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BRINGING CLINICIANS TOGETHER TO DISCUSS CURRENT DRUG THERAPY

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The following succinct analysis appeared in *Pharmacist's Letter*. Based on vol. 38. No. 8

ANTICOAGULANTS

Direct oral anticoagulant (DOAC) dosing errors continue to crop up...but you can help prevent them.

For example, evidence suggests DOACs (Eliquis, etc) are UNDERdosed almost 25% of the time for atrial fib...which is linked with increased mortality. And we know OVERdosing can lead to bleeding.

Help ensure appropriate DOAC dosing. Resist the urge to rely on memory...due to the laundry list of uses, doses, and durations.

Watch for key factors...and reevaluate the dose periodically.

Obesity. Advise usual dosing up to 120 kg or a BMI of 40.

If a DOAC is preferred for patients with a higher weight, suggest Eliquis (apixaban) or Xarelto (rivaroxaban) at usual doses...based on limited data. Otherwise, recommend warfarin.

Kidney impairment. For atrial fib, usually expect a lower dose.

For instance, think of "ABC" with Eliquis. Advise reducing the dose for patients with 2 of these 3 features...Age over 80, Body weight under 60 kg, or serum Creatinine over 1.5 mg/dL.

Recommend reducing Xarelto for CrCl under 50 mL/min.

On the other hand, don't extend atrial fib dosing "rules" to venous thromboembolism (VTE) treatment...this may undertreat acute clots.

In this case, only Savaysa (edoxaban) needs a lower dose... there's no evidence for reducing other DOACs. But avoid Pradaxa (dabigatran) for CrCl below 30 mL/min...or Xarelto below 15 mL/min.

For patients on dialysis, consider cautious use of Eliquis at the usual dose if a DOAC is preferred for atrial fib or VTE.

If you don't have access to kidney function, look for clues... such as meds being used at a lower dose or meds for kidney disease.

Interactions. Eliquis and Xarelto are metabolized by CYP3A4... and absorption of all 4 DOACs is affected by P-glycoprotein (P-gp).

For example, recommend reducing Eliquis 5 or 10 mg by half when it's used with a strong CYP3A4 and P-gp inhibitor (itraconazole, Paxlovid, etc). Avoid Xarelto in this case.

If you spot a nonstandard dose, but it isn't changed...due to patient frailty, bleeding history, etc...document your discussion.

Get our resource, Appropriate Use of Oral Anticoagulants, for help choosing a med...including in special populations (cancer, etc).

(For more on this topic, see Clinical Resource #380802 at PharmacistsLetter.com.)

Camm AJ, Cools F, Virdone S, et al. Mortality in Patients With Atrial Fibrillation Receiving Nonrecommended Doses of Direct Oral Anticoagulants. J Am Coll Cardiol. 2020 Sep 22;76(12):1425-1436.

See LEADER NOTES for answers to discussion questions.

DISCUSSION QUESTIONS

OVERVIEW OF CURRENT THERAPY

1. **What are factors that affect direct oral anticoagulant (DOAC) dosing for atrial fibrillation?**

2. **What type of study was this? How were the patients selected for inclusion?**

3. **How were the study groups defined?**

4. **How were the outcomes evaluated?**

5. **What were the outcomes of this study?**

See LEADER NOTES for answers to discussion questions.

6. **What were the strengths and weaknesses of this study?**

7. **Were the results expressed in terms we care about and can use?**

HOW SHOULD THE NEW GUIDELINES CHANGE CURRENT THERAPY?

8. **Do the guidelines change your practice? How?**

APPLY THE NEW FINDINGS TO THE FOLLOWING CASE

JE is a 73-year-old female with past medical history of hypertension and hyperlipidemia who comes to see you in clinic following recent hospital discharge during which she was diagnosed with paroxysmal atrial fibrillation. Her CHAD2DS2-VASc score was at least 3. She was prescribed the DOAC apixaban 5 mg bid at discharge; however, reports she never started the medication due to uncertainty about potential risks and side effects.

A review of JE's medications shows she is currently on lisinopril 20 mg, amlodipine 10 mg, metoprolol XL 25 mg and simvastatin 20 mg daily. Her vital signs for today's visit are: BP 135/65 mmHg, HR 95, height 5'5", weight 69 kg. Review of her inpatient labs revealed no kidney or liver impairment.

9. **How do you counsel JE regarding her available options for anticoagulation and the associated risks?**

See LEADER NOTES for answers to discussion questions.

You discuss the risks and benefits of apixaban and JE agrees to start the medication. Because DOAC dosing is so nuanced, you double-check the dose JE was prescribed.

10. What should you consider to ensure JE is receiving the correct DOAC dose?

You determine that JE was prescribed the appropriate dose of apixaban. You discuss with JE that while DOACs have fewer interactions than some other anticoagulants such as warfarin, it is important that she is aware DOACs can still have important interactions.

11. What should you keep in mind about possible DOAC interactions?

You continue to care for JE regularly in your practice over the next few years and she does well on the prescribed DOAC. About a decade later, she presents to you, now 83-years-old. Her most recent blood work shows worsening kidney function with serum creatinine of 1.7 mg/dL. You also notice that JE has lost weight as she has gotten older. Her vital signs at today's visit show a weight of 59 kg.

12. What modifications to JE's DOAC should you make at this time?

You adjust JE's apixaban dose as appropriate for her age, weight, and kidney function, and ensure JE understands the reason for the dose adjustment.

See LEADER NOTES for answers to discussion questions.

REFERENCES

Camm AJ, Cools F, Virdone S, et al. Mortality in Patients With Atrial Fibrillation Receiving Nonrecommended Doses of Direct Oral Anticoagulants. J Am Coll Cardiol. 2020 Sep 22;76(12):1425-1436.

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Additional Pharmacist's Letter Resources available at PharmacistsLetter.com
Appropriate Use of Oral Anticoagulants. Pharmacist's Letter/Prescriber's Letter. July 2022.
Oral Anticoagulants for A Fib. Pharmacist's Letter/Prescriber's Letter. June 2018.
Comparison of Oral Anticoagulants. Pharmacist's Letter/Prescriber's Letter. December 2019.
Managing Bleeding With Anticoagulants. Pharmacist's Letter/Prescriber's Letter. July 2022.
Managing Anticoagulation Patients After a Bleed. Pharmacist's Letter/Prescriber's Letter. June 2022.
Cytochrome P450 (CYP) Drug Interactions. Pharmacist's Letter/Prescriber's Letter. June 2020.
Anticoagulant Use in Cirrhosis Patients. Pharmacist's Letter/Prescriber's Letter. July 2019.

See LEADER NOTES for answers to discussion questions.