

BILH Guidance for Management of Paxlovid (nirmatrelvir-ritonavir) Interactions with Anticoagulation

APIXABAN: Increased anticoagulation effects when combined with Paxlovid

Apixaban for AFIB

If Apixaban cannot be safely adjusted <u>or</u> interrupted <u>or</u> if patient is on hemodialysis	Do NOT take Paxlovid. Consider alternative treatments for COVID-19 Molnupiravir (ORAL) and Remdesivir (IV) DO NOT interact with anticoagulants. Revisit the full guidelines to evaluate their place in therapy
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If patient is on 5mg BID	START Paxlovid and DECREASE the dose of Apixaban to 2.5mg BID. Continue for 8 days and then RESUME previous dosing of Apixaban
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If patient is on 2.5mg BID	Option 1: Do not use Paxlovid
	Option 2: Choose an alternative anticoagulant 1. HOLD Apixaban for 12-24 hours and then start both Paxlovid and the alternative anticoagulant. (ex. Enoxaparin) 2. Patient will take Paxlovid for 5 days and continue the alternative anticoagulant for 8 days. Then STOP the alternative anticoagulant and RESUME previous dose of Apixaban.
	Option 3: HOLD anticoagulation 1. Have the patient HOLD Apixaban for 24 hours before starting Paxlovid AND Continue to HOLD for 8 days (total of 9 days) Because of the prolonged time off anticoagulation, this option should only be reserved for those at very low thromboembolic risk. Low thromboembolic risk: Afib CHADSVasc < 3 and/or no hx of stroke, VTE more 1 year prior, no history of recurrent clots, no history of severe thrombophilia (APLS, homozygous factor V Leiden, etc) <u>Please be aware that having an active COVID-19 infection may increase the baseline risk of having an embolic event and this should be taken into consideration when discussing risk vs benefit with your patient.</u>

Apixaban for VTE

If Apixaban cannot be safely adjusted <u>or</u> interrupted <u>or</u> if patient is on hemodialysis	Do NOT take Paxlovid. Consider alternative treatments for COVID-19 Molnupiravir (ORAL) and Remdesivir (IV) DO NOT interact with anticoagulants. Revisit the full guidelines to evaluate their place in therapy
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If patient is on 10mg BID	1. START Paxlovid and DECREASE the dose of Apixaban to 5mg 2. Then consult anticoag for help with dosing for the duration of the 8 days
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If patient is on 5mg BID	1. START Paxlovid and DECREASE the dose of Apixaban to 2.5mg BID 2. Continue for 8 days and then RESUME previous dosing of Apixaban
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If patient is on 2.5mg BID for VTE Extended Prophylaxis	When starting Paxlovid, it is ok to continue current dosing, 2.5mg BID Note: because of the interaction with ritonavir, the patient will likely achieve therapeutic levels of anticoagulation for the 8 days
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Rivaroxaban: Increased anticoagulation effects when combined with Paxlovid	
The ritonavir component of Paxlovid can increase the concentration of Rivaroxaban by 153%.	
If Rivaroxaban cannot be safely interrupted or switched to an alternative anticoagulant	<p>Do NOT take Paxlovid. Consider alternative treatments for COVID-19</p> <p>Molnupiravir (ORAL) and Remdesivir (IV) DO NOT interact with anticoagulants. Revisit the full guidelines to evaluate their place in therapy</p>
Choose an alternative anticoagulant	<ol style="list-style-type: none"> 1. HOLD Rivaroxaban for 24-36 hours and then start both Paxlovid and the alternative anticoagulant. (ex. Enoxaparin, or half dose Apixaban). 2. Patient will take Paxlovid for 5 days and continue the alternative anticoagulant for 8 days. 3. Then STOP the alternative anticoagulant and RESUME previous dose of Rivaroxaban.
HOLD anticoagulation	<ol style="list-style-type: none"> 1. HOLD Rivaroxaban for 24 hours before starting Paxlovid 2. Start Paxlovid and continue to HOLD for 8 days (total of 9 days) <p>Because of the prolonged time off anticoagulation, this option should only be used if the patient has a LOW thromboembolic risk.</p> <p>Low thromboembolic risk: Afib CHADSVasc < 3 and/or no hx of stroke, VTE more 1 year prior, no history of recurrent clots, no history of severe thrombophilia (APLS, homozygous factor V Leiden, etc)</p> <p><u>Please be aware that having an active COVID-19 infection may increase the baseline risk of having an embolic event and this should be taken into consideration when discussing risk vs benefit with your patient.</u></p>

Edoxaban: Possible increased anticoagulation effects when combined with Paxlovid	
If Edoxaban cannot be safely interrupted or adjusted	Do NOT take Paxlovid. Consider alternative treatments for COVID-19 Molnupiravir (ORAL) and Remdesivir (IV) DO NOT interact with anticoagulants. Revisit the full guidelines to evaluate their place in therapy
Dose reduce Edoxaban by 50%	<ol style="list-style-type: none"> 1. If patient is on Edoxaban 60mg Daily DECREASE Edoxaban dose by 50% for a total of 8 days from the start of Paxlovid 2. RESUME the full dose of Edoxaban <p>Note: Recommendations are limited for patients on Edoxaban 30mg Daily - May consider switching to an alternative anticoagulant like (ex. enoxaparin) or holding Edoxaban (See below)</p>
Choose an Alternative Anticoagulant	<ol style="list-style-type: none"> 1. HOLD Edoxaban for 24 hours and then start both Paxlovid and the alternative anticoagulant. (ex. Enoxaparin) 2. Patient will take Paxlovid for 5 days and continue the alternative anticoagulant for 8 days. 3. Then STOP the alternative anticoagulant and RESUME previous dose of Edoxaban.
HOLD Anticoagulation	<ol style="list-style-type: none"> 1. HOLD Edoxaban for 24 hours before starting Paxlovid 2. Start Paxlovid and continue to HOLD for 8 more days (total of 9 days) <p>Because of the prolonged time off anticoagulation, this option should only be used if the patient has a LOW thromboembolic risk. Low thromboembolic risk: CHADSVasc < 3 and/or NO history of stroke, VTE greater than 1 year prior, NO history of recurrent clots, NO history of severe thrombophilia (NO APLS, NO homozygous factor V Leiden, etc)</p> <p><u>Please be aware that having an active COVID-19 infection may increase the baseline risk of having an embolic event and this should be taken into consideration when discussing risk vs benefit with your patient.</u></p>

Dabigatran:	
Possible increased anticoagulation effects when combined with Paxlovid	
If Dabigatran cannot be safely continued, interrupted or adjusted	Do NOT take Paxlovid. Consider alternative treatments for COVID-19 Molnupiravir (ORAL) and Remdesivir (IV) DO NOT interact with anticoagulants. Revisit the full guidelines to evaluate their place in therapy
Dabigatran for AFIB	
CrCl > 50mL/min Reduced Dose Dabigatran	1. Recommendation is to DECREASE dose to 110mg BID for 8 days when starting Paxlovid** Note: The 110 dose is NOT APPROVED for treatment of atrial fibrillation in the United States and this dose may not be covered by insurance
CrCl 30-50mL/min Reduced Dose Dabigatran	1. DECREASE dose of Dabigatran to 75mg BID and continue for 8 days** 2. Resume previous dose of Dabigatran on day 9
CrCl < 30mL/min Do NOT Combine	Do NOT take Paxlovid with Dabigatran**
**	May consider switching to an alternative anticoagulant like (ex. enoxaparin) or holding Dabigatran (See below)
Dabigatran for VTE	
Combined use with Dabigatran 150mg BID is not recommended May consider switching to an alternative anticoagulant or holding Dabigatran	
Choose an alternative anticoagulant	1. HOLD Dabigatran for 12-24 hours and then start both Paxlovid and the alternative anticoagulant. (ex. Enoxaparin) 2. Patient will take Paxlovid for 5 days and continue the alternative anticoagulant for 8 days. 3. STOP the alternative anticoagulant and RESUME previous dose of Dabigatran.
HOLD Anticoagulation	1. HOLD Dabigatran for 12-24 hours and START Paxlovid 2. Continue to HOLD Dabigatran for 8 more days (total of 9 days) and then RESUME previous dose of Dabigatran Because of the prolonged time off anticoagulation, this option should only be used if the patient has a LOW thromboembolic risk. Low thromboembolic risk: CHADSVasc < 3 and/or NO history of stroke, VTE greater than 1 year prior, NO history of recurrent clots, NO history of severe thrombophilia (NO APLS, NO homozygous factor V Leiden, etc) <u>Please be aware that having an active COVID-19 infection may increase the baseline risk of having an embolic event and this should be taken into consideration when discussing risk vs benefit with your patient.</u>

Warfarin:**Possible increased or decreased anticoagulation effects when combined with Paxlovid**

Ok to take with Paxlovid but INR should be closely monitored due to a potential decrease in INR. May consider a slight booster dose of warfarin in high-risk patients who are at the lower end of their therapeutic goal range.

Patients should contact their anticoagulation clinic to arrange for an INR check soon after taking Paxlovid.

INR testing may be difficult when patients have COVID.

Enoxaparin:**No change in anticoagulation effect expected when combined with Paxlovid**

No interaction expected with Paxlovid. Should be okay to take with Paxlovid (but this is based on limited evidence)

Recommendations for how to manage drug interactions between Paxlovid and the various anticoagulants come from the Liverpool COVID-19 Drug-Drug Interaction website and individual Package Inserts.

The recommendations in this guide are meant to serve as treatment guidance for BILH. These guidelines should not replace a provider's professional medical advice based on clinical judgment.

Be aware, research is actively ongoing in this space and practice guidelines may change from time-to-time. The authors of these guidelines have made all attempts to ensure accuracy based on current information based on the last date of revision. Users of these guidelines are strongly encouraged to confirm the information contained within them through an independent source.

References:

1. University of Liverpool COVID-19 Drug Interactions website: [Liverpool COVID-19 Interactions \(covid19-druginteractions.org\)](https://www.liverpool.ac.uk/covid19druginteractions.org/) (Accessed 6/10/22)
2. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at <https://www.covid19treatmentguidelines.nih.gov/>. Accessed [6/10/22].
3. Apixaban FDA package insert. Available at: [label \(fda.gov\)](#) Accessed 5/27/22.
4. Xarelto FDA package insert. Available at: [Xarelto \(rivaroxaban\) tablets label \(fda.gov\)](#) Accessed 5/27/22.
5. Dabigatran FDA package insert. Available at: [PRADAXA \(dabigatran etexilate mesylate\) capsules for oral use Label \(fda.gov\)](#). Accessed 5/27/22.
6. Exodaban FDA package insert. Available at: [SAVAYSA \(edoxaban\) tablets Label \(fda.gov\)](#). Accessed 5/27/22.

Revised:

5/27/2022 - Sent to BILH

6/10/2022 - Updated language surrounding alternative therapies & references attached

6/15/2022 - Updated language surrounding Paxlovid-Warfarin interaction