From The Medical Letter on Drugs and Therapeutics

Comparison Table: Some Oral Anticoagulants for VTE

In this issue of *JAMA*, a systematic review of the recent developments in the diagnosis and treatment for venous thromboembolic (VTE) disease was published.[1] Partially reprinted herein is a **Table** that was published in the March 12, 2018, issue of *The Medical Letter on Drugs and Therapeutics* summarizing the major features of different oral anticoagulants used for venous thromboembolic disease.[2] This Table accompanied a comprehensive review of the drugs used to for the treatment and prevention of VTE[3] and another online table comparing the parental anticoagulants used for VTE.[4] The Comments column from the original table appears in the Supplement.

Supplemental content

Table. Some Oral Anticoagulants for VTE

Drug	FDA-Approved Indications	Usual Adult Treatment Dosage	Usual Adult Prophylaxis Dosage[a]	Some Adverse Effects	Cost[b]
Vitamin K Antagonist					
Warfarin - generic; Coumadin (BMS); Jantoven (USL)	• Prophylaxis of DVT and PE • Treatment of DVT and PE	2-10 mg once/d	2-10 mg once/d	Vasculitis, chills, alopecia, pruritus, urticaria, abdominal pain, bloating, nausea, vomiting, diarrhea, skin necrosis **Drug Interactions:** Numerous drug interactions[c]	$7.80 64.50 10.80
Direct Thrombin Inhibitor					
Dabigatran etexilate - Pradaxa (Boehringer Ingelheim)	• Prophylaxis of DVT and PE following hip replacement surgery • Treatment of DVT and PE following 5-10 days of initial therapy with a parenteral anticoagulant • Reduction in the risk of recurrent DVT and PE following initial therapy	CrCl >30 mL/min: 150 mg bid Should not be used in patients with CrCl ≤30 mL/min	CrCl >30 mL/min: 110 mg once, then 220 mg once/d Should not be used in patients with CrCl ≤30 mL/min	Dyspepsia and gastritis-like symptoms **Drug Interactions:** Substrate of P-gp; interacts with inhibitors and inducers of P-gp[d]; NSAIDs and other antiplatelet drugs can increase the risk of bleeding Avoid coadministration with P-glycoprotein (P-gp) inhibitors in patients with CrCl <50 mL/min	400.60
Factor Xa Inhibitors					
Apixaban - Eliquis (BMS)	• Prophylaxis of DVT following hip or knee replacement surgery • Treatment of DVT and PE • Reduction in the risk of recurrent DVT and PE following initial treatment lasting at least 6 months	10 mg bid × 7 days, then 5 mg bid[e] With dual P-gp/strong CYP3A4 inhibitor: reduce dose by 50%[f]	2.5 mg bid[f]	Epistaxis, contusion, nausea, increased serum transaminases, anemia **Drug Interactions:** Substrate of CYP3A4 and P-gp; interacts with inhibitors and inducers of CYP3A4 and P-gp[d]; NSAIDs and other antiplatelet drugs can increase the risk of bleeding Should not be used concurrently with dual P-gp/strong CYP3A4 inducers	419.00
Betrixaban - Bevyxxa (Portola)	• Prophylaxis of VTE in patients hospitalized for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE	Not an FDA-approved indication	160 mg once, then 80 mg once/d for a total of 35-42 days With P-gp inhibitor: 80 mg once, then 40 mg once/d for a total of 35-42 days CrCl ≥15 to <30 mL/min: 80 mg once, then 40 mg once/d for a total of 35-42 days Should not be used in patients with CrCl <15 mL/min	Epistaxis, UTI, constipation, hypokalemia, hypertension, headache, nausea, diarrhea **Drug Interactions:** Substrate of P-gp; interacts with inhibitors and inducers of P-gp[d]; NSAIDs and other antiplatelet drugs can increase the risk of bleeding	450.00
Edoxaban - Savaysa (Daiichi-Sankyo)	• Treatment of DVT and PE following 5-10 days of initial therapy with a parenteral anticoagulant	60 mg once/d CrCl: 15-50 mL/min: 30 mg once/d With P-gp inhibitor: 30 mg once/d; ≤60 kg: 30 mg once/d	Not FDA-approved	Rash, abnormal liver function tests, anemia **Drug Interactions:** Substrate of P-gp; interacts with inhibitors of P-gp[d]; should not be used with the P-gp epistaxis inducer rifampin; NSAIDs and other antiplatelet drugs can increase the risk of bleeding	336.60

(continued)

Table. Some Oral Anticoagulants for VTE (continued)

Drug	FDA-Approved Indications	Usual Adult Treatment Dosage	Usual Adult Prophylaxis Dosage[a]	Some Adverse Effects	Cost[b]
Rivaroxaban - Xarelto (Janssen)	• Prophylaxis of DVT following hip or knee replacement surgery • Treatment of DVT and PE • Reduction in the risk of recurrent DVT and/or PE following initial treatment lasting at least 6 months	15 mg bid × 3 weeks, then 20 mg once/d[g] Should not be used in patients with CrCl <30 mL/min, in those taking dual P-gp/strong CYP3A4 inducers or inhibitors, or in those with CrCl 15-<80 mL/min taking dual P-gp/moderate CYP3A4 inhibitors	10 mg once/d Should not be used in patients with CrCl <30 mL/min, in those taking dual P-gp/strong CYP3A4 inducers or inhibitors, or in those with CrCl 15-<80 mL/min taking dual P-gp/moderate CYP3A4 inhibitors	Abdominal pain, fatigue, back pain, muscle spasms, dizziness, anxiety, depression, insomnia, pruritus, wound secretion, UTI, increased serum transaminases **Drug Interactions:** Substrate of CYP3A4 and P-gp; interacts with inhibitors and inducers of CYP3A4 and P-gp[d]; NSAIDs and other antiplatelet drugs can increase the risk of bleeding Should not be used in patients taking dual P-gp/strong CYP3A4 inducers or inhibitors or in those with CrCl 15-<80 mL/min taking dual P-gp/moderate CYP3A4 inhibitors	333.30

[a] Prophylaxis is recommended for a minimum of 10-14 days and for up to 35 days after major orthopedic surgery (Y Falck-Ytter et al. *Chest*. 2012;141:e278S).

[b] Approximate WAC for 30 days' treatment at the lowest usual adult dosage for treatment. Cost of betrixaban is based on dosage for prophylaxis. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. February 5, 2018. Reprinted with permission by First Databank, Inc. All rights reserved. ©2018. www.fdbhealth.com/policies/drug-pricing-policy/.

[c] Acetaminophen, amiodarone, cefazolin, cefotetan, ceftriaxone, clarithromycin, fluconazole, fluorquinolones, fluorouracil, fluoxetine, fluvastatin, fluvoxamine, metronidazole, phenytoin (initial use), rosuvastatin, trimethoprim-sulfamethoxazole, and voriconazole can increase the anticoagulant effect of warfarin. Barbiturates, carbamazepine, cholestyramine, colestipol, dicloxacillin, nafcillin, phenytoin, rifampin, St John's wort, and sucralfate can decrease the anticoagulant effect of warfarin (Drug interactions from *The Medical Letter*. medicalletter.org/subDIO. Accessed March 1, 2018).

[d] Inhibitors and inducers of CYP enzymes and P-glycoprotein. *Med Lett Drugs Ther*. September 18, 2017 (epub). medicalletter.org/downloads/CYP_PGP_Tables.pdf. Accessed March 1, 2018.

[e] For extended treatment after at least 6 months of treatment for DVT or PE, the dosage for reduction in risk of recurrence of VTE is 2.5 mg bid.

[f] Patients taking 2.5 mg bid should not take dual P-gp/strong CYP3A4 inhibitors.

[g] For extended treatment after at least 6 months of treatment for DVT or PE, the dosage for reduction in risk of recurrence of VTE is 10 mg once/d.

ARTICLE INFORMATION

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2. Comparison table: some oral anticoagulants for VTE. *Med Lett Drugs Ther*. 2018;60(1542):e51-e54.

3. Drugs for treatment and prevention of venous thromboembolism. *Med Lett Drugs Ther*. 2018;60(1542):41-48.

4. Comparison table: some parenteral anticoagulants for VTE. *Med Lett Drugs Ther*. 2018;60(1542):e48-e50.