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Managing Drug Interactions With Oral Anticancer Treatments

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Abstract

The use of oral anticancer treatments is widespread and vital to modern cancer treatment. Novel oral chemotherapy and targeted therapy treatments continue to receive US Food and Drug Administration approval every year, making knowledge of these agents a necessity for practitioners working in oncology. Many oral anticancer agents are prone to drug interactions that can contribute to adverse effects and decrease therapy efficacy. Potential drug-drug interactions include (1) interactions with CYP3A4 inhibitors and inducers, (2) interactions related to gastric acid suppression, (3) interactions related to prolongation of the cardiac QT interval, (4) interactions related to anticoagulant medications, and (5) drug-food and drug-herb interactions. Identifying potential drug interactions and appropriately managing them is key to preventing adverse effects and ensuring maximum efficacy while on oral anticancer therapy. Management of adverse effects increases patient compliance, ensures medication safety, and allows patients to remain on therapy. This article discusses the mechanisms of interactions and types of interacting medications. Specific recommendations are discussed.

Oral antineoplastic agents have proved essential for the treatment of many types of cancer. They may be prescribed alone, in combination with intravenous chemotherapy, or with immune checkpoint inhibitors. One difference between oral chemotherapy (OC) agents and intravenous agents is that oral agents are at higher risk for drug-drug interactions (DDIs; Rogala et al., 2019).

People with cancer are more likely to experience DDIs (Prely et al., 2022). This is partly due to older age as well as having multiple other medical disorders and needing several medications (Marcath et al., 2021). Polypharmacy includes prescribed medications, often from multiple physicians, along with over-the-counter medications, as well as herbal remedies. One study reviewed the care of 142 patients with cancer and found a mean number of medications of 9.8 per patient (Nightingale et al., 2018). Of those, 6.7 were prescribed medications, 2.6 were over-the-counter agents, and 0.5

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were herbal remedies or supplements (Nightingale et al., 2018). Another estimate revealed that 85% of ambulatory people with cancer received five or more medications, and 43% received 10 or more medications (Nightingale et al., 2015). When people with cancer take many medications, the likelihood of drug-drug and herb-drug interactions (HDIs) is greatly increased.

Different sources have found differing estimates of the frequency of DDIs in people undergoing cancer treatment. One study of 294 cancer patients found a median number of eight current chronic medications (Prely et al., 2022). They also found that 90.8% of people had at least one DDI, and 23.1% of people had HDIs. In addition, 21.7% of people had both DDIs and HDIs. Another group looked at 167 patients enrolled in SWOG trials of OC agents (Marcath et al., 2021). Using Lexicomp, researchers identified 28.7% of people with moderate or severe DDIs; a pharmacist review determined that 7.2% of these DDIs were clinically relevant. A comprehensive review identified an association of DDIs with outcome parameters such as overall survival, progression-free survival, as well as adverse effects (Sharma et al., 2019). In another study, a group of 356 patients receiving tyrosine kinase inhibitors was studied (Keller et al., 2018). A total of 244 potential DDIs were identified, 44.7% of which were described as severe (Keller et al., 2018).

Interactions can be described as pharmacokinetic interactions or as pharmacodynamic interactions. Pharmacokinetic interactions are those that change the absorption, distribution, metabolism, or elimination of the target agents. Pharmacodynamic interactions are described as interactions in which the medications alter the others' effects directly. Potential DDIs can be characterized as additive, synergistic, or antagonistic in nature (Cascorbi, 2012; Rogala et al., 2019). In addition, DDIs can be characterized by severity and likelihood of occurring. The OC might be the culprit and in other circumstances might be the target.

To complete a comprehensive drug interaction assessment, a thorough medication history must be performed (Elbeddini et al., 2021; Mackler et al., 2019). Medication reconciliation allows for the identification of DDIs as well as an opportunity to identify potentially inappropriate medications and allow for selective deprescribing. As some patients may think nononcology medications are not concerning, it is important to ask about all medications, including eye medications, blood pressure medications, and herbal remedies. Sources include patient and family recollection, prescription bottles, and pharmacy dispensing records.

Once a complete medication history has been obtained, the list should be entered into a computerized drug interaction application. There are several platforms that are freely available and others that are subscription services. In one analysis, Drugs.com was the top-performing free tool, and Lexicomp was the top-performing subscription service. There is often insufficient literature regarding the clinical significance of DDIs with OC. However, unidentified and unresolved DDIs may lead to excessive toxicity. In addition, DDIs might lead to decreased treatment effectiveness. Both can result in treatment discontinuation (Marcath et al., 2018; Sharma et al., 2019). This article will discuss DDIs related to (1) CYP3A4 inhibition and induction, (2) gastric acid inhibitors, (3) prolongation of the QTc interval, (4) anticoagulants, and (5) food and herbal remedies.

DDIs RELATED TO CYP3A4 INHIBITORS AND INDUCERS

Many OCs are hepatically metabolized through the CYP3A4 enzyme system. Inhibition and induction of CYP3A4 are examples of pharmacokinetic interactions. Ketoconazole, used to treat fungal infections, is used by the US Food and Drug Administration (FDA) as an example of a strong CYP3A4 inhibitor (Lexicomp, 2022). Use of a CYP3A4 inhibitor with a CYP3A4 substrate can lead to elevated drug levels. Neratinib (Nerlynx), a HER2 inhibitor used to treat breast cancer, is a CYP3A4 substrate (Lexicomp, 2022). In one study with ketoconazole, the maximum concentration (C_{max}) of neratinib increased by over threefold and the area under the curve (AUC) by over fourfold (Puma Biotechnology, Inc., 2017). This combination can lead to increased toxicity from the OC. CYP3A4 inhibitors are categorized by the strength of their inhibition. Strong CYP3A4 inhibitors increase the AUC of CYP3A4 substrates by ≥ fivefold

(Center for Drug Evaluation and Research, 2020). Strong CYP3A4 inhibitors include clarithromycin, idelalisib, itraconazole, ketoconazole, nefazodone, posaconazole, most protease inhibitors, and voriconazole. Moderate CYP3A4 inhibitors increase the AUC of CYP3A4 substrates by ≥ two- to < fivefold. These include aprepitant, ciprofloxacin, crizotinib, cyclosporine, diltiazem, erythromycin, fluconazole, imatinib, and verapamil.

There are also medications that induce the CYP3A4 enzyme. Rifampicin is used to treat bacterial infections, like tuberculosis, and is a strong CYP3A4 inducer (Lexicomp, 2022). When used with medications that are CYP3A4 substrates, it will decrease their serum concentration. Ribociclib (Kisqali) is an OC used to treat breast cancer and is a CYP3A4 substrate (Lexicomp, 2022). When rifampicin was used with ribociclib, the ribociclib C_{max} was reduced by 81% and the AUC by 89% (Lexicomp, 2022). This combination could lead to decreased efficacy of the OC. CYP3A4 inducers are categorized by the strength of their enzyme induction. Strong CYP3A4 inducers decrease the AUC of CYP3A4 substrates by ≥ 80% (Center for Drug Evaluation and Research, 2020). Strong CYP3A4 inducers include apalutamide, carbamazepine, enzalutamide, mitotane, phenytoin, rifampicin, and St. John's wort (Center for Drug Evaluation and Research, 2020). Moderate CYP3A4 inducers decrease the AUC of CYP3A4 substrates by ≥ 50% to < 80%. Moderate CYP3A4 inducers include bosentan, efavirenz, etravirine, phenobarbital, and primidone. Table 1 describes the dose adjustment recommendations when OCs are used with CYP3A4 inhibitors and inducers.

DDIs RELATED TO GASTRIC ACID SUPPRESSION

Numerous oral chemotherapies rely on pH for optimal absorption (Lam et al., 2016). Gastric acid suppressing (GAS) medications raise stomach pH, presenting potential for DDIs (Lam et al., 2016). For example, erlotinib (Tarceva) is a weak base that relies on low pH for absorption (Gruber et al., 2018). Raising stomach pH using GAS medications has shown to impact the solubility and absorption of erlotinib, which has translated to a significant clinical effect (Lam et al., 2016). A study following patients who were prescribed erlotinib while also taking a proton pump inhibitor (PPI) or a histamine-2 receptor antagonist (H_2RA) concomitantly found a reduced progression-free survival compared with the group taking erlotinib alone (5.3 months vs. 11.0 months, p = .029; Lam et al., 2016). Pazopanib (Votrient) is another example of an OC that is impacted by pH (Pisano et al., 2019). Patients with soft-tissue sarcoma taking concomitant GAS agents and pazopanib therapy experienced a shorter progression-free survival relative to patients taking pazopanib alone (5.3 months vs. 6.7 months; Pisano et al., 2019). Patients taking an H_2RA were counseled to take their pazopanib dose 2 hours before or 10 hours after their H_2RA dose, but pazopanib efficacy was still decreased (Pisano et al., 2019).

Furthermore, if there is a DDI between an OC and a GAS medication, the GAS agent should be tapered and discontinued to avoid the interaction, if clinically appropriate (Lam et al., 2016; Pisano et al., 2019). For patients requiring H_2RAs, dosing 2 hours after their OC dose or 10 hours before is a common strategy (Pisano et al., 2019). However, this recommendation does not always resolve the DDI. One challenge of deprescribing PPIs is the rebound acid hypersecretion (RAHS) phenomenon (Odenthal et al., 2020). To help mitigate RAHS, the dose of the PPI can be tapered (Odenthal et al., 2020). The PPI dose can be cut by half every 2 weeks until the patient is taking the lowest dose. Following that should be every-other-day dosing with H_2RA doses taken on days in which PPIs are not taken, with eventual discontinuation of the PPI (Odenthal et al., 2020). Table 2 shows administration recommendations for when OCs are used with GAS medications.

DDIs RELATED TO PROLONGATION OF THE CARDIAC QT INTERVAL

While the potential of QTc prolongation (corrected QT interval prolongation) is dependent on the medication, any significant increase in the QTc is potentially life threatening. QTc is the length of time of ventricular depolarization and repolarization on the electrocardiogram (ECG; Kim et al., 2021). The normal QTc interval in males is < 450 ms and in females is < 460 ms (Giudicessi et al., 2019). The National Cancer Institute Common Terminology Criteria for Adverse Events

Table 1. Dosage Adjustments Recommended When Oral Chemotherapies Are Used With CYP3A4 Inhibitors and Inducers

	Strong 3A4 inhibitor (e.g., clarithromycin, ketoconazole, most protease inhibitors, voriconazole)	Moderate 3A4 inhibitor (e.g., ciprofloxacin, cyclosporine, diltiazem, fluconazole, verapamil)	Strong 3A4 inducer (e.g., carbamazepine, phenytoin, rifampicin, St. John's wort)	Moderate 3A4 inducer (e.g., phenobarbital and primidone)
Abemaciclib	Avoid use with ketoconazole. Concomitant use with other CYP3A4 inhibitors requires dose reduction: 200 mg bid or 150 mg bid to 100 mg bid; 100 mg bid to 50 mg bid		Avoid concomitant use	
Abiraterone (Yonsa brand)			Increase dosing frequency to bid	
Abiraterone (Zytiga brand)	Avoid or monitor closely for adverse effects		Avoid or monitor closely for adverse effects	
Acalabrutinib	Avoid concomitant use	Reduce dose to 100 mg daily	Increase dose to 200 mg bid	
Adagrasib	Avoid until steady state concentration reached	Monitor therapy	Avoid	
Alpelisib			Avoid concomitant use	
Apalutamide	Avoid or monitor closely for adverse effects			
Asciminib	Avoid or monitor closely for adverse effects			
Avapritinib	Avoid concomitant use	Reduce dose to 100 mg daily in GIST and 50 mg daily in AdvSM	Avoid concomitant use	Avoid concomitant use
Axitinib	Reduce dose by approximately 50%, then titrate up or down based on safety and tolerability		Avoid concomitant use	Avoid concomitant use
Belumosudil			Increase to 200 mg bid	
Bosutinib	Avoid concomitant use	Avoid concomitant use	Avoid concomitant use	
Brigatinib	Reduce dose by approximately 50% (i.e., 180 mg to 90 mg or 90 mg to 60 mg)	Reduce dose by approximately 40% (i.e., 180 mg to 120 mg, 120 mg to 90 mg, or 90 mg to 60 mg)	Avoid concomitant use	Increase daily dose in 30-mg increments every 7 days as tolerated to a maximum of twice the original dose
Cabozantinib	Reduce dose by 20 mg		Increase dose by 20 mg as tolerated	
Capmatinib	Avoid or monitor closely for adverse effects		Avoid concomitant use	Avoid concomitant use

Note. AdvSM = advanced systemic mastocytosis; ALCL = anaplastic large cell lymphoma; ALK = anaplastic lymphoma kinase; bid = 2 times per day; BSA = body surface area; CML = chronic myeloid leukemia; CML-CP = chronic myeloid leukemia chronic phase; GIST = gastrointestinal stromal tumor; HER2 = human epidermal growth factor receptor 2; NSCLC = non–small cell lung cancer; Ph+ = Philadelphia chromosome positive; pNET = peripheral neuroendocrine tumor; RCC = renal cell cancer; ROS1 = ROS proto-oncogene 1. Information from Lexicomp (2022); Micromedex (2022).

Table 1. Dosage Adjustments Recommended When Oral Chemotherapies Are Used With CYP3A4 Inhibitors and Inducers (cont.)

	Strong 3A4 inhibitor (e.g., clarithromycin, ketoconazole, most protease inhibitors, voriconazole)	Moderate 3A4 inhibitor (e.g., ciprofloxacin, cyclosporine, diltiazem, fluconazole, verapamil)	Strong 3A4 inducer (e.g., carbamazepine, phenytoin, rifampicin, St. John's wort)	Moderate 3A4 inducer (e.g., phenobarbital and primidone)
Ceritinib	Reduce dose by approximately 33%, round to the nearest 150 mg dosage strength		Avoid concomitant use	
Cobimetinib	Avoid concomitant use	Avoid concomitant use	Avoid concomitant use	Avoid concomitant use
Crizotinib	Reduce dose to 250 mg daily for *ALK*- or *ROS1*-positive metastatic NSCLC and reduce dose to second dose reduction based on BSA for systemic *ALK*-positive ALCL	Avoid or monitor closely for adverse effects	Avoid concomitant use	
Dabrafenib	Avoid or monitor closely for adverse effects		Avoid or monitor closely for adverse effects	
Dasatinib	Reduce dose from 100 mg to 20 mg or 140 mg to 40 mg		Increase dose (no specific recommendations)	
Duvelisib	Reduce dose to 15 mg bid	Avoid or monitor closely for adverse effects	Avoid concomitant use	
Encorafenib	Reduce dose by approximately 66%	Reduce dose by approximately 50%	Avoid concomitant use	Avoid concomitant use
Entrectinib	If BSA is > 1.5 m^2, reduce dose to 100 mg daily; if BSA is ≤ 1.5 m^2, avoid concomitant use	If BSA is > 1.5 m^2, reduce dose to 200 mg daily; if BSA is ≤ 1.5 m^2, avoid concomitant use	Avoid concomitant use	Avoid concomitant use
Enzalutamide			Avoid concomitant use	Avoid concomitant use
Erdafitinib	Avoid or monitor closely for adverse effects		Avoid concomitant use	Increase dose to 9 mg daily based on tolerability
Erlotinib	Reduce dose in 50 mg increments		Increase dose in 50-mg increments every 2 weeks as tolerated to a maximum of 450 mg	Increase dose in 50-mg increments every 2 weeks as tolerated to a maximum of 450 mg
Everolimus	Avoid concomitant use	Reduce dose to 2.5 mg daily, can increase to 5 mg daily if tolerated	Increase dose from 10 mg to 20 mg using 5 mg increments	

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Table 1. Dosage Adjustments Recommended When Oral Chemotherapies Are Used With CYP3A4 Inhibitors and Inducers (cont.)

	Strong 3A4 inhibitor (e.g., clarithromycin, ketoconazole, most protease inhibitors, voriconazole)	Moderate 3A4 inhibitor (e.g., ciprofloxacin, cyclosporine, diltiazem, fluconazole, verapamil)	Strong 3A4 inducer (e.g., carbamazepine, phenytoin, rifampicin, St. John's wort)	Moderate 3A4 inducer (e.g., phenobarbital and primidone)
Fedratinib	Reduce dose to 200 mg daily		Avoid concomitant use	Avoid concomitant use
Gefitinib	Avoid or monitor closely for adverse effects		Increase to 500 mg daily	
Gilteritinib	Avoid or monitor closely for adverse effects			
Glasdegib	Avoid or monitor closely for adverse effects		Avoid concomitant use	
Ibrutinib	Specific recommendations for dose reduction can be found in the package insert based on ibrutinib indication and the CYP3A4 inhibitor and dose	Specific recommendations for dose reduction can be found in the package insert based on indication and CYP3A4 inhibitor and dose	Avoid concomitant use	
Idelalisib	Avoid or monitor closely for adverse effects		Avoid concomitant use	
Imatinib	Avoid or monitor closely for adverse effects		Increase by at least 50% and monitor clinical response	
Ivosidenib	Reduce dose to 250 mg daily	Avoid or monitor closely for adverse effects	Avoid concomitant use	
Ixazomib			Avoid concomitant use	
Lapatinib	Reduce dose to 500 mg daily		Increase dose gradually to 4,500 mg daily in HER2-positive metastatic breast cancer or 5,500 mg daily in hormone receptor positive, HER2-positive breast cancer based on tolerability	
Larotrectinib	Reduce dose by 50%		Double the dose	
Lorlatinib	Reduce dose to 50 mg daily		Avoid concomitant use	Increase dose to 125 mg daily
Midostaurin	Avoid or monitor closely for adverse effects		Avoid concomitant use	

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Table 1. Dosage Adjustments Recommended When Oral Chemotherapies Are Used With CYP3A4 Inhibitors and Inducers (cont.)

	Strong 3A4 inhibitor (e.g., clarithromycin, ketoconazole, most protease inhibitors, voriconazole)	Moderate 3A4 inhibitor (e.g., ciprofloxacin, cyclosporine, diltiazem, fluconazole, verapamil)	Strong 3A4 inducer (e.g., carbamazepine, phenytoin, rifampicin, St. John's wort)	Moderate 3A4 inducer (e.g., phenobarbital and primidone)
Mobocertinib	Avoid concomitant use	Reduce dose by approximately 50% and monitor closely for side effects	Avoid concomitant use	Avoid concomitant use
Neratinib	Avoid concomitant use	Avoid concomitant use	Avoid concomitant use	Avoid concomitant use
Nilotinib	Reduce dose to 300 mg daily in Ph+ CML or to 200 mg daily in Ph+ CML-CP		Avoid concomitant use	
Olaparib	Reduce dose to 100 mg bid	Reduce dose to 150 mg bid	Avoid concomitant use	Avoid concomitant use
Olutasidenib			Avoid concomitant use	Avoid concomitant use
Osimertinib	Avoid or monitor closely for adverse effects		Avoid concomitant use	
Palbociclib	Reduce dose to 75 mg daily		Avoid concomitant use	
Pazopanib	Reduce dose to 400 mg daily		Avoid concomitant use	
Pemigatinib	Reduce dose from 13.5 mg to 9 mg or 9 mg to 4.5 mg	Reduce dose from 13.5 mg to 9 mg or 9 mg to 4.5 mg	Avoid concomitant use	Avoid concomitant use
Pexidartinib	Reduce total daily dose from 800 mg to 400 mg, 600 mg to 400 mg, or 400 mg to 200 mg		Avoid concomitant use	
Pomalidomide	Avoid concomitant use		Avoid concomitant use	
Ponatinib	Reduce dose to 30 mg daily		Avoid or monitor closely for adverse effects	
Pralsetinib	Avoid concomitant use		Double the dose on day 7 of coadministration	
Regorafenib	Avoid concomitant use		Avoid concomitant use	
Ribociclib	Reduce dose to 400 mg daily		Avoid concomitant use	
Ripretinib	Avoid or monitor closely for adverse effects		Avoid concomitant use	

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Table 1. Dosage Adjustments Recommended When Oral Chemotherapies Are Used With CYP3A4 Inhibitors and Inducers (cont.)

	Strong 3A4 inhibitor (e.g., clarithromycin, ketoconazole, most protease inhibitors, voriconazole)	Moderate 3A4 inhibitor (e.g., ciprofloxacin, cyclosporine, diltiazem, fluconazole, verapamil)	Strong 3A4 inducer (e.g., carbamazepine, phenytoin, rifampicin, St. John's wort)	Moderate 3A4 inducer (e.g., phenobarbital and primidone)
Ruxolitinib	Specific recommendations for dose reduction can be found in the package insert based on ruxolitinib indication and the CYP3A4 inhibitor and dose	For fluconazole: Specific recommendations for dose reduction can be found in the package insert based on ruxolitinib indication and the CYP3A4 inhibitor and dose	Avoid or monitor closely for adverse effects	
Selpercatinib	Reduce dose from 120 mg bid to 40 mg bid or 160 mg bid to 80 mg bid	Reduce dose from 120 mg bid to 80 mg bid or 160 mg bid to 120 mg bid	Avoid concomitant use	Avoid concomitant use
Selumetinib	If dose is 25 mg/m^2 bid to 20 mg/m^2 bid; if dose is 20 mg/m^2 bid to 15 mg/m^2 bid	If dose is 25 mg/m^2 bid to 20 mg/m^2 bid; if dose is 20 mg/m^2 bid to 15 mg/m^2 bid	Avoid concomitant use	Avoid concomitant use
Sonidegib	Avoid concomitant use	Avoid concomitant use	Avoid concomitant use	Avoid concomitant use
Sorafenib			Avoid concomitant use	
Sunitinib	Reduce dose to 37.5 mg daily in GIST or RCC and to 25 mg daily in pNET		Increase dose to a maximum of 87.5 mg daily in GIST and RCC or to 62.5 mg daily in pNET in 12.5 mg increments	Increase dose to a maximum of 87.5 mg daily in GIST and RCC or to 62.5 mg daily in pNET in 12.5 mg increments
Tazemetostat	Avoid concomitant use	Reduce total daily dose by 50%	Avoid concomitant use	Avoid concomitant use
Tepotinib			Avoid concomitant use	
Tivozanib			Avoid concomitant use	
Tucatinib			Avoid concomitant use	
Vandetanib			Avoid concomitant use	
Vemurafenib	Avoid concomitant use		Increase dose by 240 mg as tolerated	
Venetoclax	Reduce dose by at least 75% if at steady daily dose; concomitant use is contraindicated at initiation and during ramp-up phase	Reduce dose by at least 50%	Avoid concomitant use	Avoid concomitant use
Zanubrutinib	Reduce dose to 80 mg daily	Reduce dose to 80 mg bid	Avoid concomitant use	Avoid concomitant use

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Table 2. Administration Recommendations for When Oral Chemotherapies Are Used With Gastric Acid Suppressing Medications

Medication	Antacids	H_2RAs	PPIs
Acalabrutinib capsules[a]	Separate by 2 hours	Take 2 hours before H_2RA	Contraindicated: Use H_2RA/antacid
Bosutinib	Separate by 2 hours	Separate by 2 hours	Contraindicated: Use H_2RA/antacid
Capecitabine	–	–	Monitor therapy
Dacomitinib	–	Take 6 hours before or 10 hours after H_2RA	Contraindicated: Use H_2RA/antacid
Dasatinib	Separate by 2 hours	Contraindicated: Use antacid	Contraindicated: Use antacid
Erlotinib	Separate by several hours	Take 2 hours before or 10 hours after H_2RA	Contraindicated: Use H_2RA/antacid
Gefitinib	Take 6 hours before or 6 hours after	Take 6 hours before or 6 hours after H_2RA	Separate by 12 hours
Infigratinib	Separate by 2 hours	Take 2 hours before or 10 hours after H_2RA	Contraindicated: Use H_2RA/antacid
Methotrexate	–	–	Switch to H_2RA/antacid if high dose
Neratinib	Take 3 hours after antacid	Take 2 hours before or 10 hours after H_2RA	Contraindicated: Use H_2RA/antacid
Nilotinib	Separate by 2 hours	Take 2 hours before or 10 hours after H_2RA	Contraindicated: Use H_2RA/antacid
Palbociclib	–	–	Consider antacid/H_2RA
Pazopanib	Separate by several hours	Contraindicated: Use antacid	Contraindicated: Use antacid
Pexidartinib	Separate by 2 hours	Take 2 hours before or 10 hours after H_2RA	Contraindicated: Use H_2RA/antacid
Selpercatinib	Separate by 2 hours	Take 2 hours before or 10 hours after H_2RA	Contraindicated: Use H_2RA/antacid
Sorafenib	–	–	Monitor therapy
Sotorasib	Take 4 hours before or 10 hours after antacid	Contraindicated: Use antacid	Contraindicated: Use antacid

Note. H_2RA = histamine-2 receptor antagonist; PPIs = proton pump inhibitors. Information from Lexicomp (2022); Micromedex (2022).
[a]The new tablet formation does not have gastric acid suppressing interactions.

defines QTcP as grade 1 at 450 ms to 480 ms, grade 2 at 481 ms to 500 ms, grade 3 at > 501 ms or > 60 ms from baseline, and grade 4 with torsades de pointes, polymorphic ventricular tachycardia, or signs or symptoms of serious arrhythmias (Kim et al., 2021). An increased QTc can result in syncope, seizures, or sudden death (Nachimuthu et al., 2012). Patients at higher risk include women, those of older age, those with preexisting cardiac rhythm disorders, and those with congenital long QT syndrome.

When a patient is starting an OC with QTc prolongation characteristics, the risk can be reduced by correcting any electrolyte abnormalities (potassium, magnesium, and calcium), stopping the use of diuretics if possible, stopping any other medications that are associated with QTcP, and checking an ECG for any baseline QTc prolongation. Most OCs with the potential for QTc prolongation have recommendations for monitoring the ECG after initiation; these are shown in Table 3.

Table 3. QT Prolongation Monitoring Recommendations

Medication	FDA-approved indications	QTcP frequency	Monitoring recommendations
Asciminib	Philadelphia chromosome–positive chronic myelogenous leukemia	1%–10%	Monitor if history of cardiovascular risk factors
Adagrasib	Non–small cell lung cancer	10%–30%	ECG and electrolytes at baseline, and as clinically necessary for high-risk patients
Bosutinib	Chronic myelogenous leukemia	1%–10%	NA
Ceritinib	Non–small cell lung cancer	1%–10% to 10%–30%	ECG and electrolytes periodically in high-risk patients
Crizotinib	Non–small cell lung cancer	1%–10%	ECG and electrolytes in high-risk patients
Dasatinib	Chronic myelogenous leukemia, acute lymphoblastic leukemia	< 1%	ECG in high-risk patients
Encorafenib	Melanoma	< 1%	Monitor high-risk patients
Entrectinib	Non–small cell lung cancer, solid tumors	1%–10%	ECG and electrolytes at baseline and periodically
Gilteritinib	Acute myeloid leukemia	1%–10%	ECG at baseline on days 8 and 15 of cycle 1, and before the start of the next two subsequent treatment cycles
Glasdegib	Acute myeloid leukemia	1%–10%	ECG at baseline, 1 week after initiation, once monthly for 2 months following initiation, and as clinically necessary
Ivosidenib	Acute myeloid leukemia	10%–30%	ECG at baseline, at least once weekly for the first 3 weeks of therapy, and once monthly for duration of therapy. Monitor electrolytes at baseline and periodically
Lapatinib	Breast cancer	< 1%	Consider ECG at baseline and periodically in high-risk patients
Lenvatinib	Renal cell carcinoma, hepatocellular carcinoma, thyroid cancer, endometrial carcinoma	1%–10%	ECG and electrolytes in high-risk patients
Midostaurin	Acute myeloid leukemia, mast cell leukemia	10%–30%	Consider ECG in high-risk patients
Mobocertinib	Non–small cell lung cancer	1%–10%	ECG and electrolytes at baseline and as clinically necessary. Avoid strong and moderate CYP3A inhibitors or drugs known to prolong QTc interval
Nilotinib	Chronic myelogenous leukemia	1%–10%	ECG and electrolytes at baseline. ECG at 7 days and with dose change
Osimertinib	Non–small cell lung cancer	1%–10%	Monitor ECG and electrolytes periodically in high-risk patients
Pacritinib	Myelofibrosis	1%–10%	ECG and electrolytes at baseline and periodically.
Pazopanib	Renal cell carcinoma, soft tissue sarcoma	1%–10%	ECG and electrolytes at baseline and periodically
Ribociclib	Breast cancer	1%–10%	ECG at baseline, at day 14 of cycle 1, at start of cycle 2, and as clinically indicated. Electrolytes at baseline and at beginning and end of the first six cycles.

Note. NA = not available; FDA = US Food and Drug Administration; QTcP = prolongation of the corrected QT interval on the ECG; ECG = electrocardiogram; GIST = gastrointestinal stromal tumor; TSH = thyroid stimulating hormone. Information from Lexicomp (2022); Micromedex (2022).

Table 3. QT Prolongation Monitoring Recommendations (cont.)

Medication	FDA-approved indications	QTcP frequency	Monitoring recommendations
Selpercatinib	Lung cancer, thyroid cancer	10%–30%	Assess QT interval, electrolytes, and TSH at baseline and periodically during treatment. Monitor QT interval more frequently when used with strong and moderate CYP3A inhibitors or drugs known to prolong QTc interval
Sorafenib	Renal cell cancer, hepatocellular cancer, differentiated thyroid cancer	< 1%	ECG and electrolytes in high-risk patients
Sunitinib	Renal cell carcinoma, GIST, pancreatic neuroendocrine tumor	< 1%	Consider ECG at baseline and periodically with electrolytes
Vandetanib	Medullary thyroid cancer	10%–30%	Monitor electrolytes at baseline and periodically. ECG at baseline, 2–4 weeks, and 8–12 weeks after initiation, then every 3 months or as clinically necessary
Vemurafenib	Melanoma	30%–50% to > 50%	Monitor electrolytes at baseline and with dosage adjustments. Monitor ECG at baseline, 15 days post initiation, then monthly for 3 months, then every 3 months thereafter and with dose adjustments
Vorinostat	Cutaneous T-cell lymphoma	1%–10%	NA

Note. NA = not available; FDA = US Food and Drug Administration; QTcP = prolongation of the corrected QT interval on the ECG; ECG = electrocardiogram; GIST = gastrointestinal stromal tumor; TSH = thyroid stimulating hormone. Information from Lexicomp (2022); Micromedex (2022).

If QTcP is identified, serum electrolytes should be drawn, the offending OC agent may be stopped, and status should be monitored until levels have normalized (Kim et al., 2021). If the QTc interval is ever > 500 ms or > 60 ms above baseline, the offending therapy should be stopped immediately and the ECG monitored until QTc returns to normal (Porta-Sánchez et al., 2017). A cardiologist may be consulted for further assistance.

Vemurafenib (Zelboraf) is a BRAF inhibitor used in the treatment of melanoma and other malignancies. QTc prolongation has been reported in up to 55% of study participants. It is recommended that ECG monitoring be done at baseline, at 15 days after start, then monthly for 3 months, then every 3 months thereafter, and with any dosing adjustments. If a person taking vemurafenib experiences a QTc > 500 ms, it should be held at least until the subsequent QTc is < 500 ms. In addition, any electrolyte abnormalities should be corrected, and any modifiable risk factors should be eliminated if possible. If the QTc remains longer than 500 ms, the vemurafenib should be permanently discontinued and other potential cancer treatments evaluated. Table 3 lists monitoring recommendations for potential QT prolongation with OCs.

DDIs RELATED TO ANTICOAGULATION

Patients with cancer have an increased risk of venous thromboembolism and bleeding events due to multifactorial dysregulation of all three elements of the Virchow's triad (Mosarla et al., 2019). Historically, low-molecular-weight heparin has been the preferred anticoagulant option. More recently, the National Comprehensive Cancer Network (NCCN, 2022) has also recommended the direct oral anticoagulants (DOACs) apixaban, edoxaban, and rivaroxaban as preferred agents for patients without gastric or gastroesophageal lesions (NCCN, 2022). Dabigatran and warfarin may be selected as alternatives when preferred options are not appropriate.

Drug-drug interactions involving DOACs commonly involve the P-glycoprotein (P-gp) transporter or the CYP system (Wiggins et al., 2020) Among the DOACs, the metabolism of apixaban and rivaroxaban are particularly affected by CYP enzymes (metabolism by CYP3A4:

rivaroxaban 50%, apixaban 20%–25%, edoxaban < 4%, and dabigatran 0%). The prescribing information of apixaban and rivaroxaban recommend avoiding the concomitant use of combined P-gp and strong CYP3A4 inhibitors or inducers. Although edoxaban is a substrate of P-gp transporter, the labeling of edoxaban only recommends avoiding rifampin, a P-gp inducer, whereas no dose reduction is recommended for P-gp inhibitors. For dabigatran, the prescribing information recommends avoiding concomitant use of P-gp inducers, whereas dose reduction or avoidance of dabigatran is recommended for P-gp inhibitors based on renal function. However, the prescribing information does not provide a formal clinical recommendation. Therefore, potential risks may still exist, and caution should be exercised with consideration and monitoring of concomitant use of chemotherapy agents that inhibit or induce CYP enzymes (Wiggins et al., 2020). Warfarin is metabolized by CYP2C9, CYP2C19, CYP3A4, and CYP1A2. Concomitant use of OC agents that inhibit or induce these enzymes warrant close monitoring of international normalized ratio and signs and symptoms of bleeding, or in some cases avoided for such OC agents such tamoxifen and imatinib (Gleevec).

Certain oral anticancer agents are associated with increased risk of major hemorrhage. Serious and fatal hemorrhage have been reported in the clinical trials of dasatinib (Sprycel) as well as Bruton tyrosine kinase inhibitors such as ibrutinib (Imbruvica), acalabrutinib (Calquence), and zanubrutinib (Brukinsa). The concomitant use of anticoagulants with these agents may further increase the risk of hemorrhage. Therefore, the risks and benefits should be carefully considered, and signs and symptoms of bleeding should be closely monitored if these agents are administered. Table 4 provides a summary of anticipated drug-drug interactions between anticoagulants and common oral anticancer agents that affect CYP enzyme activity or P-gp transport.

DRUG-FOOD AND DRUG-HERB INTERACTIONS

Food-drug interactions with OC agents largely effect the absorption or metabolism of the OC medication, and this can affect the bioavailability of the agent (Veerman et al., 2020; Schlichtig et al., 2019; Singh & Malhotra, 2004). During a meal, the stomach pH rises to help digest the food. Many OC agents are weakly basic molecules, and an increase in stomach pH reduces the formation of the soluble ionized form, thereby reducing oral absorption. The FDA criteria regarding food-drug absorption interactions require the AUC and maximum concentration (C_{max}) levels to be between 80% to 125% of the reference levels for bioequivalence. However, many beverages such as soda, fruit, and energy drinks have an acidic pH of about 4. In cola drinks, this is due to phosphoric acid. There can be a difference in OC absorption with meals with a high-fat vs. a low-fat content. Some OC agents are lipophilic and would tend to have a higher solubility with a high-fat meal. Other changes with food intake include slowing of gastric emptying and gastrointestinal transit time as well as increasing hepatic blood flow, and these factors may also impact absorption rates. One special example is capecitabine, which is recommended to be taken within 30 minutes of a meal. Although food intake reduces the rate and extent of absorption, it does even out the blood levels of this prodrug and reduces toxicity (Veerman et al., 2020; Singh & Malhotra, 2004).

The FDA and the drug's manufacturer provide administration recommendations, with priority directed to reduce potential toxicity, while also maintaining efficacy (Veerman et al., 2020). Those OC agents whose oral absorption is decreased by food intake should be administered on an empty stomach. Those OC agents whose absorption is not affected by food intake can be taken with food or on an empty stomach, depending on the patient's choice. Those OC agents whose absorption is increased by food intake must rely on drug-specific recommendations based on the potential adverse effects (Veerman et al., 2020).

There are foods that may inhibit CYP3A4 metabolism of OC agents. Some of these include garlic, red wine, and grapefruit (Veerman et al., 2020; Schlichtig et al., 2019; Singh et al., 2004). Except for grapefruit, there are no standard recommendations due to different amounts and types of intake. Compounds in grapefruit, such as naringenin, bergamottin, bergapten, and dihydroxybergamottin, act as inhibitors of intestinal CYP3A4. The blood

Table 4. Potential Interactions Between and Proposed Management for Anticoagulants and Common OCs

Anticoagulants	Oral chemotherapy agent	Mechanism	Management
All anticoagulants	Dasatinib Ibrutinib Acalabrutinib Zanubrutinib	The anticancer agents are associated with increased risk of hemorrhage and may enhance anticoagulant effects	Monitor for signs and symptoms of bleeding. Dasatinib: Associated with thrombocytopenia and potentially severe bleeding events. Zanubrutinib: Discontinue if intracranial hemorrhage of any grade occurs.
Warfarin	Tamoxifen	Agent may increase serum concentration of vitamin K antagonist	Avoid combination. Combined use is contraindicated in US labeling due to increased risk of bleeding from increased anticoagulant response.
	Imatinib[a]	CYP3A4 and CYP2C9 inhibitor	US package insert recommends use of low-molecular-weight or standard heparin instead of warfarin. If warfarin must be coadministered, monitoring of INR and signs and symptoms of bleeding should be increased.
	Adagrasib[a] Bicalutamide Cabozantinib[b] Capecitabine Ceritinib Erlotinib Etoposide Gefitinib Pexdartinib Regorafenib Rucaparib Selumetinib Sorafenib Toremifene Vemurafenib Venetoclax Vismodegib[b] Vorinostat	Inhibitors of CYP2C9, CYP2C19 and/or CYP3A4	Monitor for increased anticoagulant effects, monitor PT and INR and signs and symptoms of bleeding.
	Alpelisib Apalutamide[a] Dabrafenib Lorlatinib[a] Mitotane	CYP2C9 inducer: alpelisib, apalutamide, dabrafenib, apalutamide, lorlatinib CYP3A4 inducer: mitotane	Monitor for decreased effects of warfarin including decreased INR, thrombosis.
	Enzalutamide	CYP3A4 inducer	Avoid concurrent use of warfarin and enzalutamide if possible. If combination must be used, monitor for reduced anticoagulant effects from warfarin.

Note. PT = prothrombin time; INR = international normalized ratio of the prothrombin time; eCrCl = estimated creatinine clearance. Information from Lexicomp (2022); Micromedex (2022).
[a]Oral chemotherapy agent appears more than once in table.
[b]Based on a single case report.

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levels of the OC may be increased resulting in excess toxicities. It has not been determined if there is a safe low level of grapefruit intake that would not cause problems, but it is known that about 200 mL to 240 mL of juice does inhibit these enzymes (Veerman et al., 2020; Singh et al., 2004).

There are also some herbal remedies that might affect the blood levels of OC agents. Although a comprehensive review is beyond the scope of this summary, one notable example is St. John's wort (*Hypericum perforatum*), which is an inducer of hepatic CYP3A4 as well as an inhibitor of P-gp-medicated drug efflux. Concomitant use may alter levels of OC medications. Other examples include echinacea, green tea extract, and turmeric, which can inhibit CYP3A4. As reliable

Table 4. Potential Interactions Between and Proposed Management for Anticoagulants and Common OCs

Anticoagulants	Oral chemotherapy agent	Mechanism	Management
Apixaban and rivaroxaban	Ceritinib Idelalisib	Strong CYP3A4 inhibitor	Monitor for evidence of bleeding, If used with a P-gp inhibitor, rivaroxaban should be avoided and apixaban should be avoided or dose adjusted.
	Crizotinib Duvelisib Imatinib[a] Fedratinib Nilotinib Ribociclib	Moderate CYP3A4 inhibitor	Monitor for increased bleeding. If used with a P-gp inhibitor, avoid rivaroxaban in patients with renal impairment (eCrCL of 15 to 80 mL/min) unless the benefit justifies potential risk.
	Adagrasib[a] Tucatinib	Strong CYP3A4 inhibitor and P-gp inhibitor	Avoid rivaroxaban. Reduce apixaban dose by 50% in patients receiving 5 mg or 10 mg twice daily. Avoid apixaban in patients receiving a dose of 2.5 mg twice daily.
	Enzalutamide	Strong CYP3A4 inducer	Avoid apixaban use with strong CYP3A4 inducers whenever possible. Rivaroxaban: Consider an alternative anticoagulant. If the patient is also using a P-gp inducer, apixaban and rivaroxaban should be strictly avoided.
	Lorlatinib[a]	Moderate CYP3A4 inducer and P-gp inducer	Monitor for reduced apixaban and rivaroxaban efficacy.
	Apalutamide[a]	Strong CYP3A4 inducer and P-gp inducer	Avoid apixaban. Avoid rivaroxaban.
	Erdafitinib Ivosidenib	CYP3A4 inducer	Monitor for reduced efficacy of apixaban and rivaroxaban.
Apixaban	Cabozantinib[b]	Possible enhanced side effects of cabozantinib.	Monitor for signs of bleeding, thrombocytopenia, and neutropenia.
Edoxaban and dabigatran	Adagrasib[a] Apalutamide[a] Lorlatinib[a]	P-gp inducer	Avoid combination with dabigatran. Avoid combination with edoxaban if possible. If concomitant use is required, edoxaban efficacy may be decreased.
	Capmatinib Erdafitinib Gilteritinib Lapatinib Neratinib Osimertinib Tepotinib Tucatinib Vemurafenib	P-gp inhibitor	Monitor for excessive anticoagulation responses such as bruising and bleeding. Avoid combination with dabigatran in reduced renal function (if CrCL < 30 mL/min for treatment of atrial fibrillation or less than 50 mL/min for other indications of dabigatran)

Note. PT = prothrombin time; INR = international normalized ratio of the prothrombin time; eCrCl = estimated creatinine clearance. Information from Lexicomp (2022); Micromedex (2022).
[a]Oral chemotherapy agent appears more than once in table.
[b]Based on a single case report.

Table 5. Oral Chemotherapy Administration Recommendations

Oral chemotherapy agent	Recommendation	
Abemaciclib	Take with or without food	Avoid grapefruit and grapefruit juice
Abiraterone	Zytiga: Take on empty stomach at least 1 hr before or at least 2 hr after food Yonsa: Take with or without food	NA
Acalabrutinib	Take with or without food	NA
Adagrasib	Take with or without food	NA
Afatinib	Take on empty stomach at least 1 hr before or at least 2 hrs after food	NA
Alectinib	Take with food	NA
Alpelisib	Take with food	NA
Apalutamide	Take with or without food	NA
Asciminib	Take on empty stomach at least 2 hr before or at least 1 hr after food	NA
Avapritinib	Take on empty stomach at least 1 hr before or at least 2 hr after food	NA
Axitinib	Take with or without food	Avoid grapefruit and grapefruit juice
Azacitidine	Take with or without food	NA
Bexarotene	Take with food	NA
Binimetinib	Take with or without food	NA
Bosutinib	Take with food	Avoid grapefruit and grapefruit juice
Brigatinib	Take with or without food	Avoid grapefruit and grapefruit juice
Cabozantinib	Take on empty stomach at least 1 hr before or at least 2 hr after food	Avoid grapefruit and grapefruit juice
Capecitabine	Take within 30 minutes after meal	NA
Capmatinib	Take with or without food	NA
Ceritinib	Take with food (450-mg dose)	Avoid grapefruit and grapefruit juice
Chlorambucil	Take on empty stomach	NA
Cobimetinib	Take with or without food	Avoid grapefruit and grapefruit juice
Crizotinib	Take with or without food	Avoid grapefruit and grapefruit juice
Cyclophosphamide	Take with or without food	NA
Dabrafenib	Take on empty stomach at least 1 hr before or at least 2 hr after food	NA
Dacomitinib	Take with or without food	NA
Darolutamide	Take with food	NA
Dasatinib	Take with or without food. May take with food if stomach upset	Avoid grapefruit and grapefruit juice
Decitabine/ cedazuridine	Take on empty stomach at least 2 hr before or at least 2 hr after food	NA
Duvelisib	Take with or without food	NA

Note. NA = not applicable. Information from Lexicomp (2022).

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Table 5. Oral Chemotherapy Administration Recommendations (cont.)

Oral chemotherapy agent	Recommendation	
Enasidenib	Take with or without food	NA
Encorafenib	Take with or without food	Avoid grapefruit and grapefruit juice
Entrectinib	Take with or without food	Avoid grapefruit and grapefruit juice
Enzalutamide	Take with or without food	NA
Erdafitinib	Take with or without food	NA
Erlotinib	Take on empty stomach at least 1 hr before or at least 2 hr after food	Avoid grapefruit and grapefruit juice
Etoposide	Take with or without food	NA
Everolimus	Take with or without food, but should be consistent	Avoid grapefruit and grapefruit juice
Fedratinib	Take with or without food, but a higher-fat meal decreases GI upset	NA
Futibatinib	Take with or without food	NA
Gefitinib	Take with or without food	Avoid grapefruit and grapefruit juice
Gilteritinib	Take with or without food	NA
Glasdegib	Take with or without food	NA
Ibrutinib	Take with or without food	Avoid grapefruit, grapefruit juice, and Seville oranges
Idelalisib	Take with or without food	NA
Imatinib	Take with food to reduce GI upset	Avoid grapefruit and grapefruit juice
Infigratinib	Take on empty stomach at least 1 hr before or at least 2 hr after food	NA
Ivosidenib	Take with or without food	NA
Ixazomib	Take on empty stomach at least 1 hr before or at least 2 hr after food	NA
Lapatinib	Take on empty stomach at least 1 hr before or at least 2 hr after food	Avoid grapefruit and grapefruit juice
Larotrectinib	Take with or without food	Avoid grapefruit and grapefruit juice
Lenalidomide	Take with or without food	NA
Lenvatinib	Take with or without food	NA
Lomustine	Take on empty stomach to reduce nausea	NA
Lorlatinib	Take with or without food	NA
Melphalan	Take on empty stomach to enhance oral absorption	NA
Mercaptopurine	Take with or without food	NA
Methotrexate	Take with or without food	NA
Midostaurin	Take with or without food	Avoid grapefruit and grapefruit juice
Mitotane	Take with or without food	NA

Note. NA = not applicable. Information from Lexicomp (2022).

Table 5. Oral Chemotherapy Administration Recommendations (cont.)

Oral chemotherapy agent	Recommendation	
Mobocertinib	Take with or without food	NA
Neratinib	Take with food	Avoid grapefruit and grapefruit juice
Nilotinib	Take on empty stomach at least 1 hr before or at least 2 hr after food	Avoid grapefruit and grapefruit juice
Niraparib	Take with or without food	NA
Olaparib	Take with or without food	Avoid grapefruit, grapefruit juice, and Seville oranges
Olutasidenib	Take on empty stomach at least 1 hr before or at least 2 hr after food	NA
Osimertinib	Take with or without food	NA
Pacritinib	Take with or without food	NA
Palbociclib	Take with or without food	Avoid grapefruit and grapefruit juice
Pazopanib	Take on empty stomach at least 1 hr before or at least 2 hr after food	Avoid grapefruit and grapefruit juice
Pemigatinib	Take with or without food	NA
Pexidartinib	Take on empty stomach at least 1 hr before or at least 2 hr after food	Avoid grapefruit and grapefruit juice
Pomalidomide	Take with or without food	NA
Ponatinib	Take with or without food	Avoid grapefruit and grapefruit juice
Pralsetinib	Take on empty stomach at least 1 hr before or at least 2 hr after food	NA
Procarbazine	Take with or without food. Avoid alcohol and tyramine-containing foods to reduce adverse effects	NA
Ribociclib	Take with or without food	Avoid grapefruit and grapefruit juice
Ripretinib	Take with or without food	NA
Rucaparib	Take with or without food	NA
Ruxolitinib	Take with or without food	Avoid grapefruit and grapefruit juice
Selinexor	Take with or without food	NA
Selpercatinib	Take with or without food	NA
Selumetinib	Take on empty stomach at least 2 hr before or at least 1 hr after food	NA
Sonidegib	Take on empty stomach at least 1 hr before or at least 2 hr after food	NA
Sorafenib	Take on empty stomach at least 1 hr before or at least 2 hr after food	NA
Sotorasib	Take with or without food	NA
Sunitinib	Take with or without food	Avoid grapefruit and grapefruit juice
Talazoparib	Take with or without food	NA
Tazemetostat	Take with or without food	NA

Note. NA = not applicable. Information from Lexicomp (2022).

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Table 5. Oral Chemotherapy Administration Recommendations (cont.)

Oral chemotherapy agent	Recommendation	
Temozolomide	Take on empty stomach to reduce GI upset	NA
Tepotinib	Take with food	NA
Thalidomide	Take at least 1 hr after evening meal	NA
Thioguanine	Take with or without food	NA
Tivozanib	Take with or without food	NA
Topotecan	Take with or without food	NA
Trametinib	Take on empty stomach at least 1 hr before or at least 2 hrs after food	NA
Tretinoin	Take with food to enhance oral absorption	NA
Trifluridine/tipiracil	Take with food	NA
Tucatinib	Take with or without food	NA
Umbralisib	Take with food	NA
Vandetanib	Take with or without food	NA
Vemurafenib	Take with or without food	Avoid grapefruit and grapefruit juice
Venetoclax	Take with food	Avoid grapefruit, grapefruit juice, and Seville oranges
Vismodegib	Take with or without food	NA
Vorinostat	Take with food	NA
Zanubrutinib	Take with or without food	Avoid grapefruit, grapefruit juice, and Seville oranges

Note. NA = not applicable. Information from Lexicomp (2022).

information regarding HDIs with OCs is limited, it is important to consult trustworthy resources such as the Memorial Sloan Kettering Cancer Center About Herbs database (Memorial Sloan Kettering Cancer Center, 2022) and the Natural Medicines database (Therapeutic Research Center, 2022). Table 5 provides recommendations for the oral administration of OC agents.

PATIENT CARE AND DECISION-MAKING

When a patient starts an OC treatment, it is vital to consider potential DDIs. A thorough medication history should be taken, including prescribed and over-the-counter medications and herbal remedies. Using published literature as well as drug interaction databases, all potential interactions should be identified. When assessing potential drug interactions, consider the likelihood of the interaction happening, the likelihood of harm from the interaction, the potential severity of the interaction, and the quality of evidence of the potential interaction.

Using principles of deprescribing, it might be appropriate to eliminate some interacting medications (Halli-Tierney et al., 2019). With the remaining medications, it is important to weigh the risks and benefits of continuing or discontinuing any agent. Alternatives that might not interact should be explored. If combinations of interacting medications should be maintained, it will be important to enhance monitoring plans to rapidly discover adverse effects as they start. Likewise, when an interacting medication is withdrawn, it is important to revisit dosing and monitoring plans. Attention to potential drug interactions with OC agents can reduce toxicity and potentially enhance anticancer effects.

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The authors have no conflicts of interest to disclose.

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