Pharmacy Update:

HPTN 084 Version 3.0 dated 12AUG2021

Katherine Shin, PharmD

Protocol Pharmacist
Pharmaceutical Affairs Branch/DAIDS/NIAID/NIH

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Protocol and SSP Updates

- Changes between HPTN 084 Protocol Version 2.0 dated 06NOV2019 and HPTN 084 Version 3.0 dated 12AUG2021
  - Review Appendix VIII of HPTN 084 Protocol Version 3.0: Procedures for Offering Open Label (OL) Cabotegravir- The Next Part of HPTN 084
- Changes between Study Products Consideration Section 8 Version 2.1 dated 20JAN2021 to updated version of Study Products Consideration Section 8 of SSP to be issued by HPTN 084 protocol team in the next few weeks
  - Review updated Study Product Considerations (Section 8) of HPTN 084 SSP when issued
    - Specific updates to SSP Section 8 in relation to issuance of unblinded study products in when implementing Appendix VIII, HPTN 084 Protocol Version 3.0

Updated SSP (to be issued): Participants Assigned to the TDF/FTC Arm in Steps 1 and 2

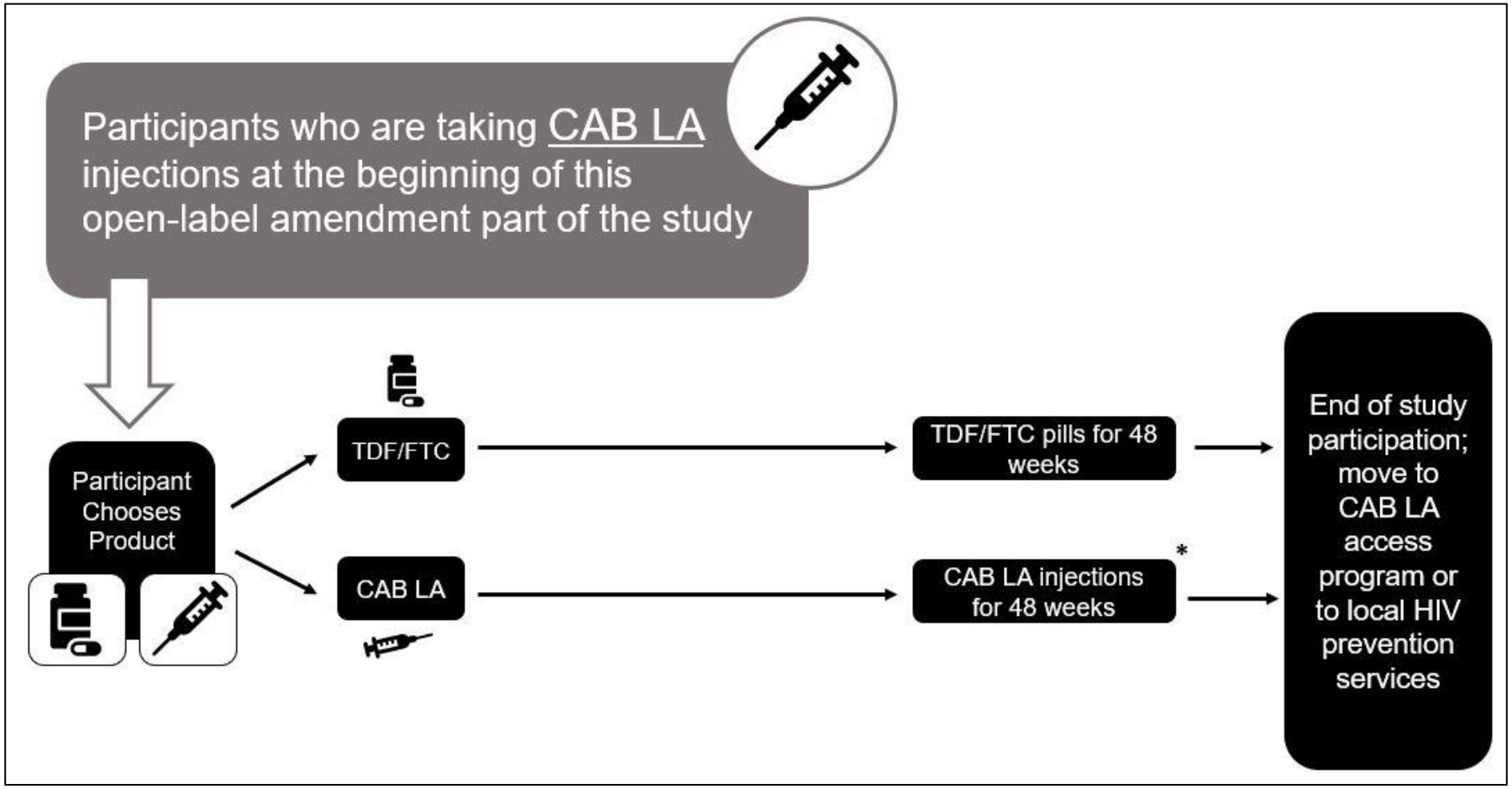
- When the participant has been informed of her randomized assignment to the TDF/FTC arm, a new prescription for un-blinded oral active TDF/FTC signed by an authorized prescriber must be provided to the site pharmacist.

- The pharmacist will take the following steps to prepare and dispense un-blinded active oral TDF/FTC to the participant:
  - **Retrieve oral active TDF/FTC bottle with two part-label from Step 2 supply** (in version 2.1 of SSP)**.**
  - Retain both the un-blinded part and the blinded part of the two-part label on the TDF/FTC bottle. Do not tear off the un-blinded part of the two-part label from the bottle.
  - Place pharmacist prepared participant-specific un-blinded label in such a way that the blinded part of the two-part label on the bottle is covered.

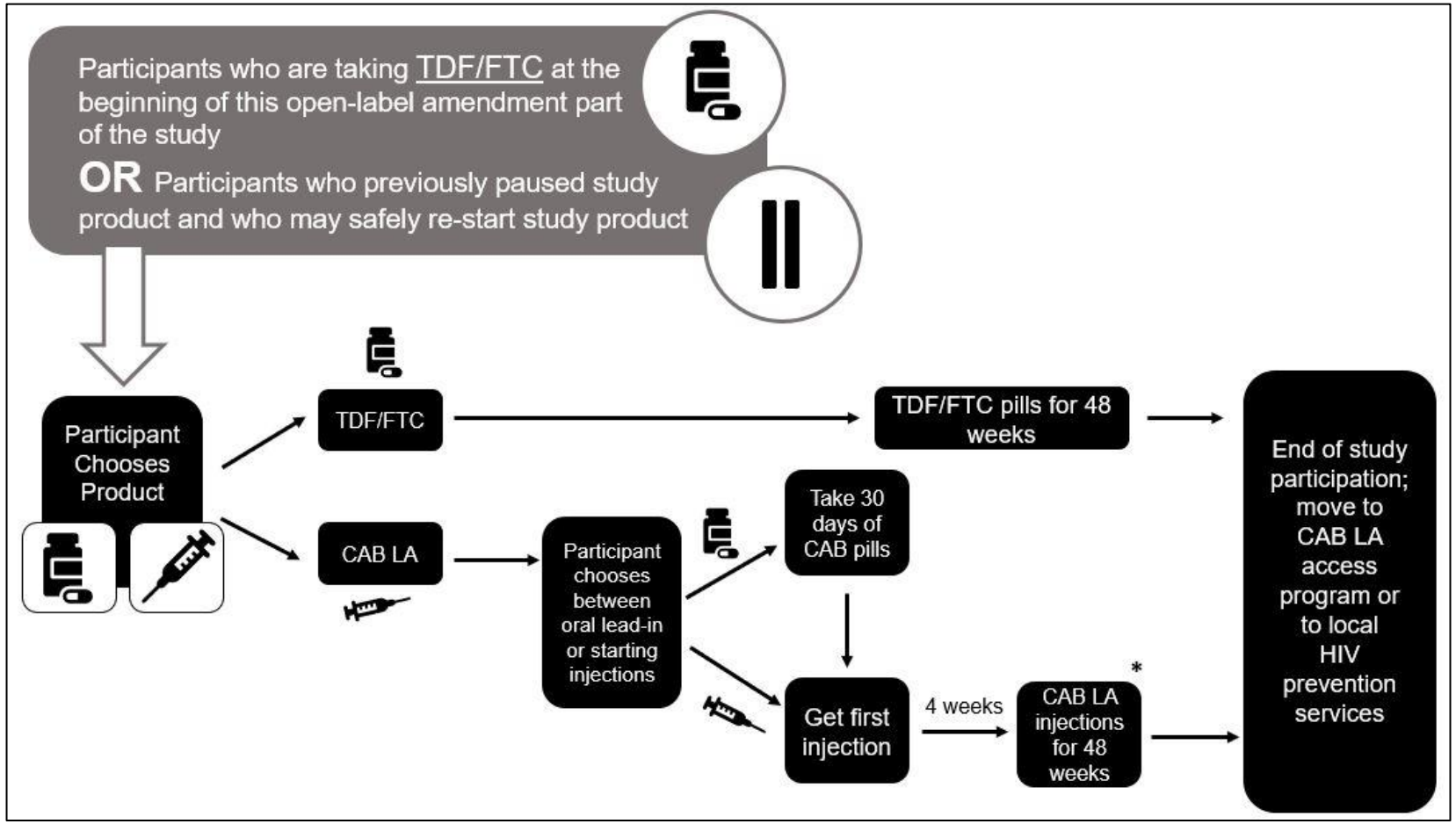
- The pharmacist-prepared, participant-specific, un-blinded oral active TDF/FTC bottle will have the manufacturer's unblinded part of the two-part label and site pharmacist generated participant-specific un-blinded label visible on the prepared bottle before dispensation.

- **Alternatively, retrieve open-label oral active TDF/FTC supply from Step 3 supply if the site no longer has oral active TDF/FTC bottles with a two-part label from Step 2 supply due to no further supply of oral TDF/FTC from Step 2 supply available at the CRPMC to distribute to sites. Place pharmacist prepared participant-specific un-blinded label on the open-label oral active TDF/FTC bottle from Step 3 supply and dispense (in updated SSP version to be issued).**

Updated Schema



Updated Schema (continued)



Steps 4a, 4b, 4c, 4d, and 5

- Step 4a
- Step 4b
- Step 4c
- Step 4d
- Step 5

- Participants who transition from TD/FTC or re-start CAB LA may choose from two options (Step 4a or Step 4b) before starting Step 4c.

Step 4a

- Participants Initially Randomized to TDF/FTC Who Elect to Move to OL CAB LA with Optional Oral Lead-in first

  - **CAB 30 mg tablet, one tablet orally once daily for 4 weeks, with or without food**, prior to initiating CAB-LA injection. This is an optional oral CAB lead-in prior to receiving CAB-LA injection for participants originally randomized to TDF/FTC.

Step 4b

- Participants Initiating or Re-starting CAB LA without the Optional Oral Lead-in; the Initial Dose Visit, CAB LA Loading Dose

  - **CAB-LA 600 mg administered as one 3 mL (600 mg) IM in the gluteal muscle one time** at Step 4b visit. The participant will then transition to Step 4c four weeks later. This is for participants who are initiating CAB for the first time with or without oral CAB (Step 4a) or for participants who have been on cabotegravir during the study but have had a long absence of visits (>15 weeks since prior injection) and require a reload of cabotegravir injection.

Step 4c

- Participants on Maintenance Doses of CAB LA or TDF/FTC

  - <u>CAB LA Maintenance Doses</u>
    - **CAB-LA 600 mg administered as one 3 mL (600 mg) IM in the gluteal muscle every 8 weeks for no longer than a total of 48 weeks.** This is for participants transitioning from Step 4b, or for participants originally randomized to cabotegravir who choose to continue it and do not need reloading dose.

  - <u>TDF/FTC Maintenance Doses</u>
    - **TDF/FTC 300 mg/200 mg fixed dose combination tablet, one tablet orally once daily, with or without food for no longer than a total of 48 weeks.**

Step 4d

- Participants who become pregnant in Step 4 and first 8 weeks of Step 5, who have had at least one CAB LA injection ever and Participants who are Breastfeeding

  - **CAB-LA 600 mg administered as one 3 mL (600 mg) IM in the gluteal muscle every 8 weeks for no longer than a total of 48 weeks.**

    – If participant declines to continue CAB LA during pregnancy or breastfeeding will be offered OL TDF/FTC. **TDF/FTC 300 mg/200 mg fixed dose combination tablet, one tablet orally once daily, with or without food for no longer than a total of 48 weeks per protocol.**

Step 5

- Participants Taking OL TDF/FTC for 48 Weeks after Premature CAB LA discontinuation

  - **TDF/FTC 300 mg/200 mg fixed dose combination tablet, one tablet orally once daily, with or without food for no longer than a total of 48 weeks per protocol.**

    – This is for participants who received OL CAB LA in Step 4 and who discontinue CAB-LA early for safety or other reasons will have the option to transition to Step 5.

Preparation of Unblinded Oral CAB Study Product

- The pharmacist will take the following steps to prepare and dispense un-blinded active oral CAB to the participant:
  - Retrieve oral active CAB 30mg tablet bottle with two part-label from Step 1 supply.
  - Retain both the un-blinded part and the blinded part of the two-part label on the CAB bottle. Do not tear off the un-blinded part of the two-part label from the bottle.
  - Place pharmacist-prepared, participant- specific, un-blinded label in such a way that the blinded part of the two-part label on the bottle is covered.
  - The pharmacist prepared, participant-specific, un-blinded oral active CAB bottle will have the manufacturer's unblinded part of the two-part label and site pharmacist generated participant specific un-blinded label visible on the prepared bottle before dispensation.
  - The participant specific label must be in accordance with the local regulations, and the DAIDS Pharmacy Guidelines manual.

Preparation of Unblinded Oral TDF/FTC Study Product

- The pharmacist will take the following steps to prepare and dispense un-blinded active oral TDF/FTC to the participant:

  - Retrieve oral active TDF 300 mg/FTC 200 mg with two-part label from Step 2 supply.
  - Retain both the un-blinded part and the blinded part of the two-part label on the TDF/FTC bottle. Do not tear off the un-blinded part of the two-part label from the bottle.
  - Place pharmacist prepared participant-specific un-blinded label in such a way that the blinded part of the two-part label on the bottle is covered.

Preparation of Unblinded Oral TDF/FTC Study Product (continued)

- The pharmacist-prepared, participant-specific, un-blinded oral active TDF/FTC bottle will have the manufacturer's unblinded part of the two-part label and site pharmacist generated participant-specific un-blinded label visible on the prepared bottle before dispensation.

- Alternatively, retrieve open-label oral active TDF/FTC supply from Step 3 supply if the site no longer has oral active TDF/FTC bottles with a two-part label from Step 2 supply due to no further supply of oral TDF/FTC from Step 2 supply available at the CRPMC to distribute to sites. Place pharmacist prepared participant-specific un-blinded label on the open-label oral active TDF/FTC bottle from Step 3 supply and dispense.

- The participant specific label must be in accordance with the local regulations and the DAIDS Pharmacy Guidelines manual.

Preparation of Unblinded Injectable CAB LA 600 mg/3mL

- The pharmacist will take the following steps to prepare and dispense unblinded active injectable CAB-LA in a syringe to the participant:

  - Retrieve injectable CAB-LA vial(s) from storage.
  - Prepare the injectable CAB LA dose in a syringe using aseptic technique under a pharmacy BSC Class 2 or better as detailed in Appendix 8 of the protocol. The overlay tape that covers the syringe barrel of the prepared unblinded, injectable CAB-LA in a syringe is not required.
  - Place pharmacist-prepared participant-specific un-blinded label on the prepared syringe.

  - The participant specific CAB LA label must be in accordance with the protocol, local regulations and the DAIDS Pharmacy Guidelines manual.

CAB-LA Injectable Study Product Packaging Reminder

- CAB-LA injectable suspension in single use vial containing 400 mg/2 mL or 600 mg/3 mL is to be stored up to 30°C (up to 86°F), do not freeze.

Training and Documentation – Pharmacy Records

- Document training of HPTN 084 Version 3.0 protocol, updated SSP and study related documents of the PoR and all applicable pharmacy staff
- Document initial and periodic training of aseptic technique and study product preparation of pharmacy staff
- Updated prescription template(s) which incorporate new Steps 4a, 4b, 4c, 4d, and 5

Communication and Study Product Supply

- Maintain close communication among site team
  - Participant clinic scheduling

- Maintain adequate supply of study products
  - Order study products in advance to arrive at least 2 months before the current supply is depleted or expires
  - Order study products in sufficient quantity (up to 6-month supply order at a given time for sites outside of South Africa)

Thank You

National Institute of Allergy and Infectious Diseases

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Questions