New Drug Overview

Lifyorli (relacorilant)

RDL Category: Antineoplastics

Introduction

Disease Background:

- Cancers of the epithelial ovaries, fallopian tubes, and peritoneum are clustered together as it is thought they evolve from the same origin (*Smrke et al 2026*).
  - High-grade serous epithelial ovarian carcinoma (EOC), fallopian tube, and peritoneal carcinomas are thought to be a single clinical entity due to common clinical behavior and treatment (*Chen and Berek 2025*).
- It is estimated that close to 90% of primary malignant ovarian tumors are epithelial cancers (*Smrke et al 2026*).
  - In the US, ovarian cancer generally affects older adults who are older than 64 years of age.
    - In 2022, a surveillance concluded that ovarian cancer was the 7th most frequently diagnosed cancer globally in women (excluding nonmelanoma skin cancer).
- Persistent and/or frequent symptoms reported for clinical presentation include pelvic and/or abdominal pain, bloating, difficulty with eating or early satiety, diarrhea and/or constipation, vaginal bleeding, or urinary urgency/frequency (*Smrke et al 2026*).
- Lifyorli was FDA approved in 2026.

Pharmacology/Usage

- Lifyorli (relacorilant) is a reversible glucocorticoid receptor (GR) antagonist antineoplastic agent. In functional in vitro assays with the mineralocorticoid receptor, relacorilant demonstrated no agonist or antagonist activity. In human cell-line derived xenograft models, relacorilant enhanced apoptosis and antitumor activity when administered with paclitaxel.
  - Cortisol binding to the GR is immunosuppressive, decreasing secretion of pro-inflammatory cytokines. GR antagonism may indirectly activate the immune system; relacorilant inhibited the cortisol-induced reduction of tumor necrosis factor alpha and interferon gamma in stimulated peripheral blood mononuclear cells.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Lifyorli (relacorilant)
• In combination with nab-paclitaxel for the treatment of adults with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received one to three prior systemic treatment regimens, at least one of which included bevacizumab.	✔

(Prescribing information: Lifyorli 2026)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Lifyorli (relacorilant)	Capsules: 25mg, 100mg -Swallow whole; do not crush, chew, dissolve or split the capsules.	PO	Take 150mg PO once on the day before, the day of, and the day after each nab-paclitaxel infusion until disease progression or unacceptable toxicity. Take with food. -The recommended dosage for nab-paclitaxel is 80mg/m^2 administered as an IV infusion on days 1, 8, and 15 of each 28-day cycle until disease progression or unacceptable toxicity. Refer to the prescribing information for more information on nab-paclitaxel administration. Do not substitute with other paclitaxel formulations.	• If a dose of Lifyorli is missed by less than 12 hrs, take the missed dose. If a dose is missed by 12 hours or more, skip the missed dose and take the next dose at the regularly scheduled time. Do not take 2 doses at the same time to make up for a missed dose. • If vomiting occurs after taking Lifyorli, do not take an additional dose. • Refer to the prescribing information for dosage modifications for adverse reactions. • Avoid Lifyorli in combination with nab-paclitaxel in patients with moderate or severe hepatic impairment.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Lifyorli in combination with nab-paclitaxel was assessed in a multicenter, open-label, active-controlled, randomized, two-arm trial (ROSELLA) that included patients with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer.
  - Patients were permitted to receive up to 3 prior lines of systemic therapy and prior bevacizumab was required.
    - The trial excluded patients who required chronic or frequent use of glucocorticoids.
  - Patients (N=381) were randomized to receive:
    - Lifyorli 150mg PO the day before, the day of, and the day after administration of nab-paclitaxel 80mg/m^2 IV infusion on days 1, 8, and 15 of each 28-day cycle (N=188), or
    - Nab-paclitaxel 100mg/m^2 IV infusion on days 1, 8, and 15 of each 28-day cycle (N=193).
    - Treatment was administered until disease progression or unacceptable toxicity.
  - The median age of included patients was 62 years (range 26 to 86) and 71% were White. Nearly all patients had an Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 (69%) or 1 (30%). In addition, 9% had received 1 prior line of systemic therapy, 48% of patients had received 2 prior lines of systemic therapy, and 44% of patients had received 3 prior lines of systemic therapy. All patients received prior bevacizumab.
  - Tumor response assessments occurred every 8 weeks for the first 40 weeks and every 12 weeks thereafter.

- The major efficacy outcome measures were progression-free survival (PFS) assessed by blinded independent central review (BICR) and overall survival (OS). PFS was evaluated per Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1.
  - Results suggested that Lifyorli demonstrated a statistically significant improvement in PFS and OS for patients randomized to Lifyorli in combination with nab-paclitaxel compared to nab-paclitaxel monotherapy.
  - Results are presented in the table below, which was adapted from the prescribing information.

Table 3. Efficacy results

	Lifyorli + nab-paclitaxel (N=188)	**Nab-paclitaxel (N=193)**
Progression-free Survival (PFS) by BICR		
Number (%) of patients with events	113 (60%)	121 (63%)
Median, months	6.5	5.5
Hazard Ratio; p-value	0.70; p=0.0076	
Overall Survival (OS)		
Number (%) of patients with events	129 (69%)	159 (82%)
Median, months	16.0	11.9
Hazard Ratio; p-value	0.65; p=0.0004	

Clinical guidelines

- **National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Ovarian Cancer, including Fallopian Tube Cancer and Primary Peritoneal Cancer** (*NCCN 2026*).
  - Albumin-bound paclitaxel/relacorilant were added to the NCCN guidelines.
    - This combination was added as preferred under recurrence therapy for platinum-resistant disease with notes that it should be for patients who have been treated with up to 3 lines of therapy and prior bevacizumab, and that steroid premedication should not be used.

Safety summary

- **Contraindications:**
  - In patients receiving systemic glucocorticoids for lifesaving purposes (eg, immunosuppression after organ transplantation) as Lifyorli antagonizes the effect of glucocorticoids.

- **Box Warning:** None.

- **Warnings and precautions:**
  - Lifyorli in combination with nab-paclitaxel can cause neutropenia, including febrile neutropenia and severe infections. The median time to onset of neutropenia was 15 days (range 8 to 329). In addition, 38% of patients initiated granulocyte colony-stimulating factor (G-CSF) during the first or second cycle of therapy.
    - Monitor complete blood counts prior to each weekly treatment with Lifyorli and as clinically indicated.

- Based on the severity of neutropenia, delay, reduce dose or permanently discontinue Lifyorli in combination with nab-paclitaxel. Consider short-acting G-CSF administration as applicable.
- Consider the possibility of concurrent adrenal insufficiency, especially in the setting of serious infection. Inform patients to promptly report any episodes of fever to their healthcare provider.

○ Lifyorli can cause adrenal insufficiency, which can occur at any time during Lifyorli treatment. The risk of adrenal insufficiency is increased in situations of stress. Consider whether supplemental glucocorticoids are required in the perioperative period in patients who have received Lifyorli within 30 days of surgery.
- Monitor patients receiving Lifyorli for signs and symptoms of adrenal insufficiency. Serum cortisol levels do not provide an accurate assessment of adrenal insufficiency in patients receiving Lifyorli.
- Withhold Lifyorli and administer glucocorticoid therapy if adrenal insufficiency is suspected. High doses of supplemental glucocorticoids may be needed to overcome the glucocorticoid receptor antagonism produced by Lifyorli
  - When deciding on the duration of glucocorticoid treatment, consider the long half-life of relacorilant and that glucocorticoid receptor antagonism may occur for up to 6 days after the last dose of Lifyorli.
- After resolution of adrenal insufficiency, resume previous dose, reduce dose or permanently discontinue Lifyorli based on severity.
- Educate patients on the symptoms associated with adrenal insufficiency and advise them to contact a healthcare provider if they occur.

○ Use of Lifyorli in patients taking systemic glucocorticoids for other conditions may exacerbate these conditions.
- Monitor patients for reduced effectiveness of Lifyorli and glucocorticoids in patients receiving both.
  - Patients who require chronic or frequent use of glucocorticoids were excluded from clinical trials of Lifyorli in combination with nab-paclitaxel.
- Lifyorli is contraindicated in patients receiving systemic glucocorticoids for lifesaving purposes.

- **Common adverse drug reactions**:

○ Listed % incidence for adverse drug reactions= reported % incidence for drug (Lifyorli plus nab-paclitaxel) minus reported % incidence for nab-paclitaxel for all grades that occurred in ≥10% of patients. Please note that an incidence of 0% means the incidence was the same as or less than comparator.
- The most frequently reported adverse events included fatigue (9%), edema (7%), pyrexia (6%), nausea (9%), diarrhea (13%), stomatitis (10%), rash (14%), nail disorders (7%), decreased appetite (10%), cough (9%), dizziness (9%), and dysgeusia (8%).
- Laboratory abnormalities included hemoglobin decreased (10%), leukocytes decreased (5%), neutrophils decreased (9%), and platelets decreased (14%).

- **Drug interactions:**

○ Both relacorilant and paclitaxel are CYP3A substrates.
- Avoid coadministration of Lifyorli plus nab-paclitaxel with strong CYP3A inducers.

○ Paclitaxel is a substrate of CYP2C8 and CYP3A and relacorilant is a CYP3A substrate.
- Monitor for reduced effectiveness of Lifyorli plus nab-paclitaxel with CYP2C8 inducers and moderate CYP3A inducers.

○ Paclitaxel is a substrate of CYP2C8.
- Monitor for increased adverse reactions and modify the dosage for adverse reactions as recommended when used with CYP2C8 inhibitors.

○ Relacorilant is a strong CYP3A inhibitor.
- Avoid concomitant use unless otherwise recommended in the prescribing information for CYP3A substrates.

- Relacorilant is a weak CYP2C8 inducer.
  - Avoid concomitant use with certain CYP2C8 substrates unless otherwise recommended in the prescribing information for CYP2C8 substrates where minimal concentration changes may lead to reduced effectiveness.
- Avoid coadministration in patients with other medical conditions requiring systemic glucocorticoids when possible. If coadministration cannot be avoided, monitor patients for reduced effectiveness of Lifyorli and glucocorticoids.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that based on findings in animals, Lifyorli can cause fetal harm when administered to a pregnant woman. There are no available data on use in pregnant women to inform drug-associated risk.
    - Advise pregnant women and females of reproductive potential of the potential risk to a fetus.
    - Verify pregnancy status in women of reproductive potential prior to starting Lifyorli.
      - Advise females of reproductive potential to use effective contraception during treatment with Lifyorli and for 1 week after the last dose.
      - Advise male patients with female partners of reproductive potential to use effective contraception during treatment with Lifyorli and for 1 week after the last dose.
  - The safety and efficacy of use in the pediatric population have not been established.

Conclusion

- High-grade serous epithelial ovarian carcinoma (EOC), fallopian tube, and peritoneal carcinomas are thought to be a single clinical entity due to common clinical behavior and treatment (*Chen and Berek 2025*).
- Lifyorli is an oral glucocorticoid receptor antagonist 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 one to three prior systemic treatment regimens, at least one of which included bevacizumab.
  - Use is contraindicated in patients receiving systemic glucocorticoids for lifesaving purposes.
- The efficacy of Lifyorli in combination with nab-paclitaxel was assessed in a randomized, multicenter, open-label, active-controlled trial that included patients with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer.
  - The major efficacy outcome measures were progression-free survival (PFS) assessed by blinded independent central review (BICR) and overall survival (OS).
    - Results suggested that Lifyorli demonstrated a statistically significant improvement in PFS and OS for patients randomized to Lifyorli in combination with nab-paclitaxel compared to nab-paclitaxel monotherapy.
- Lifyorli has been added to guidelines as a preferred therapy but the guidelines note that it is for patients who have been treated with up to 3 lines of therapy and prior bevacizumab.

- It is recommended that Lifyorli should be non-recommended with conditions in order to confirm the appropriate diagnosis and clinical parameters for use.

- **RDL Placement:**
  - ☐ Recommended
  - ☒ Non-Recommended with Conditions

References

- Chen LM, Berek JS. Epithelial carcinoma of the ovary, fallopian tube, and peritoneum: Clinical features and diagnosis. UpToDate website. Last updated July 7, 2025. Accessed June 16, 2026. www.uptodate.com.
- Lifyorli. Package insert. Corcept Therapeutics Incorporated; March 2026.
- National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Ovarian Cancer, including fallopian tube cancer and primary peritoneal cancer. Version 4.2026-April 10, 2026. Accessed June 16, 2026. www.nccn.com.
- Smrke A, Ko YJ, Fedorowicz Z. Epithelial Ovarian, Fallopian Tube, and Primary Peritoneal Cancer. Dynamed Website. Last updated April 24, 2026. Accessed June 16, 2026. https://www.dynamed.com.

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