carboplatin, cisplatin, docetaxel, doxorubicin, gemcitabine, nab-paclitaxel, oxaliplatin, or paclitaxel); **AND**
   E. Treatment is not prescribed in combination with glucocorticoids; **AND**
   F. Member meets <u>one</u> (1 or 2) of the following:
      1. Biomarker testing was completed and resulted in an actionable biomarker†; **AND**

i. For PD-L1 positive disease: treatment with PD-L1 directed therapy (i.e. pembrolizumab (Keytruda)*, etc.) has been ineffective, contraindicated or has not been tolerated; **OR**
    a. Member does not have a PD-L1 positive disease based on negative biomarker testing; **OR**
ii. For FRα positive disease: treatment with mirvetuximab soravtansine-gynx (Elahere)* has been ineffective, not tolerated, or contraindicated; **OR**
    a. Member does not have FRα positive disease based on negative biomarker testing; **OR**

2. Provider attestation biomarker testing cannot be completed

*Please note: medications notated with an asterisk may require additional review.

†Note: Actionable biomarkers include but not limited to, HER2 status (by IHC), PD-L1 (IHC, CPS), BRCA1/2, HRD status, MSI, MMR, TMB, BRAF, KRAS, FRa (FOLR1), RET, and NTRK1/2/3. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker.

II. Relacorilant (Lifyorli) is considered investigational when used for all other conditions, including but not limited to:
    F. Treatment in low-grade serous ovarian cancer (LGSOC), borderline ovarian tumors, platinum-sensitive disease, treatment naïve patients
    G. Endogenous hypercortisolism
    H. Endometrial, cervical, pancreatic, and prostate cancer

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Relacorilant (Lifyorli) will be used in combination with nab-paclitaxel* (Abraxane); **AND**
IV. Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

Supporting Evidence

I. Relacorilant (Lifyorli) is a selective glucocorticoid receptor antagonist (SGRA) indicated in combination with nab-paclitaxel for the treatment of adults with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received 1-3 prior systemic treatment regimens, at least one of which included bevacizumab.
II. The recommended dose for relacorilant (Lifyorli) is 150 mg taken orally once daily for three consecutive days on the day before, the day of, and the day after each weekly 80 mg/m^2 nab-

paclitaxel (Abraxane) infusion given for three weeks of a four week cycle, until disease progression or unacceptable toxicity.

III. Platinum resistant disease is defined as progression of disease less than six months after completing platinum containing therapy OR progression on primary or recurrence therapy OR stable or persistent disease (if not on maintenance therapy) OR complete remission and relapse less than 6 months after completing chemotherapy.

IV. Current treatment typically consists of sequential single-agent chemotherapy with or without bevacizumab, with increasing use of biomarker-directed therapies in eligible patients. Patients with advanced epithelial ovarian cancer are treated with debulking surgery, platinum doublet chemotherapy, and maintenance therapy with bevacizumab and/or a poly (adenosine diphosphate-ribose) polymerase (PARP) inhibitor. Combination chemotherapy with a platinum drug (i.e., carboplatin) and a taxane (i.e., paclitaxel) is the first-line chemotherapy in patients with ovarian cancer. Standard-of-care treatment options for patients with PROC include weekly nab-paclitaxel (albumin-bound paclitaxel), pegylated liposomal doxorubicin [PLD], gemcitabine, or topotecan administered as monotherapy or with bevacizumab. However, there is a rapid emergence of resistance to these treatments, approximately 70% of patients relapse and are incurable. Patients may respond to retreatment with platinum-based regimens initially, but eventually all develop platinum-resistant ovarian cancer (PROC), which has a median survival of approximately one year.

V. Tumor biomarker testing is recommended to include tests to identify potential benefits from targeted therapeutics that have tumor-specific or tumor-agnostic benefit including if prior testing did not include these markers. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Key biomarker-driven treatment options include mirvetuximab soravtansine-gynx (Elahere) and pembrolizumab (Keytruda), both of which are restricted to defined populations. Mirvetuximab soravtansine-gynx (Elahere) is indicated for patients with folate receptor alpha (FRα) -positive tumors, representing approximately 30% to 40% of patients with PROC. Pembrolizumab (Keytruda) is indicated in combination with paclitaxel, with or without bevacizumab, for patients with PD-L1–positive disease (CPS ≥1). However, these therapies require biomarker testing to confirm eligibility, which may introduce additional testing and access considerations.

VI. The National Comprehensive Cancer Network (NCCN) ovarian cancer (including fallopian tube cancer and primary peritoneal cancer) clinical practice guidelines (version 4.2026) recommend tumor biomarker testing prior to initiation of therapy for persistent/recurrent disease, if not previously done. Tumor biomarker analysis is recommended to include, tests to identify potential benefit from targeted therapeutics that have tumor-specific or tumor-agnostic benefit including, but not limited to, HER2 status (by immunohistochemistry [IHC]), PD-L1 (IHC, combined positive score [CPS]), *BRCA1/2*, HRD status, microsatellite instability (MSI), mismatch repair (MMR), tumor mutational burden (TMB), *BRAF*, *KRAS*, FRα (FOLR1), *RET*, and *NTRK1/2/3* if prior testing did not include these markers. Multigene panel testing (MGPT) may be particularly important in LCOC with limited approved therapeutic options. There are a variety of treatment options for recurrence therapy for platinum-resistant disease (including cytotoxic therapy, targeted therapy, hormone, therapy, and immunotherapy). Preferred cytotoxic therapies

include docetaxel, gemcitabine, liposomal doxorubicin ± bevacizumab, weekly paclitaxel ± bevacizumab, oral cyclophosphamide + bevacizumab, and topotecan ± bevacizumab (category 2A). Relacorilant (Lifyorli) and nab-paclitaxel is listed amongst the "Preferred" cytotoxic therapies (category 2A) (for patients who have been treated with up to three lines of therapy and prior bevacizumab). Other "Mirvetuximab soravtansine-gynx intravenous infusion (Elahere) is recommended as targeted therapy for FRα-expressing tumors (≥ 75% positive tumor cells) [category 1].

VII. The efficacy and safety of relacorilant (Lifyorli) was evaluated in the ROSELLA trial, a Phase 3, randomized, open-label, global multicenter study in women with recurrent, platinum-resistant, high-grade (grade 3) serous epithelial ovarian, primary peritoneal, or fallopian tube cancer (N=381). Eligible participants received 1 to 3 lines of prior systemic anticancer therapy, including ≥1 prior line of platinum therapy and prior treatment with bevacizumab. Participants were randomized 1:1 to receive intermittently dosed relacorilant (Lifyorli) in combination with nab-paclitaxel or nab-paclitaxel monotherapy. The primary endpoint was progression-free survival (PSF) assessed by blinded independent central review (BICR v1.1) and overall survival (OS).

VIII. Tumor response assessments occurred every 8 weeks for the first 40 weeks and every 12 weeks thereafter. The trial excluded patients who required chronic or frequent use of glucocorticoids. There is no biomarker-based requirement for participant selection. Subjects remained on study treatment until disease progression per RECIST version 1.1 as determined by the investigator, unmanageable toxicity, or until other criteria for discontinuation of study treatment were met.

- In the combination arm, the dose of nab-paclitaxel was reduced because relacorilant is a strong inhibitor of CYP3A4, which metabolizes nab-paclitaxel. Thus, the lower dose of nab paclitaxel in the combination arm (80 mg/m2) compared to the control arm (100 mg/m2) was chosen based on the pharmacokinetic data. Additionally, nab-paclitaxel does not require corticosteroid premedication. Since corticosteroids activate the same glucocorticoid receptor that relacorilant is designed to modulate, using them together would work against the drug's mechanism, making nab-paclitaxel the more compatible chemotherapy for this regimen.

IX. Baseline characteristics were generally well balanced across both arms of the trial. The number of prior lines of therapy were similar across both arms. Nine percent of patients had received one prior line of systemic therapy, 48% of patients had received two prior lines of systemic therapy, and 44% of patients had received three prior lines of systemic therapy. For platinum-resistant disease, 39% of patients received prior systemic therapy: all patients received prior bevacizumab, 99.5% had received a prior taxane (19% in the last line of therapy and 4% in the platinum-resistant setting) and 61% had received a prior PARP inhibitor. Of patients who had received a prior PARP inhibitor, 78% had radiographic progression while receiving the PARP inhibitor.

X. In ROSELLA, the median PFS was 6.5 months (95% CI: 5.6, 7.4) in the relacorilant (Lifyorli) in combination with nab-paclitaxel arm and 5.5 months (95% CI: 3.9, 5.9) in the nab-paclitaxel arm (HR 0.70 [95% CI: 0.54, 0.91]; p-value 0.0076), resulting in a 30% reduction in risk of progression or death. Median OS was 16 months (95% CI: 13, 18.3) in the relacorilant (Lifyorli) in

combination with nab-paclitaxel arm and 11.9 months (95% CI: 10, 13.8) in the nab-paclitaxel arm (HR 0.65 [95% CI: 0.51, 0.83]; p-value 0.0004), resulted in a 35% reduction in risk of death. Combination therapy with relacorilant (Lifyorli) and nab-paclitaxel, compared with nab-paclitaxel alone, improved median PFS by about one month and provided an improvement in OS by about 4.2 months, respectively. The overall response rate (ORR) was numerically higher for relacorilant (Lifyorli) and nab-paclitaxel, but not statistically significant at 36.9% for relacorilant (Lifyorli). While the PFS improvement was statistically significant, the magnitude of PFS benefit is less than the scanning interval (every eight weeks) and is not considered clinically meaningful. The results of median OS were both statistically significant and clinically meaningful. Study limitations include the open-label design and the applicability of these results to patients with greater than three lines of anticancer therapy. There are no head-to-head trials or prospective data to inform optimal sequencing.

XI. The safety of combination relacorilant (Lifyorli) and nab-paclitaxel was assessed in a pooled analysis where the overall the AE profile for the combination was consistent with the known safety profile of nab-paclitaxel monotherapy. More patients on relacorilant (Lifyorli) experienced adverse events, where the most common AE experienced by more than 20% of patients decreased hemoglobin, decreased neutrophils, fatigue, nausea, diarrhea, decreased platelets, rash, and decreased appetite. The overall Grade ≥ 3 AEs including neutropenia, anemia, and fatigue and overall serious AEs were numerically higher with relacorilant in combination with nab-paclitaxel, which had slightly longer treatment exposure, compared with nab-paclitaxel monotherapy (~1 month). Specific serious AEs of febrile neutropenia, sepsis, and infections and infestations were infrequent. Dose modifications due to AE were numerically higher in the relacorilant (Lifyorli) in combination with nab-paclitaxel group (73% vs 55%), but overall discontinuations due to AEs were comparable between the two treatment groups (<10%).

XII. The prescribing information for relacorilant (Lifyorli) includes warnings and precautions for neutropenia and severe infections, adrenal insufficiency, exacerbation of conditions treated with glucocorticoids and embryo-fetal toxicity. Relacorilant (Lifyorli) is contraindicated in patients receiving systemic glucocorticoids for lifesaving purposes (e.g., immunosuppression after organ transplantation) because relacorilant (Lifyorli) antagonizes the effect of glucocorticoids.

Investigational or Not Medically Necessary Uses

I. Relacorilant (Lifyorli) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Treatment in low-grade serous ovarian cancer (LGSOC), borderline ovarian tumors, platinum-sensitive disease
      i. In the ROSELLA trial population, patients were excluded if they had primary platinum-refractory disease (progression within 1 month of first-line platinum therapy), low-grade serous ovarian cancer (LGSOC), borderline ovarian tumors, platinum sensitive disease, or required recent or ongoing glucocorticoid use.

Therefore, restricting treatment to this population ensures alignment with clinical evidence.

B. Endogenous hypercortisolism
    i. Relacorilant (Lifyorli) previously received a complete response letter (CRL) from the FDA for an application in endogenous hypercortisolism (Cushing's syndrome), with the agency citing the need for additional evidence of efficacy. This regulatory action was not related to the ovarian cancer program.

C. Endometrial, cervical, pancreatic, and prostate cancer
    i. Relacorilant (Lifyorli) is currently being evaluated in these indications and use is considered experimental and investigational at this time. Additional studies for relacorilant (Lifyorli) are ongoing. The Phase 2 BELLA trial is evaluating relacorilant (Lifyorli) in combination with nab-paclitaxel and bevacizumab in ~270 patients with PROC, with primary completion expected in late 2026.

Appendix

I. The recommended dosage of relacorilant (Lifyorli) is 150 mg orally once on the day before, the day of, and the day after each nab-paclitaxel infusion (9 doses in 28-day cycle).
II. The recommended dosage for nab-paclitaxel is 80 mg/m2 administered as an intravenous infusion on Days 1, 8 and 15 of each 28-day cycle until disease progression or unacceptable toxicity
III. First Dose modification: 125 mg once the day before, the day of and the day after the nab-paclitaxel infusion. Members should permanently discontinue relacorilant (Lifyorli) if unable to tolerate after one dose reduction.
IV. Contraindications/Precautions: relacorilant (Lifyorli) is a glucocorticoid receptor antagonist which may make systemic glucocorticoids less effective. Similarly, coadministration of systemic glucocorticoids may make relacorilant (Lifyorli) less effective. Concurrent systemic glucocorticoid therapy for conditions (e.g.., autoimmune disorders) antagonizes the effect of glucocorticoids and systemic glucocorticoids may exacerbate these conditions. It is recommended to monitor patients for reduced effectiveness of relacorilant (Lifyorli) and glucocorticoids in patients receiving both. Patients who require chronic or frequent use of glucocorticoids were excluded from clinical trials of relacorilant (Lifyorli) in combination with nab-paclitaxel. Additionally, relacorilant (Lifyorli) is contraindicated in patients receiving systemic glucocorticoids for lifesaving purposes (e.g., immunosuppression after organ transplantation). Pretreatment (before chemotherapy) with glucocorticoids is also not recommended.
V. Chemotherapy regimens for ovarian cancer may include bevacizumab monotherapy, docetaxel, gemcitabine, paclitaxel, carboplatin/paclitaxel, liposomal doxorubicin, carboplatin/liposomal doxorubicin, carboplatin/docetaxel, paclitaxel/bevacizumab.

References

1. Lifyorli Prescribing Information. Redwood City, CA: Corcept Therapeutics Incorporated; March 2026.
2. Formulary Dossier for relacorilant in combination with nab-paclitaxel. Corcept Therapeutics Incorporated; April 2026.

3. Olawaiye AB, Gladieff L, O'Malley DM, et al. Relacorilant and nab-paclitaxel in patients with platinum-resistant ovarian cancer (ROSELLA): An open-label, randomised, controlled, phase 3 trial. *Lancet*. 2025; 405(10496): 2205-2216.
4. National Comprehensive Cancer Network. Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer Version 4.2026. Available at: Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer - Guidelines Detail. Accessed June 9, 2026.
5. Herzog TJ, Armstrong DK, Brady MF, et al. Ovarian cancer clinical trial endpoints: Society of Gynecologic Oncology white paper. *Gynecol Oncol.* 2014;132(1):8-17. doi:10.1016/j.ygyno.2013.11.008

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
Long-acting Granulocyte Colony Stimulating Factor (G-CSF) Policy	Neutropenia
sorafenib, pazopanib (multi-targeted tyrosine kinase inhibitors) Policy	Off-label use noted: • Sorafenib/topotecan (2A) • Pazopanib (2B)

Policy Implementation/Update

Action and Summary of Changes	Date
Policy created	08/2026