A note from the study chair
Thomas Ortel MD, PhD
Duke University Medical Center, Durham, NC

ACTIV-4c
COVID-19 Post-Hospital Thrombosis Prevention Study

Welcome to the ACTIV-4 Post-Hospital Thrombosis Prevention Study and Thank You for helping in the fight against COVID-19! We are sorry you have been in the hospital with COVID-19. We truly hope you are feeling better and can recover comfortably back at home. When you signed up for the ACTIV-4 Post-Hospital study, you learned that a positive COVID-19 diagnosis is one of several factors that can lead to a higher risk of blood clots. Your participation in the Post-Hospital Thrombosis Prevention Study is helping us discover the best course of treatment for people like you who have had COVID-19. We are so grateful for your help.

The study team is here to assure your safety and success in the study. If you have questions or concerns, call the study number at 855-322-6509 and we will do our best to help.

Your ACTIV-4 Study Kit includes:

- **One bottle of study pills with 70 pills** (2 for each day and a few extra). The pills will be either Apixaban 2.5 mg, also known as Eliquis, or matching pills which contain no active medication.
- **A wallet card** with important information you or others may need during the study period. We suggest you keep this with you while you are in the study.
- **A study calendar** to help you keep track of taking your study pills and follow-ups.
- **A letter for any doctors** that you might see during the study. This letter will tell them everything they need to know about the study.
- **A guide to staying on track** including information about what to expect from follow-ups, when to seek medical attention, and advice on starting new medication while in this study.

Please follow these instructions on how to take your study pills

- **Every day,** take 1 pill in the morning and 1 pill in the evening, about 12 hours apart.
- **If you miss a pill,** take it as soon as you remember. If it's less than 6 hours until it's time for the next pill just skip the missed dose and take the next one at the regular scheduled time.
- **Do not take 2 pills at the same time.**

IMPORTANT: If you have any questions or need help related to the study **please call 855-322-6509** and ask to speak to the pharmacist.

IMPORTANT

Talk to your doctor before starting any of these medicines while you are in the study. Or, you can call 855-322-6509 to talk to a study pharmacist.

Blood-thinning medications:

- Eliquis (Apixaban) (*other than your study medicine*)
- Aggrenox (Dipyridamole)
- Aspirin
- Brilinta (Ticagrelor)
- Coumadin (Warfarin)
- Effient (Prasugrel)
- Fragmin (Dalteparin)
- Lovenox (Enoxaparin)
- Plavix (Clopidogrel)
- Pradaxa (Dabigatran)
- Savaysa (Edoxaban)
- Xarelto (Rivaroxaban)

Pain Medication (taken daily):

- Advil or Motrin (Ibuprofen)
- Aleve (Naproxen)

Try taking Tylenol (Acetaminophen) if you need pain relief.

If you have questions related to the study **please call the study number at 855-322-6509**

ACTIV-4c

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YOUR GUIDE TO STAYING ON TRACK WITH THE ACTIV-4C POST-HOSPITAL STUDY

All of these materials and other information are available on the study website

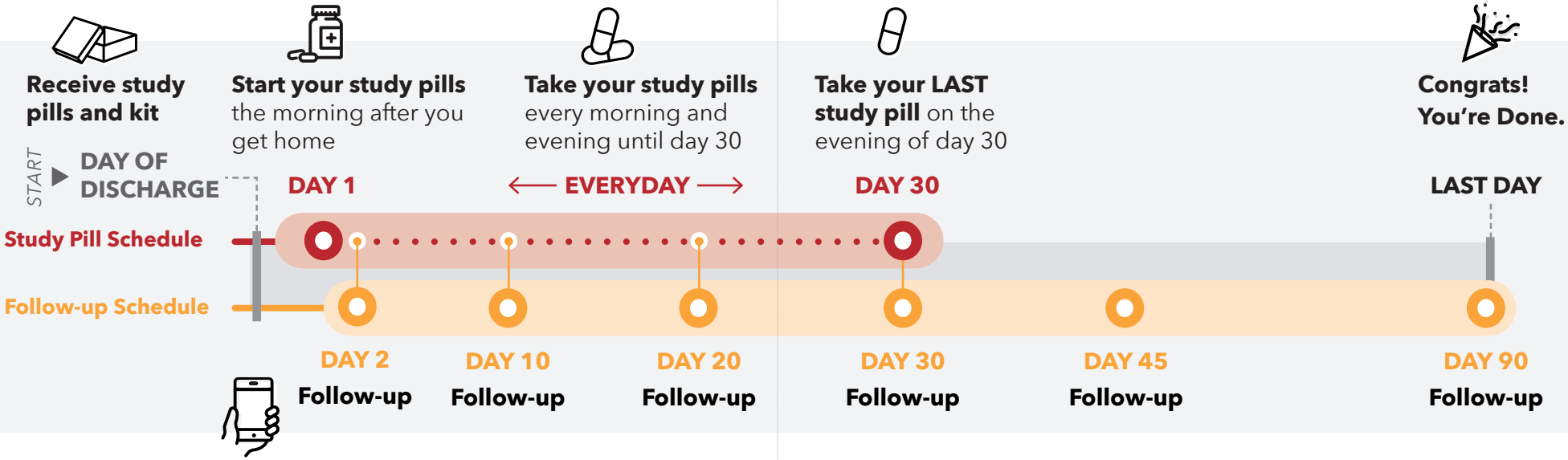
ACTIV4c.org

12.20.2020

WHAT TO EXPECT OVER THE NEXT 90 DAYS

ACTIV-4c
COVID-19 Post-Hospital Thrombosis Prevention Study

Day-by-day guide



Some helpful tips

- **Take your study pills around the same time** each morning and evening.
- **Use a reminder system to help you with your pills and follow-ups!**
  We have included a tracking calendar in your kit, but adding reminders into your phone would be helpful as well!
- **If you miss any doses, be sure to let the study team know** during your follow-ups.
- **Stop taking your pills on day 30** even if you still have pills left in the bottle. If you need to know what day to stop taking your pills, a study team member can help you figure it out.

What to expect during follow-ups

- Follow-ups help us look out for your safety and assess how you are doing in the study. **Be ready to discuss the below information:**
  - *Are you still taking your study pills?*
  - *Have you had any medical issues since your last follow-up?*
  - *Have you started taking any new medications since your last follow-up?*
  - *How do you feel about your Mobility, Self-Care, Usual Activities, Pain/ Discomfort, and Mood?*
- Your follow-up may not be on the exact day listed after discharge, but **expect your follow-ups within one week of that day.**
- Survey/call times will vary depending on which follow-up it is, **but they may take from 5 - 15 minutes to complete.**

STUDY PILL TRACKER AND CALENDAR

ACTIV-4c
COVID-19 Post-Hospital Thrombosis Prevention Study

Study pill **start date:** ___/___/___

*****Begin study pills the morning after your discharge to home. This is your ***study pill start date.***

Study pill **end date:** ___/___/___

*End study pills 30 days after your discharge even if you still have study pills left. This is your **study pill end date.***

Expect follow up survey

Day of the week:							
Week 1	study pill start day ☐ AM* ☐ PM day 1	☐ AM ☐ PM day 2	☐ AM ☐ PM 3	☐ AM ☐ PM 4	☐ AM ☐ PM 5	☐ AM ☐ PM 6	☐ AM ☐ PM 7
2	☐ AM ☐ PM 8	☐ AM ☐ PM 9	☐ AM ☐ PM day 10	☐ AM ☐ PM 11	☐ AM ☐ PM 12	☐ AM ☐ PM 13	☐ AM ☐ PM 14
3	☐ AM ☐ PM 15	☐ AM ☐ PM 16	☐ AM ☐ PM 17	☐ AM ☐ PM 18	☐ AM ☐ PM 19	☐ AM ☐ PM day 20	☐ AM ☐ PM 21
4	☐ AM ☐ PM 22	☐ AM ☐ PM 23	☐ AM ☐ PM 24	☐ AM ☐ PM 25	☐ AM ☐ PM 26	☐ AM ☐ PM 27	☐ AM ☐ PM 28
5	☐ AM ☐ PM 29	*study pill end day ☐ AM ☐ PM day 30					

Congratulations. You're done taking your study pills!

...but keep an eye out for follow-up contact via email/text or phone on days 45 and 90!

INSTRUCTIONS

1. Write the date that you take your first dose in the green box labeled **study pill start date.** Your site coordinator or RCC agent can help you find your **study pill end date** which is 30 days after you go home. Write that date in the 2nd green box.

2. Write the **Day of the week** when you took your first dose in the yellow box.

3. Then, write the other six days of the week across the top of the calendar.

For example, if you take your first pill on Wednesday, you will write: ***Wednesday*** in the yellow box followed by ***Thursday, Friday, Saturday, etc.***

NOTES / QUESTIONS

IMPORTANT: If you have any questions or need help related to the study please **call the study number at (855) 322-6509**.

visit **ACTIV4c.org**

12.20.2020

DISPOSING OF YOUR EXTRA STUDY PILLS

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You can dispose of your study pills in your household trash as long as you follow these 4 steps:

1

Mix pills with unappealing substance

Remove the pills from the original container and mix them with something undesirable, like used coffee grounds, dirt, or cat litter. This makes the medicine less appealing to children and pets and unrecognizable to someone who might go through the trash looking for drugs.

2

Place in a sealed container

Put the mixture in something you can close (a re-sealable zipper storage bag, empty can, or other container) to prevent the drug from leaking or spilling out.

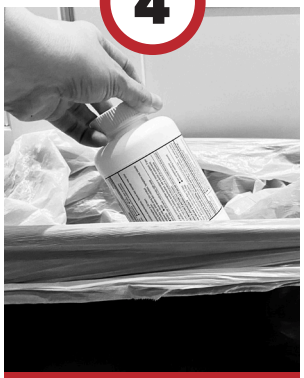
Do not throw the pills out inside their original container.

3

Throw in household trash

Throw the container with the substance and the pills in your household garbage.

4



Throw empty pill bottle into trash

Throw the empty pill bottle away in your household garbage as well.

DO I NEED TO SEEK MEDICAL ATTENTION?

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Seek immediate medical attention if you experience ANY of the following symptoms:

- **Pain or swelling in one leg**
- **Increased difficulty breathing**
- **New chest pain**
- **New numbness or weakness on one side**
- **New difficulty speaking**

Likelihood of severe bleeding is rare, but **if you experience any of the following types of unexpected bleeding, seek medical attention.**

- Bleeding from a cut that lasted **more than 5 minutes** even though you applied direct constant pressure
- A nosebleed that lasted **more than 30 minutes**, or **more than 3 to 4 nose bleeds in one week**
- Blood in your urine or stool, or dark black stools
- Coughing up or vomiting blood
- **Heavier than normal** menstrual bleeding such as the need to change a large menstrual pad or tampon every hour for 3 or more consecutive hours because it was soaked

If you have more questions, please call the study number at 855-322-6509

12.21.2020

ACTIV-4 Post-Hospital Thrombosis Prevention Study

I am participating in a randomized, double-blind, placebo-controlled study to compare the effectiveness and safety of antithrombotic therapy with no anti-thrombotic therapy after hospitalization for COVID-19.

For urgent questions about this study, please call 855-322-6509.

ACTIV-4c

COVID-19 Post-Hospital Thrombosis Prevention Study

In this randomized, double-blind, placebo-controlled study, this person has received a 30-day supply to take 1 pill in the morning and 1 pill at night.

This person is receiving one of the following treatments:

Apixaban	2.5mg morning and evening
Placebo	morning and evening

Information for your doctor about the ACTIV-4c Post Hospital Thrombosis Prevention Study

ACTIV-4c
COVID-19 Post-Hospital Thrombosis Prevention Study

There is evidence of an increased incidence of thromboembolic complications in COVID-19 positive patients, particularly those who require care in the hospital.

Your patient has agreed to participate in a large, multi-national, NIH-funded study to evaluate the efficacy and safety of antithrombotic strategies in COVID-19 positive adults following discharge from the hospital.

The main aim of this 90-day study is to compare the effectiveness and safety of antithrombotic therapy vs. no antithrombotic therapy after hospitalization for COVID-19. The primary endpoint is the composite of symptomatic deep vein thrombosis, pulmonary embolism, other venous thromboembolism, ischemic stroke, myocardial infarction, other arterial thromboembolism, and all-cause mortality by 30 days post-discharge from the hospital.

In this randomized, double-blind, placebo-controlled trial, your patient has a 30-day supply of pills to take, 1 in the morning and 1 at night. Concomitant single anti-platelet therapy is allowed in this study, and your patient may be taking aspirin or another antiplatelet therapy unrelated to this study.

Your patient was assigned to one of the following treatments as part of this study:

Apixaban (Eliquis)	2.5mg twice daily	30-day duration
Placebo	Matching pills twice daily	30-day duration

Study participants will be followed for an additional 60 days after completion of the study medication.

Study Chair: Thomas Ortel, MD, PhD, Duke University Medical Center, Durham, NC

If you have general questions about the trial or require emergency unblinding, **please feel free to call the Study Communication Center at 855-322-6509.**

visit **ACTIV4c.org**