Table 2: Drug-Drug Interactions of Common Chemotherapeutic Agents and Warfarin

Chemotherapy Drug	Effect on INR*	Mechanism	Suggested Management
Cabozantinib Ceritinib Regorafenib Rucaparib Vemurafenib	↑	Inhibition of warfarin metabolism (CYP2C9)	Closely monitor INR and signs/symptoms of bleeding, especially during chemotherapy initiation and discontinuation. Adjust dose of warfarin accordingly.
Carboplatin Doxorubicin Erlotinib Gefitinib Mesna Romidepsin Vincristine	↑	Unknown	Closely monitor INR and signs/symptoms of bleeding, especially during chemotherapy initiation and discontinuation. Adjust dose of warfarin accordingly.
Dasatinib Ibrutinib Ibritumomab Nintedanib Obinutuzumab	↑	Additive clinical effect	↑ anticoagulant effects and increased risk of bleeding. Consider the benefit to risk ratio of anticoagulant therapy. If concomitant therapy is necessary, use caution and frequently monitor platelet counts and evidence of bleeding or hemorrhagic events.
Fluoropyrimidines (capecitabine, 5-fluorouracil)	↑	Inhibition of warfarin metabolism (CYP2C9)	Avoid co-administration if possible and consider a substitute for warfarin during chemotherapy. Case reports of altered coagulation parameters, bleeding, and death have been reported. If concurrent use is clinically necessary, closely monitor INR frequently and signs/symptoms of bleeding. Adjust dose of warfarin accordingly. Occurrence can be within several days to months after initiation of chemotherapy and may be seen 1 month after discontinuation. The effect is time- and dose-dependent, with further warfarin dose reductions needed with each cycle.†
Imatinib	↑	Inhibition of warfarin metabolism (CYP3A4 and CYP2C9)	The manufacturer recommends LMWH or standard heparin instead of warfarin in patients requiring heparin.† If concomitant therapy of warfarin and imatinib is unavoidable, increased frequency of INR monitoring and signs/symptoms of bleeding is necessary. Greatest effects are seen with discontinuation or initiation of imatinib therapy or dose changes.
Tamoxifen	↑	Unknown	Concurrent administration is contraindicated in high-risk women.† In clinical situations where concomitant therapy is unavoidable, use lower warfarin doses and closely monitor the INR and signs/symptoms of bleeding.
Mercaptopurine Nilotinib	↓	Unknown	Closely monitor for loss of efficacy and INR levels. Dose adjustments may be required to maintain desired level of anticoagulation.
Dabrafenib Ivosidenib	↓	Induction of warfarin metabolism (CYP2C9)	Avoid co-administration if possible and consider a substitute for warfarin during chemotherapy.† If concurrent use is clinically necessary, closely monitor for loss of efficacy and INR levels, especially during chemotherapy initiation and discontinuation. Dose adjustments may be required to maintain desired level of anticoagulation.
* Color denotes severity of interaction as follows:			

- *Red.* Major interaction; Black Box warning and/or strong clinical effects; avoid combination.
- *Orange.* Moderate interaction; known, reliable mechanism of interaction such as enzyme effects, protein binding, etc. Data demonstrate that there is a clinically significant drug interaction. Individual risk-benefit assessment for each patient should be considered with concomitant therapy. Actions such as aggressive monitoring or empiric dose changes should be taken to minimize toxicity. Alternative agents should be chosen if risks outweigh benefits.
- *Yellow.* Minor interaction; potential interaction between the agents; however, benefits usually outweigh risks. Evidence may be limited to only case reports. Appropriate monitoring plan should be implemented; a small number of patients may need dose adjustments or consideration of alternative agent.

† Package insert recommendation.