# FDA Approved Indications and Dosages

## Apixaban (Eliquis®)

**NVAF**
- 5 mg PO BID
- 2.5 mg PO BID: If ≥ 2 of the following: age ≥80 years, weight ≤60 kg or Cr ≥ 1.5 mg/dL
- Usage in Cr > 2.5 mg/dL or CrCl < 25 mL/min is based on pharmacokinetics and not on clinical studies. Caution is advised.

**VTE treatment**
- 10 mg PO BID for 7 days, then 5 mg PO BID
- No dose adjustment based on renal function
- Usage in CrCl < 25 mL/min is based on pharmacokinetics and not on clinical studies. Caution is advised.

**VTE secondary prevention**
- 2.5 mg PO BID
- CrCl < 25 mL/min: no clinical studies

**VTE prophylaxis in THR/TKR**
- Start 12-24 hours postop
- THR: 2.5 mg BID PO for 35 days
- TKR: 2.5 mg BID PO for 12 days
- CrCl <30 mL/min: no clinical studies

## Edoxaban (Savaysa®)

**NVAF**
- CrCl > 95 mL/min: NOT recommended (drug may be cleared too rapidly and adequate drug levels not attained)
- CrCl 51-95 mL/min: 60 mg PO once daily
- CrCl 15-50 mL/min: 30 mg PO once daily
- CrCl < 15 mL/min: not recommended

**VTE treatment**
- Begin after 5-10 days of initial therapy with a parenteral anticoagulant
- CrCl > 50 mL/min: 60 mg PO once daily
- CrCl 15-50 mL/min or weight ≤60 kg or on P-gp inhibitors*: 30 mg PO once daily

**VTE secondary prevention**
- Not approved

**VTE prophylaxis in THR/TKR**
- Not approved

## Rivaroxaban (Xarelto®)

**NVAF**
- CrCl > 50 mL/min: 20 mg PO once daily with evening meal
- CrCl 15-50 mL/min: 15 mg PO once daily with evening meal
- CrCl < 15 mL/min: not recommended

**VTE treatment**
- CrCl >30 mL/min: 15 mg PO BID for 21 days, then 20 mg PO daily
- CrCl <30 mL/min: not recommended

**VTE secondary prevention**
- CrCl >30 mL/min: 20 mg PO daily
- CrCl <30 mL/min: not recommended

**VTE prophylaxis in THR/TKR**
- Start 6-10hr post-op
- THR: 10 mg PO daily for 35 days
- TKR: 10 mg PO daily for 12 days
- Avoid in CrCl < 30mL/min

## Dabigatran (Pradaxa®)

**NVAF**
- CrCl >30 mL/min: 150 mg PO BID
- CrCl 15-30 mL/min: 75 mg PO BID
- CrCl < 15 mL/min: not recommended

**VTE treatment and secondary prevention**
- For VTE treatment, an initial 5-10 days of parenteral anticoagulation is required before initiating dabigatran
- CrCl >30 mL/min: 150 mg PO BID
- CrCl ≤30 mL/min: not recommended

**VTE prophylaxis in THR/TKR**
- Not approved

| | Apixaban (Eliquis®) | Edoxaban (Savaysa®) | Rivaroxaban (Xarelto®) | Dabigatran (Pradaxa®) |
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| **Dosage Forms** | Tablets: 2.5 mg, 5 mg | Tablets: 15 mg, 30 mg, 60 mg | Tablets: 10 mg, 15 mg, 20 mg | Capsules: 75 mg, 150 mg<br>- Once bottle opened, use within 4 months.<br>- Keep bottle tightly closed and store in original package to protect from moisture. Close immediately after use.<br>- Do not put in pillbox or medication organizer<br>- Keep in original container; remove only at time of use. |
| **Able to Crush Medication** | • Yes<br>• Both 2.5 mg and 5 mg tablets may be crushed and suspended in 60 mL D5W and immediately delivered through an NGT<br>• No information available regarding oral administration of crushed and suspended tablets | • No data are available regarding the bioavailability upon crushing and/or mixing of edoxaban tablets into food, liquids, or administration through feeding tubes | • Yes<br>• The 15 mg or 20 mg tablets may be crushed and mixed with applesauce for oral or with 50 mL of water for NG or gastric tube feeding (avoid if distal to the stomach)<br>• After administration, oral or enteral feeding should immediately follow the dose | • No<br>• Do not chew, break, or open capsules! (bioavailability increases by 75% if opened) |
| **Administration with food** | With or without food | With or without food | • 20 mg: with food<br>• 15 mg: with food<br>• 10 mg: with or without food | With or without food |
| **Half-life** | • 8-15 hours | • 10-14 hours | • 5-13 hours | • 12-17 hours |
| **T-Max** | • 3-4 hours | • 1-2 hours | • 2-4 hours | • 1-3 hours |
| **Metabolism** | • Renal 27%<br>• Hepatic73% | • Renal 50%<br>• Metabolism, biliary/ intestinal 50% | • 2/3 renal (66%) and hepatic<br>• 1/3 eliminated non-metabolized | • Renal 80% |
| **Side Effects** | • Bleeding<br>• Thrombocytopenia<br>• Hypersensitivity reaction | • Bleeding<br>• Abnormal LFTs<br>• Rash<br>• Anemia | • Bleeding<br>• Thrombocytopenia<br>• Hypersensitivity reaction<br>• Stevens-Johnson Syndrome<br>• Agranulocytosis<br>• Hepatitis | • Bleeding<br>• GI: dyspepsia, abdominal and epigastric pain<br>• GI bleed<br>• Thrombocytopenia<br>• Hypersensitivity reaction |

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| **Evidence for VTE Prophylaxis for THR vs. Enoxaparin** | **ADVANCE 3**<br>- Superior with no difference in bleeding | Not approved for this indication<br>**STARS J-V** (hip replacement)<br>- Superior with no difference in bleeding<br>**STARS J-IV** (hip fracture)<br>- Similar with no difference in bleeding | **RECORD 1 and RECORD 2**<br>Superior with no difference in bleeding | Not approved for this indication<br>**RE-NOVATE I**<br>**RE-NOVATE II**<br>- Non-inferior |
| **Evidence for VTE Prophylaxis for TKR vs. Enoxaparin** | **ADVANCE 2**<br>- Superior with no difference in bleeding | Not approved for this indication<br>**STARS E-3**<br>- Superior with no difference in bleeding | **RECORD 3 and RECORD 4**<br>- Superior with no difference in bleeding | Not approved for this indication<br>**RE-MODEL/RE-MOBILIZE**<br>- Non-inferior |
| **Evidence for VTE Management vs. Heparin/VKA** | **AMPLIFY**<br>- Non-inferior: recurrent VTE/ mortality<br>- Major bleeding: lower | **HOKUSAI VTE STUDY**<br>- Non-inferior: recurrent VTE<br>- Superior: fatal and intracranial bleeding, clinically relevant bleeding | **EINSTEIN**<br>- Non-inferior: recurrent VTE/ mortality<br>- Major bleeding: lower (pooled analysis) | **RE-COVER**<br>- Non-inferior: recurrent VTE/ mortality<br>- Major bleed: similar<br>- Clinically relevant non-major and any bleed: lower |
| **Evidence for VTE Risk Reduction after Initial Treatment** | **AMPLIFY-EXT**<br>- Superior vs. placebo with similar major bleeding | Not approved for this indication (not studied) | **EINSTEIN-EXT**<br>• Superior vs. placebo with higher major bleeding | • **RE-SONATE**<br>- Superior vs. placebo, higher major bleeding<br>• **RE-MEDY**<br>- Non-inferior vs. warfarin, similar major bleeding |
| **Management of Bleeding** | • No specific antidote<br>• Charcoal: within 6 hours of last ingestion<br>• Life-threatening bleeding: consider PCC (Kcentra®), aPCC (FEIBA®), rVIIa (NovoSeven®)<br>• Not dialyzable<br>• See supplemental document ‡ | • No specific antidote<br>• No information available on the use of charcoal<br>• Life-threatening bleeding: consider PCC (Kcentra®), aPCC (FEIBA®), rVIIa (NovoSeven®)<br>• Not dialyzable<br>• See supplemental document ‡ | • No specific antidote<br>• Charcoal: within 2 hours of last ingestion<br>• Life-threatening bleeding: consider PCC Kcentra®), aPCC (FEIBA®), rVIIa (NovoSeven®)<br>• Not dialyzable<br>• See supplemental document‡ | • No specific antidote<br>• Charcoal: within 2 hours of last ingestion<br>• Life-threatening bleeding: PCC (Kcentra®), aPCC (FEIBA®), rVIIa (NovoSeven®)<br>• Hemodialyzable<br>• See supplemental document ‡ |
| **Peri-procedural Anticoagulation** | • See supplemental document‡ | • See supplemental document‡ | • See supplemental document‡ | • See supplemental document‡ |

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| **Switching between Anticoagulants** | **From warfarin**<br>- Start when INR < 2<br><br>**To warfarin**<br>- Start warfarin and consider bridging agent at next apixaban due time<br>- Start INR monitoring 2 days after stopping apixaban (initial INR values may be falsely elevated by apixaban)<br>- Stop bridging agent once goal INR is achieved<br><br>**From LMWH/UFH**<br>- Start apixaban 0-2 hours prior to next scheduled LMWH dose or at the time of UFH infusion discontinuation<br><br>**To LMWH/UFH**<br>- Start LMWH/UFH at next apixaban due time<br><br>**To/from other TSOAC**<br>- Start at the scheduled due time of the other agent | **From warfarin**<br>- Start when INR ≤ 2.5<br><br>**To warfarin**<br>- Oral Option<br>- If patient taking 60 mg edoxaban, reduce to 30 mg and begin warfarin.<br>- If patient taking 30 mg, reduce to 15 mg and begin warfarin.<br>- INR must be measured at least weekly and just prior to edoxaban dose to minimize edoxaban influence on INR. When INR ≥2, discontinue edoxaban.<br>- Parenteral option<br>- Administer parenteral anticoagulant and warfarin at time of next scheduled edoxaban dose. When INR ≥2, discontinue parenteral anticoagulant.<br><br>**From LMWH/UFH**<br>- LMWH: Start edoxaban at time of next scheduled LMWH dose<br>- UFH: Start edoxaban 4 hours after discontinuation of UFH infusion.<br><br>**To LMWH/UFH**<br>- Start LMWH/UFH at next edoxaban due time<br><br>**To/from other TSOAC**<br>- Start at the scheduled due time of the other agent | **From warfarin**<br>- Start when INR < 3<br><br>**To warfarin**<br>- Start warfarin and consider bridging agent at next rivaroxaban due time<br>- Start INR monitoring 2 days after stopping rivaroxaban (initial INR values may be falsely elevated by rivaroxaban)<br>- Stop bridging agent once goal INR is achieved<br><br>**From LMWH/UFH**<br>- Start rivaroxaban 0-2 hours prior to next scheduled LMWH dose or at the time of UFH infusion discontinuation<br><br>**To LMWH/UFH**<br>- Start LMWH/UFH at next rivaroxaban due time.<br><br>**To/from other TSOAC**<br>Start at the scheduled due time of the other agent | **From warfarin**<br>- Start when INR < 2<br><br>**To warfarin**<br>- Start warfarin . . .<br>- CrCl≥50 mL/min: 3 days<br>- CrCl 30-50 mL/min: 2 days<br>- CrCl 15-30 mL/min: 1 day<br>. . . before stopping dabigatran<br>- Start INR monitoring 2 days after stopping dabigatran (initial INR values may be falsely elevated by dabigatran)<br><br>**From LMWH/UFH**<br>- Start dabigatran 0-2 hours prior to next scheduled LMWH dose or at the time of UFH infusion discontinuation<br><br>**To LMWH/UFH**<br>- Start LMWH/UFH . . .<br>- CrCl≥30 mL/min: 12 hours after the last dabigatran dose<br>- CrCl<30 mL/min: 24 hours after the last dabigatran dose<br><br>**To/from other TSOAC**<br>- Start at scheduled due time of other agent |