



Clinical Pharmacology & Toxicology Pearl of the Week

Edoxaban (Lixiana)

- ✓ Edoxaban is the latest Direct Oral Anticoagulant (DOAC) to be approved for use in Canada.
- ✓ It has the same mechanism of action as Rivaroxaban and Apixaban, and acts as a direct Factor Xa inhibitor.
- ✓ It has been approved by Health Canada for the following indications:
 - Non-Valvular Atrial Fibrillation (NVAf) to prevent stroke & systemic embolism (NVAf is defined as: AFib in the absence of mechanical heart valves, rheumatic mitral stenosis, or moderate/severe non-rheumatic mitral stenosis)
 - Acute venous thromboembolism (VTE) treatment & prevention of recurrent VTE

Edoxaban pharmacokinetics:

- Peak plasma concentrations occur 1–2 h following oral administration.
- Oral bioavailability is 62%, and unlike rivaroxaban, does not seem to be affected by food.
- Edoxaban is a P-glycoprotein substrate in the gut, liver and kidneys, and therefore is subject to drug-drug interactions that can either increase or decrease it's serum concentration.
- Minimal metabolism via CYP3A4 occurs.
- Those with mild-moderate hepatic impairment do not have any major alterations in pharmacokinetics. (The drug is contraindicated in advanced liver disease)
- Up to 70% of the drug is eliminated unchanged, with up to 50% of the drug being renally cleared.
- Edoxaban has an elimination half-life of 10-14 hours.

Edoxaban Dosing Recommendations:

Stroke Prevention in Non-Valvular Atrial Fibrillation	<ul style="list-style-type: none"> ● 60mg Once Daily if CrCl > 50mL/min* ● 30 mg Once Daily if one or more of the following: <ul style="list-style-type: none"> ○ CrCl 30-50mL/min ○ Body weight ≤ 60Kg ○ Concomitant P-gp Inhibitor (excluding amiodarone or verapamil) 	CrCl<30 mL/min Not Recommended
Acute DVT/PE Treatment	Parenteral Anticoagulant x 5-10 days, then edoxaban as per AF dosing	
Hip & Knee Replacement	Not approved	

*Sub-group analysis reports reduced efficacy if CrCl greater than 95mL/min, but is limited by low event rates⁵

Edoxaban Drug-Drug interactions

- ✓ Edoxaban should not be used in conjunction with strong CYP3A4
- ✓ Avoid concomitant use of P-glycoprotein inducers (phenytoin, rifampicin, phenobarbital, and carbamazepine).

References:

1. <http://thrombosiscanada.ca/wp-content/uploads/2018/02/Edoxaban-2018Feb16.pdf>
2. <https://www.rxfiles.ca/rxfiles/uploads/documents/CLOT-Edoxaban-Checklist-Final-CPP.pdf>



The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click [HERE](#) for clinical issues the CP service can assist with.



The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1.