Potential Drug Interactions

- **Loading dose** should be decreased by 25% for patients receiving amiodarone.
- Drug interactions with warfarin may occur via several mechanisms, including impairment of absorption, induction or inhibition of metabolism, competition for protein-binding sites, and platelet inhibition. Drugs that inhibit or induce P-450 2C9 (responsible for metabolism of S-warfarin) may have the greatest effect on INR.
- Complementary/alternative medications known to have potential to *increase* warfarin effects include bromelains, danshen, dong quai, garlic, gingko biloba, ginseng and omega 3 fish oil.
- Complementary/alternative medications known to have potential to *decrease* warfarin effects include CoQ10 and St. John's Wort.
- INR should be monitored more frequently in pediatric patients who are already on warfarin therapy and are starting on antibiotics.
- Warfarin dosing can be adjusted to permit use of some medications that have an effect on warfarin metabolism. Please consult Hematology for adjustment recommendations.

Table 6. Commonly used Drugs in Children that affect INR Values

Drug	INR Effect	Mechanism
Amiodarone	Increase	Decreases warfarin metabolism
Antifungal agents	Increase	Fluconazole, ketoconazole, and miconazole (vaginal) decrease warfarin metabolism
Barbiturates	Decrease	Increase warfarin metabolism
Carbamazepine	Decrease	Increase warfarin metabolism
Cephalosporins	Increase	Inhibits production of vitamin K dependent clotting factors
Ciprofloxacin	Increase	Displace warfarin from binding sites (possible mechanism; not fully known)

Clarithromycin	Increase	Decrease warfarin metabolism
Contraceptives (Oral)	Increase	Increase clotting factor synthesis; may inhibit oxidative metabolism
Corticosteroids	Increase	Produce hypercoagulability; may have ulcerogenic effects
Delaviridine	Increase	May inhibit warfarin metabolism
Erythromycin	Increase	Decrease warfarin metabolism
Ibuprofen	Increase	May inhibit warfarin metabolism in addition to platelet inhibition
Indomethacin	Increase	May inhibit warfarin metabolism in addition to platelet inhibition
Isoniazid	Increase	May inhibit warfarin metabolism
Losartan	Increase	May inhibit warfarin metabolism
Omeprazole	Increase	May inhibit of warfarin metabolism
Metronidazole	Increase	Inhibits metabolism of S-isomer
Nicardipine	Increase	May inhibit warfarin metabolism
Pantoprazole	Increase	May inhibit warfarin metabolism
Penicillins	Increase	May enhance warfarin metabolism; May reduce GI flora synthesis of vitamin K
Phenytoin / fosphenytoin	Decrease	Increase warfarin metabolism; induces warfarin metabolism; displaces warfarin from protein-binding sites; enhances metabolism of clotting factors
Rifampin	Decrease	Induces hepatic enzymes, increases warfarin metabolism
Sulfamethoxazole - Trimethoprim (Bactrim)	Increase	Sulfonamide component may stereo-selectively inhibit S-isomer metabolism

Vitamin K (ADEK, Centrum, Viactiv)	Decrease	Effects of oral anticoagulants are directly antagonized by the excessive ingestion of foods or dietary supplements containing vitamin K
Zafirlukast	Increase	May inhibit warfarin metabolism

Other important interactions		
Drug	**Effect**	**Mechanism**
Aspirin, NSAIDs	Increased risk of bleed	Inhibition of platelet aggregation
Anti-platelet agents (dipyridamole, clopidrogel, ticlopidine, cilostazol)	Increased risk of bleed	Inhibition of platelet aggregation

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These guidelines do not establish a standard of care to be followed in every case. It is recognized that each case is different and those individuals involved in providing health care are expected to use their judgment in determining what is in the best interests of the patient based on the circumstances existing at the time. It is impossible to anticipate all possible situations that may exist and to prepare guidelines for each. Accordingly these guidelines should guide care with the understanding that departures from them may be required at times.

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