The new oral anticoagulants rivaroxaban (Xarelto), dabigatran etexilate (Pradaxa), and apixaban (Eliquis), and the investigational oral anticoagulant edoxaban all appear to be effective and safe for treatment of acute venous thromboembolism. Rivaroxaban was non-inferior to standard therapy in reducing the rate of recurrent VTE. The rate of major or clinically relevant non-major bleeding, the primary safety endpoint, was the same in both groups. A second randomized open-label study (EINSTEIN-PE) in 4832 patients with PE found that rivaroxaban was non-inferior to enoxaparin plus a vitamin K antagonist in reducing the rate of recurrent VTE with a similar rate of major or clinically relevant non-major bleeding.

Dabigatran etexilate (Pradaxa) — A 6-month, randomized, double-blind trial (RE-COVER) in 2539 patients compared dabigatran to warfarin for treatment of acute VTE after initial treatment with a parenteral anticoagulant. Twice-daily dabigatran was non-inferior to warfarin in preventing recurrent VTE or VTE-related death, the primary efficacy endpoint. Rates of major bleeding were similar in the two groups.

Apixaban (Eliquis) — A 6-month, randomized, double-blind trial (AMPLIFY) in 5395 patients compared apixaban alone to enoxaparin plus warfarin for treatment of acute VTE. Twice-daily apixaban was non-inferior in preventing recurrent VTE or VTE-related death (the primary efficacy endpoint). Major bleeding, the primary safety outcome, occurred less frequently with apixaban (0.6% vs. 1.8%).

Edoxaban — In a randomized, double-blind trial of 8240 patients with acute VTE first treated with unfractionated heparin or LMWH, once-daily edoxaban (not FDA-approved) was non-inferior to warfarin in preventing recurrent VTE or VTE-related death (the primary endpoint). Patients taking edoxaban had a significantly lower rate of major or clinically relevant non-major bleeding (8.5% vs. 10.3%).

CONCLUSION — The new oral anticoagulants rivaroxaban (Xarelto), dabigatran etexilate (Pradaxa), and apixaban (Eliquis), and the investigational oral anticoagulant edoxaban all appear to be effective and safe for treatment of acute venous thromboembolism.
but data in older and sicker patients are limited. They do not require INR monitoring and do not have dietary restrictions, but they have short half-lives that increase the risk of thrombosis with missed doses and no specific antidote to reverse their anticoagulant effect.


Table 1. Oral Anticoagulants for Treatment of Venous Thromboembolism

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of Action</th>
<th>Usual Dosage</th>
<th>Cost ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin – generic</td>
<td>Vitamin K antagonist</td>
<td>2-10 mg² once/d</td>
<td>$6.00</td>
</tr>
<tr>
<td>(Coumadin)</td>
<td></td>
<td></td>
<td>43.00</td>
</tr>
<tr>
<td>Rivaroxaban – (Xarelto)</td>
<td>Direct factor Xa inhibitor</td>
<td>15 mg bid for 3 wks, then 20 mg once/d</td>
<td>265.00</td>
</tr>
<tr>
<td>Apixaban – (Eliquis)</td>
<td>Direct factor Xa inhibitor</td>
<td>10 mg bid for 7 days, then 5 mg bid²</td>
<td>265.00</td>
</tr>
<tr>
<td>Dabigatran etexilate – (Pradaxa)³</td>
<td>Direct thrombin inhibitor</td>
<td>150 mg bid²</td>
<td>265.00</td>
</tr>
</tbody>
</table>

1. Approximate wholesale acquisition cost of 30 days’ treatment at the lowest daily dose. Source: AnalySource® Monthly (Selected from FDB Medi-knowledge™) December 5, 2013. Reprinted with permission by FDB, Inc. All rights reserved. ©2013. www.fdbhealth.com/policies/drug-pricing-policy. Actual retail prices may be higher.

2. Monitor INR daily and adjust dose until in therapeutic range (2-3) for >24 hours.

3. With food; avoid use with combined P-glycoprotein and strong CYP3A4 inhibitors or inducers, or in patients with CCl <30 mL/min.

4. Not FDA-approved for treatment of VTE.

5. Not studied in patients with acute VTE who are taking strong CYP3A4 inhibitors or who have CCI <25 mL/min or serum creatinine >2.5 mg/dL.

6. Avoid use with P-glycoprotein inducers; not studied for acute VTE in patients who have CCI <30 mL/min.

Coming Soon in The Medical Letter:

Omacetaxine Mepesuccinate (Symbr kitty) for CML
Sofosbuvir (Sovaldi) for Chronic Hepatitis C
Tobramycin Inhalation Solution (Bethkis) for Cystic Fibrosis

Coming Soon in Treatment Guidelines:

Drugs for HIV Infection
Treatment of Atrial Fibrillation