EJPMR, 2026, 13(11), 637-642 **Review Article** **Impact Factor: 8.158**

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

ISSN (O): 2394-3211
ISSN (P): 3051-2573
Coden USA: EJPMAG

APIXABAN AS A DIRECT FACTOR XA INHIBITOR: A COMPREHENSIVE REVIEW OF PHARMACOKINETICS, CLINICAL EFFICACY, AND SAFETY

[1]*Mr. Abhijeet Ramprasad Shinde, [2]Mr. Sainath Laxman Shingane, [3]Ms. Yogeshwari Madhukar Gaikwad, [4]Mr. Maharudra S. Rakh

[1,2]Students of JSPM COBP and RC Gadhi.
[3]Ass. Proff. of JSPM COBP and RC Gadhi.
[4]Principal of JSPM's COBP & RC Shivajinagar Gadhi.

***Corresponding Author: Mr. Abhijeet Ramprasad Shinde**
Students of JSPM COBP and RC Gadhi.

DOI: https://doi.org/10.5281/zenodo.24128023

How to cite this Article: [1]*Mr. Abhijeet Ramprasad Shinde, [2]Mr. Sainath Laxman Shingane, [3]Ms. Yogeshwari Madhukar Gaikwad, [4]Mr. Maharudra S. Rakh. (2026). Apixaban As A Direct Factor Xa Inhibitor: A Comprehensive Review Of Pharmacokinetics, Clinical Efficacy, And Safety. European Journal of Pharmaceuticaland Medical Research, 13(11), 637–642.
This work is licensed under Creative Commons Attribution 4.0 International license.

Article Received on 04/10/2026 **Article Revised on 25/10/2026** **Article Published on 01/11/2026**

ABSTRACT

Apixaban is a selective, reversible oral factor Xa inhibitor used to prevent and treat thromboembolic disorders. This review summarises its pharmacology, pharmacokinetics, mechanism, clinical uses, and safety. By inhibiting factor Xa, Apixaban reduces thrombin generation and clot formation. It has about 50% oral bioavailability, a 12-hour half-life, and multiple elimination routes; renal excretion accounts for roughly 27% of clearance. Uses include stroke prevention in non-valvular atrial fibrillation, treatment of deep vein thrombosis and pulmonary embolism, prevention of recurrent venous thromboembolism, and thromboprophylaxis after hip or knee replacement. Clinical trials support its efficacy and favourable benefit-risk profile versus conventional anticoagulants in appropriately selected patients. Bleeding is the main adverse effect; interactions, organ impairment, and specific patient groups require consideration. Although routine international normalized ratio monitoring is unnecessary, regular clinical assessment and appropriate laboratory tests help ensure safety. Apixaban offers convenient, effective anticoagulation, but individualised prescribing and ongoing monitoring are essential to optimize outcomes and limit complications.

KEYWORDS: Apixaban, factor Xa inhibitor, anticoagulant, thromboembolic disorders, atrial fibrillation, venous thromboembolism, bleeding risk.



INTRODUCTION

Thromboembolic disorders are major causes of morbidity and mortality. Atrial fibrillation raises the risk of ischemic stroke, while deep vein thrombosis and pulmonary embolism are forms of venous thromboembolism.

Anticoagulants limit clot formation or growth and play a central role in prevention and treatment for appropriately selected patients. Traditional vitamin K antagonists, especially warfarin, have several limitations, including a narrow therapeutic range, numerous food and drug interactions, and the need for regular international normalized ratio (INR) monitoring. Direct oral anticoagulants were developed to target specific coagulation factors and provide more predictable effects. Apixaban is an oral, selective, reversible factor Xa inhibitor. This review summarizes its pharmacology, pharmacokinetics, clinical uses, evidence of efficacy, safety, and limitations. Anticoagulants remain the

primary means of preventing and treating thrombosis. Unfractionated heparin, low-molecular-weight heparin, fondaparinux, and warfarin have been studied and used extensively, while direct thrombin inhibitors are typically reserved for patients with complications or those requiring intervention. Novel oral anticoagulants have emerged from clinical development and are expected to replace older agents because they are easier to use and have more favourable pharmacodynamics profiles. Haemorrhage is the main adverse event of concern with all anticoagulants. Given their widespread use, clinicians need a sound understanding of anticoagulant pharmacology, dosing, and toxicity. Warfarin and other vitamin K antagonists (VKAs) are highly effective oral anticoagulants; however, their use is limited by a narrow therapeutic window, interactions with medications and food, and the need for frequent monitoring. Direct oral anticoagulants, including dabigatran (a direct thrombin inhibitor) and direct factor Xa (FXa) inhibitors such as rivaroxaban, apixaban, edoxaban, and betrixaban, have been developed to address some of the limitations associated with VKAs. These agents permit fixed dosing without routine therapeutic monitoring.[1,2] Apixaban, a direct FXa inhibitor, has been approved in many countries for several indications. Results from the pivotal phase III clinical trials supporting its approval showed that apixaban is an important alternative to existing anticoagulant therapies, including VKAs, aspirin, and low-molecular-weight heparin (LMWH), with an improved benefit-risk profile. In patients with nonvalvular atrial fibrillation (NVAF), apixaban 5 mg twice daily (BID) significantly reduced the risk of stroke or systemic embolism by 21%, major bleeding by 31%, and death by 11% compared with warfarin.[3]

Physical and Chemical overview of Apixaban

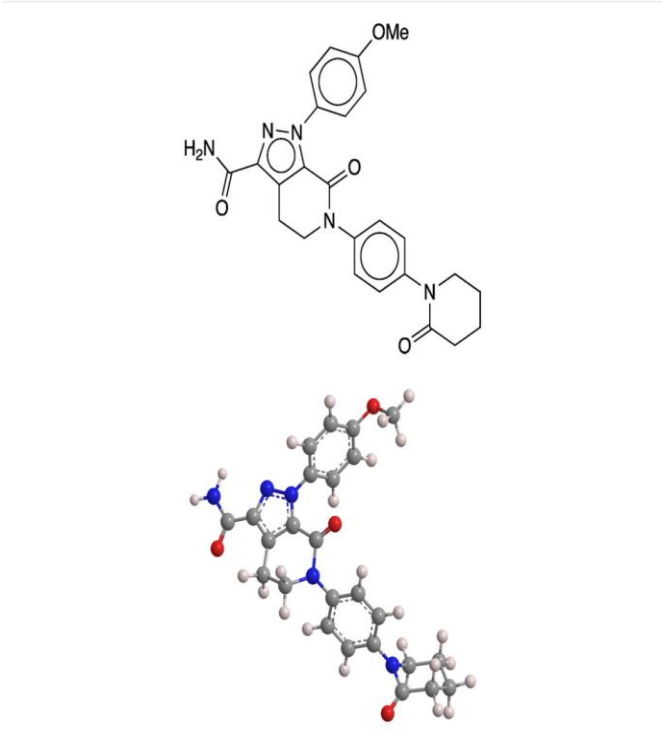


Fig. 1: Chemical structure of Apixaban.



Fig. 2: Apixaban drug Powder & Tablets.

Chemical properties

Table 1: Chemical properties.

Parameters	Description
Chemical Formula	C25 H25 N50
Molecular Weight / Molar Mass	~459.50 g/mol (exact: 459.497 g/mol)
CAS Number	503612-47-3
IUPAC name	1-(4-methoxyphenyl)-7-oxo-6-[4-(2-oxopiperidin-1-yl)phenyl]-4,5-dihydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide
LogP	~2.70
Hydrogen Bond Acceptors	6
Rotatable Bonds	5

Physical properties

Table 2: Physical properties.

Parameters	Description
Melting point	235-240°c
Appearance	Solid crystalline powder
Solubility	Low aqueous solubility
Half-life	Approximately 12 hours (range: 8–15 hours)
Oral Bioavailability	Approximately 50%
Plasma proteins binding	Approximately 87%

Table 3: Solubility profile of Apixaban.

Solvent	Solubility	Observation
Water	2.86≈0.13ug/ml	Practically soluble
DMSO	5.23±0.25mg/ml	Freely soluble
DMF	3.16±0.32mg/ml	Freely soluble
Dichloromethane	4.34±0.26mg/ml	Freely soluble
Ethanol	214.83±0.65mg/ml	Slightly soluble
Methanol	243.26±0.31ug/ml	Slightly soluble
Acetonitrile	196.76±0.92ug/ml	Slightly soluble

Pharmacology of Apixaban

- **Pharmacokinetics**

Absorption: Apixaban is taken orally and has an absolute bioavailability of about 50%.[16]

Distribution: Approximately 87% is bound to plasma proteins.

Metabolism: Apixaban is metabolised mainly by CYP3A4, with other pathways also contributing, and is a substrate of P-glycoprotein (P-gp). Elimination: Multiple pathways are involved, with renal excretion accounting for approximately 27% of total clearance. Half-life: In adults, the apparent half-life is about 12 hours.

These properties may be affected by organ function, age, and interacting medicines, making patient-specific assessment important.[17]

- **Pharmacodynamics and monitoring**

Apixaban reduces factor Xa activity and thrombin generation. It may affect prothrombin time, INR, and activated partial thromboplastin time, but these changes can vary, so these tests aren't suitable for routine monitoring of its anticoagulant effect. When measurement is clinically necessary, a suitably calibrated chromogenic anti-factor Xa assay may help estimate drug exposure. Routine INR-guided dose adjustments aren't needed, but ongoing clinical follow-up and appropriate laboratory evaluation remain important.

- **Mode of Action**

Apixaban is a potent, direct, oral, reversible, and highly selective FXa inhibitor (inhibitory constant = 0.08 nM [0.037 ng/mL] at 25 °C) that does not require antithrombin III to exert its antithrombotic activity [4,5]. It inhibits both free and clot-bound FXa, as well as prothrombinase activity, thereby limiting clot growth. By inhibiting FXa, Apixaban reduces thrombin generation and thrombus development. Although it has no direct effect on platelet aggregation, it indirectly inhibits thrombin-induced platelet aggregation. In a rabbit arteriovenous shunt thrombosis model, Apixaban inhibited thrombus formation in a dose-dependent manner (half-maximal inhibitory concentration = 329 nM). Mode of action is showed in the figure 2.

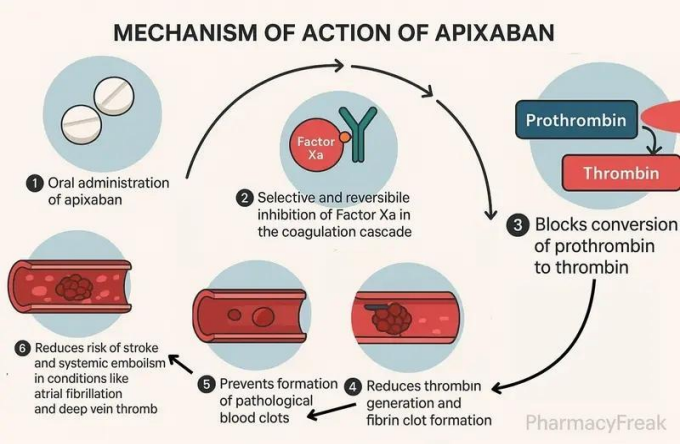


Figure 3: Mechanism of action of Apixaban.

❖ **Molecular Docking and Mechanism of Factor Xa Inhibition by Apixaban**

Apixaban is a selective, reversible, direct inhibitor of coagulation factor Xa. By binding to factor Xa, it reduces the conversion of prothrombin into thrombin, thereby decreasing fibrin formation and blood clot development. Molecular docking can help examine how Apixaban binds to factor Xa and the molecular interactions involved. The figure illustrates the conceptual binding interactions and the mechanism underlying apixaban's anticoagulant activity. The schematic representation of molecular docking and Mechanism of Factor Xa Inhibition of blocking is shown in figure 4.as below.

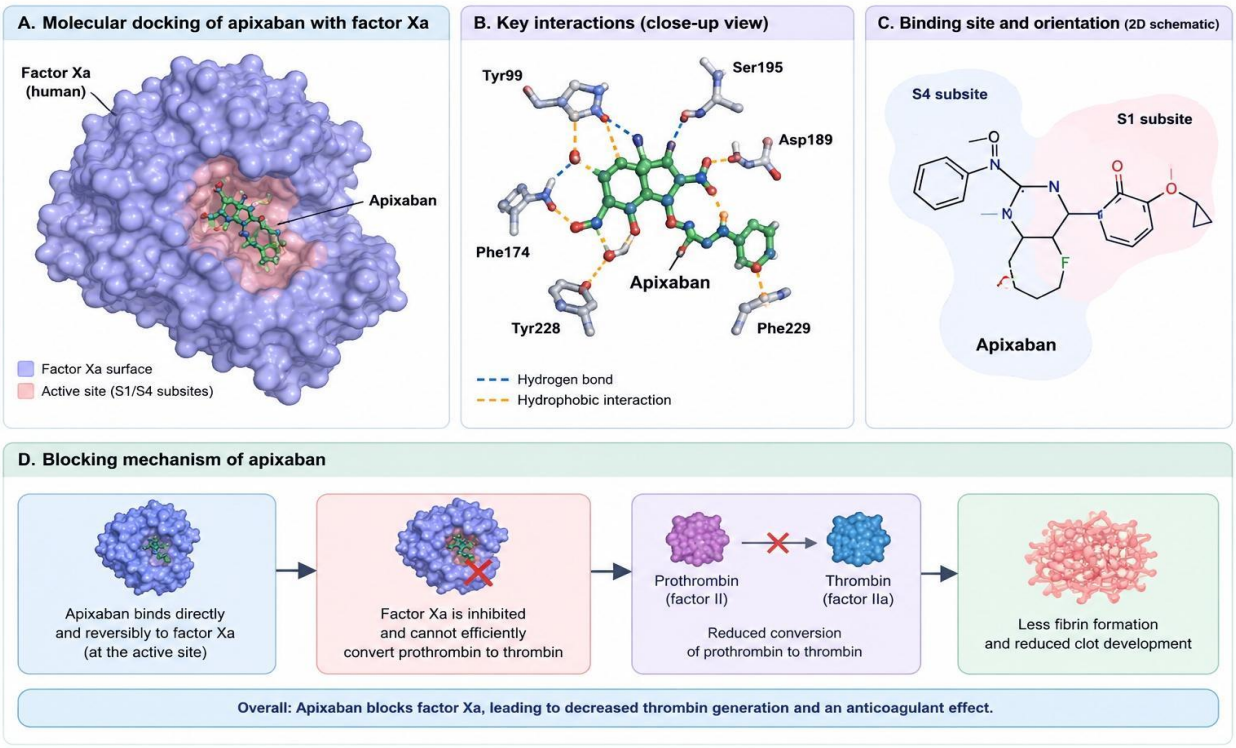


Figure 4: Schematic representation of molecular docking and Mechanism of Factor Xa Inhibition.[6]

- **Protein Binding and Distribution**

In humans, approximately 87% of apixaban binds to plasma proteins, primarily albumin.[7] Among healthy subjects taking apixaban, protein binding was about 93%. Binding was similar in subjects with end-stage renal disease (ESRD; creatinine clearance [CrCl] <15 mL/min) and those with mild-to-moderate hepatic impairment, suggesting these conditions do not alter apixaban protein binding.[8,9] Apixaban has a volume of distribution of about 21 Suggesting it is distributed mainly in extracellular fluid, including vascular and interstitial fluid. Its blood-to-plasma ratio in humans is 0.9:1, indicating even distribution between plasma and red blood cells . Whether apixaban or its metabolites are excreted in human breast milk is unknown. A tissue distribution study in rats found that apixaban was excreted in milk at about 10% of the maternal dose.[33] In rats, the milk-to-plasma AUC0-08 ratio was 30:1, indicating that apixaban can accumulate in milk.[10]

- **Metabolism and Elimination**

Total plasma clearance of Apixaban is ~ 3. 3 L/h, while renal clearance is ~ 0. 9 L/h (~ 27% of total clearance), as determined in two intravenous (IV) studies.[11,12] The apparent elimination half- life (t ½) is ~ 12 h. Apixaban is eliminated through multiple pathways, including metabolism, biliary and renal elimination of unchanged parent compound, and direct intestinal excretion.

Apixaban is not a high- extraction- ratio drug.[13,14] The metabolic pathways for Apixaban include O-demethylation, hydroxylation, and sulfation of hydroxylated 0-demethyl Apixaban. Metabolism occurs primarily via cytochrome P 450 (CYP) 3 A 4/5, with minor contributions from CYP 1 A 2, CYP 2 C 8, CYP 2 C9, CYP 2 C 19, and CYP 2 J 2. After an oral dose, unchanged Apixaban is the major drug- related component in human plasma, with no active circulating metabolites. After oral administration of a 20 mg radiolabelled dose, 56.0% was recovered in faeces and 24. 5% was eliminated in urine. Unchanged Apixaban was the major component in both faeces (60.7%) and urine (87.7%). When bile was collected following administration of the 20-mg dose, 46. 7% was recovered in faeces and 28. 8% in urine. Radioactivity identified in biliary excreta during a 5- h collection window accounted for approximately 5% of total radioactivity recovery, suggesting that biliary excretion is a minor Elimination pathway. Faecal recovery therefore consisted of Both absorbed and unabsorbed drug,

because total Radioactivity recovered in faeces exceeded that in bile. In experiments in bile duct- cannulated rats and dogs, 20-50% of an IV dose of Apixaban was excreted in faeces, identifying direct intestinal excretion as a contributor to Apixaban elimination. Direct intestinal excretion also appears to play a role in humans.[15]

Administration

Available Dosage Forms and Strengths

Apixaban is available as 2.5 mg and 5 mg oral tablets. The dose depends on the treatment indication, the patient's age, serum creatinine, and body weight.

Adult Dosage

Patients with DVT or PE should take 10 mg twice daily for 7 days, followed by 5 mg twice daily.

In the European Union (EU) and the United States, the FDA has approved Apixaban for prophylaxis after hip and knee replacement surgery. The recommended dose for DVT prophylaxis after either procedure is 2.5 mg orally twice daily. Treatment should begin 12 to 24 hours after surgery and continue for 12 days after knee replacement or approximately 35 days after hip replacement.[18]

The recommended dose for patients with nonvalvular atrial fibrillation is 5 mg twice daily. For patients who meet at least 2 of the 3 criteria below, reduce the 5 mg dose of Apixaban to 2.5 mg twice daily.

Age 80 or older

Serum creatinine greater than or equal to 1.5 mg/dL

Body weight less than or equal to 60 kg

If a dose is missed, the patient should take it as soon as possible on the same day and then resume the twice-daily schedule. Do not take a double dose to make up for a missed dose. Other administration options: Patients who have difficulty swallowing whole tablets may be able to crush 2.5 mg or 5 mg Apixaban tablets, suspend them in water, apple juice, 5% dextrose in water (D5W), or applesauce, and take the mixture orally immediately. The crushed tablets remain stable for up to 4 hours. Alternatively, the tablets may be crushed and suspended in 60 mL of water or D5W for prompt administration through a nasogastric tube.[20]

Pregnancy consideration

A limited amount of data is available on the use of Apixaban tablets in pregnant women and the associated risk of major congenital disabilities, adverse outcomes, or miscarriage. The treatment with the drug may lead to an increased risk of bleeding during pregnancy and delivery. As per the American College of Obstetricians and Gynaecologists (ACOG), the use of dabigatran and anti-Xa Inhibitors (such as rivaroxaban, apixaban, and edoxaban) is not recommended during pregnancy due to the limited availability of safety data about the well-being of the mother, foetus, and breastfeeding neonate. Research involving human placental studies has indicated the passage of these inhibitors across the placenta, warranting caution regarding potential indirect effects on foetal blood coagulation.[19]

Paediatric patient

The safety and efficacy of Apixaban tablets have not been established in paediatric patients.

- **Clinical applications**

1. Treatment of deep vein Thrombosis.
2. Stroke prevention
3. Treatment of pulmonary embolism
4. Anticoagulant therapy management
5. Bleeding risk monitoring
6. Alternative to Warfarin
7. Post operative thrombophylaxis.

- **Adverse effects**

1. Bleeding : must common adverse effect (about 1-10%)
2. Nausea
3. Anaemia
4. Bruising
5. Haematoma
6. Epistaxis
7. Gingival haemorrhage
8. Increased liver enzymes
9. Hypersensitivity reactions
10. Rectal haemorrhage
11. Haematuria

DISCUSSION

Clinical evidence supports Apixaban for several thromboembolic disorders. Its selective factor Xa inhibition, oral dosing, and predictable effects offer Advantages over vitamin K antagonists for many patients. ARISTOTLE supported stroke and systemic embolism prevention in atrial fibrillation; AMPLIFY supported acute VTE treatment; and AMPLIFY-EXT showed reduced recurrent VTE with extended therapy. However, Apixaban is not suitable for everyone. Bleeding risk, interactions, organ impairment, adherence, and planned procedures may complicate treatment. Trials enroll selected populations, limiting generalizability to some medically complex patients. Although routine INR monitoring is unnecessary, follow-up remains essential: periodically review renal and hepatic function, medications, bleeding and thrombotic risks, and ongoing treatment need. Continued pharmacovigilance and research can help optimise use in underrepresented populations.[21,22]

CONCLUSION

Apixaban is an oral, direct factor Xa inhibitor used to help prevent stroke and systemic embolism in eligible patients with non-valvular atrial fibrillation. It is also used to treat DVT and PE, prevent recurrent VTE, and reduce the risk of blood clots after certain orthopaedic procedures. Major trials support its effectiveness in the

populations studied. Its predictable effects and the fact that doses do not need routine adjustment based on INR testing can make treatment more convenient. However, bleeding risks, medication interactions, organ impairment, and individual contraindications remain important to consider. Safe use depends on choosing appropriate patients, reviewing medications, following up clinically, and following current prescribing guidance.

REFERENCES

1. Wonkyung Byon, Samira Garonzik, Rebecca A. Boyd, Charles E. Frost. Apixaban: A Clinical Pharmacokinetic and Pharmacodynamics Review Clinical Pharmacokinetics, 2019; 58: 1265–1279.
2. Bristol-Myers Squibb. Coumadin (warfarin sodium) prescribing Information. 2017. http://packageinserts.bms.com/pi/pi_couma Din.pdf. Accessed 2 Feb 2018.
3. Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek E, Hanna M, et al. Apixaban versus warfarin in patients with atrial Fibrillation. N Engl J Med., 2011; 365(11): 981–92.
4. Pinto DJ, Orwat MJ, Koch S, Rossi KA, Alexander RS, Small-Wood A, et al. Discovery of 1-(4-methoxyphenyl)-7-oxo-6-(4-(2-oxopiperidin-1-yl)phenyl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-C]pyridine-3-carboxamide (apixaban, BMS-562247), a highly Potent, selective, efficacious, and orally bioavailable inhibitor of Blood coagulation factor Xa. J Med Chem., 2007; 50(22): 5339–56.
5. Luettgen JM, Knabb RM, He K, Pinto DJ, Rendina AR. Apixaban Inhibition of factor Xa: microscopic rate constants and inhibition Mechanism in purified protein systems and in human plasma. J Enzyme Inhib Med Chem., 2011; 26(4): 514–26.
6. Raghavan N, et al. Apixaban metabolism and pharmacokinetics. Drug Metabolism and Disposition, 2009; 37(1): 74–81
7. He K, Luettgen JM, Zhang D, He B, Grace JE Jr, Xin B, et al. Preclinical pharmacokinetics and pharmacodynamics of apixaban, a potent and selective factor Xa inhibitor. Eur J Drug Metab Pharmacokinetic, 2011; 36(3): 129–39.
8. Wang X, Tirucherai G, Marbury TC, Wang J, Chang M, Zhang D, Et al. Pharmacokinetics, pharmacodynamics, and safety of Apixaban in subjects with end-stage renal disease on hemodialysis. J Clin Pharmacia, 2016; 56(5): 628–36.
9. Frost C, Yu Z, Wang J, Li T, Ziegler C, Schuster A, et al. Single-Dose safety and pharmacokinetics of apixaban in subjects with Mild or moderate hepatic impairment. Clin Pharmacology Ther., 2009; 85(1): S34.
10. Wang L, He K, Maxwell B, Grossman SJ, Tremaine LM, Hum-Phreys WG, et al. Tissue distribution and elimination of [14C]Apixaban in rats. Drug Metab Dispos, 2011; 39(2): 256–64.
11. Bristol-Myers Squibb, Pfizer EEIG. EU summary of product Characteristics: Eliquis(apixabantablets).2018.http://www.ema.Europa.eu/docs/en_GB/document_library/EPAR_Product_InforMation/human/002148/WC500107728.pdf. Accessed 8 Apr 2019.
12. Bristol-Myers Squibb Company PI. Eliquis (apixaban) prescribing information, 2018. http://packageinserts.bms.com/pi/pi_eliquIs.pdf. Accessed 14 Jun 2018.
13. Raghavan N, Frost CE, Yu Z, He K, Zhang H, Humphreys WG, Et al. Apixaban metabolism and pharmacokinetics after oral Administration to humans. Drug Metab Dispos, 2009; 37(1): 74–81.
14. Wang X, Mondal S, Wang J, Tirucherai G, Zhang D, Boyd RA, Et al. Effect of activated charcoal on Apixaban pharmacokinetics In healthy subjects. Am J Cardiovascular Drugs, 2014; 14(2): 147–54.
15. Zhang D, He K, Herbst J, Kolb J, Shou W, Wang L, et al. Char-Acterization of efflux transporters involved in distribution and Disposition of apixaban. Drug Metab Dispos, 2013; 41(4): 827–35.
16. Byon W, Garonzik S, Boyd RA, Frost CE. Apixaban: A Clinical Pharmacokinetic and Pharmacodynamics Review. Clin Pharmacokinetic, Oct. 2019; 58(10): 1265-1279. [PMC free article] [PubMed].
17. Yao X, Inselman JW, Ross JS, Izem R, Graham DJ, Martin DB, Thompson AM, Ross South worth M, Siontis KC, Ngufor CG, Nath KA, Desai NR, Nallamothu BK, Saran R, Shah ND, Noseworthy PA. Comparative Effectiveness and Safety of Oral Anticoagulants Across Kidney Function in Patients With Atrial Fibrillation. Circ Cardiovascular Qual Outcomes, Oct. 2020; 13(10): e006515. [PMC free article] [PubMed].
18. Rooney T, Barrack RL, Clohisy JC, Nunley RM, Lawrie CM. Is Apixaban Safe and Effective for Venous Thromboembolism Prophylaxis After Primary Total Hip and Total Knee Arthroplasties? J Arthroplasty, Jul., 2021; 36(7S): S328-S331. [PubMed].
19. American College of Obstetricians and Gynaecologists' Committee on Practice Bulletins—Obstetrics. ACOG Practice Bulletin No. 196: Thromboembolism in Pregnancy. Obstet Gynecol, Jul. 2018; 132(1): e1-e17. [PubMed].
20. Agrawal A, Manna B. Apixaban. [Updated 2024 Feb 22]. In: Stat Pearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507910/
21. Granger CB, Alexander JH, McMurray JJV, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med., 2011; 365: 981–992. Doi:10.1056/NEJMoa1107039.
22. Agnelli G, Buller HR, Cohen A, et al. Apixaban for extended treatment of venous thromboembolism. N Engl J Med., 2013; 368: 699–708. Doi:10.1056/NEJMoa1207541.