

Section 7. Study Product Considerations for Non-Pharmacy Staff

This section provides information and instructions for non-pharmacy staff related to the ordering and administration of MTN-011 study product for study participants. Associated instructions for the pharmacy staff are provided in the MTN-011 Pharmacist Study Product Management Procedures Manual, which will be made available to each site Pharmacist of Record (PoR) by the MTN Pharmacist. Please also refer to related information in Sections 4 and 5 of this manual.

7.1 Study Product Regimens

This open label study involves 40 couples, two cohorts of 20 couples each. The first cohort is a Single Dose/BAT Cohort (Group 1) and the second cohort is a Multiple Dose Cohort (Group 2). Female participants in both cohorts will insert tenofovir 1% gel.

Table 7-1a
Group 1 Participant Gel Schedule

Gel	Visit	Number of doses dispensed	Location of use
-1 hr	3a	1	Hotel or comparable location
	4a	1	Clinic
-24 hr	5a	1	Clinic
	6a	1	Clinic
BAT	7a	2	Hotel or comparable location

**Table 7-1b
Group 2 Participant Gel Schedule**

Gel	Visit	Number of doses dispensed	Location of use
	2	7*	1 Clinic 5 Home
-1 hr	3a	1	1 Hotel or comparable location
	4	7*	1 Clinic 5 Home
	5	1	1 Clinic
-72 hr	6	8*	1 Clinic 6 Home
	8	8*	1 Clinic 6 Home

*Participants will be given one extra dose

7.2 Dispensing from the Pharmacy to Research Staff

7.2.1 Initial Ordering and Dispensation

Two prescription forms will be used for this study, Group 1 Prescription and Group 2 Prescription. Prescriptions will be produced as two-part no carbon required (NCR) forms pre-printed with the site (CRS) name, DAIDS site ID number, and site (CRS) location (Appendix 7-1 and 7-2). After recording the PTID and other details on the prescription, clinic staff will separate the two sheets of the form and the white original will be delivered to the pharmacy. The yellow copy will be retained in the participant's study notebook in the clinic.

The study product for MTN-011 will only be dispensed directly to research study staff, who will then deliver the study product to the participant. The study prescription (and study gel request slip, see below) are expected to be faxed or scanned to the pharmacy by clinic staff. Upon receipt of a completed and signed MTN-011 prescription, the PoR will prepare the participant-specific study gel. The study product may be prepared based on faxed/scanned copies but will only be dispensed upon receipt of the original document. The study product will be delivered to the participant for administration in the clinic, home or hotel (or comparable location), depending on the visit.

7.2.2 Gel Re-Supply During Follow-up

At each follow-up visit when gel is dispensed, study staff will determine whether a participant remains eligible for continued study product use per specifications listed in section 9 of the protocol. These sections list conditions under which gel use should be held, either temporarily or permanently. The site Investigator of Record (IoR) is responsible for ensuring that these protocol specifications are followed for all participants.

Clinic staff will dispense gel during follow-up using the Study Product Request Slip (Appendix 7-3).

The MTN-011 Study Product Slip Request is a two-part no carbon required (NCR) document that is available from SCHARP. Site staff will be provided with bulk supplies throughout the course of the study. The Study Product Slip will be used to inform the pharmacy if product needs to be held (permanently or temporarily), or resumed. The Study Product Slip will also be used to order study product during follow-up visits, as indicated below.

Participants in Group 1 will receive one prefilled applicator of tenofovir 1% gel at visits 3a, 4a, 5a and 6a. At visit 3a the participant will administer the dose approximately 1 hour prior to coitus at the hotel site. At Visits 4a and 5a the dose will be administered in the clinic. Visit 4a is gel administration without coitus and at Visit 5a the gel is administered in the clinic 24 hours prior to coitus. At Visit 6a, gel is once again administered without coitus. At Visit 7a participants will receive 2 prefilled applicators of tenofovir 1% gel. Both of these doses will be administered at the hotel site. One of these doses will be inserted approximately 1 hour prior to coitus and a second dose will be inserted approximately one hour after coitus.

Participants in Group 2 will be dispensed 7 doses of tenofovir 1% gel at Visit 2. These applicators will be dispensed as individually wrapped applicators in a suitable container. Of these 7 doses 1 applicator will be vaginally inserted in the clinic at Visit 2. The content of one applicator of gel will be vaginally inserted at home for the next five consecutive days. The participants will however, take home 6 prefilled applicators which will allow for one extra dose should an applicator become unusable for any reason. At Visit 3a the couple will be given one applicator for insertion at the hotel site which will be administered approximately 1 hour prior to coitus. Similar to Visit 2, at Visit 4 participants in Group 2 will be dispensed 7 doses of tenofovir 1% gel. Of these 7 doses 1 will be administered in the clinic at Visit 4, and for the next five consecutive days the participant will vaginally insert the content of one applicator of gel. The participants will however, take home 6 prefilled applicators which will allow for one extra dose should an applicator become unusable for any reason. At Visit 5 participants will receive one applicator of tenofovir 1% gel for insertion at the clinic.

At Visit 6 and Visit 8 participants will be dispensed 8 applicators of tenofovir 1% gel. At both Visit 6 and 8, participants will vaginally insert one applicator of tenofovir 1% gel followed by daily insertion of gel at home for the next six consecutive days. Participant will take home 7 applicators which will allow for one extra dose should an applicator become unusable for any reason. Visit 7a and 9 should take place approximately 72 hours after the last dose.

All study product dispensation must be documented on the Study Product Accountability CRF for Group 1 and Group 2.

7.3 Gel Use Instructions

All participants will be instructed on how to insert the gel and will be counseled to insert the entire contents of one applicator into the vagina. For vaginal administration of the study gel on consecutive days at home, participants should be advised to insert the gel at approximately the same time each day. Participants should be advised that it may be preferable to administer the gel before the longest period of rest to minimize the potential for leakage. Site staff may offer panty liners to participants to assist with leakage. If a participant misses one of the consecutive day doses, she must insert vaginally the missed dose as soon as possible, unless the next dose is estimated to be due within six hours. If the next dose is estimated to be due within six hours, the missed dose must be skipped. The next dose will be inserted vaginally as originally scheduled.

Detailed instructions for insertion of study gel are listed in Figure 7.1 below and Appendix 7-5. For further reference, a listing of frequently asked questions related to product use, and answers to these questions, is provided in Appendix 7-6.

Figure 7.1
Gel Administration Instructions for MTN-011

Removing the Applicator:

- Tear open the wrapper
- Remove the applicator
- Remove the blue cap

Inserting the Applicator:

- Choose a comfortable position to insert the applicator, for example lying on your back with your knees bent or standing up with one leg raised and resting on an object
- Hold the filled applicator about half-way along the barrel
- Gently insert the filled applicator into the vagina as far as it will comfortably go
- Slowly press the plunger until it stops to deposit the gel into the vagina
- Withdraw the applicator from the vagina

** Note: Study Staff should inform participants that they may experience some minor gel leakage from the vagina, when inserting the filled applicator into the vagina*

Save the Applicator:

- Place used and unused applicators in separate bags provided by study staff and return to the clinic
- Discard the wrapper and cap.

7.4 Return of Used and Unused Study Gel Supplies

After study staff count all used and unused applicators and document the product count on the Study Product Accountability CRF; all unused study gel supplies should be returned to the pharmacy as soon as possible. The Record of Receipt (see Appendix 7-3), in the Pharmacy should indicate in the comments section that the study gel was returned and initialed by the research study staff member. Following documentation, used applicators should NOT be returned to the pharmacy; rather site staff should dispose of used applicators in appropriate biowaste containers in accordance with applicable biowaste requirements.

Participants who are permanently discontinued from study product use will be instructed to return all study product to the site. The PoR will store returned *unused* study products in designated areas within the study pharmacy. Used applicators will be disposed of in the clinic.

It is anticipated that for participants in Group 2 an unused applicator may be available and should be returned to the clinic following Visits 2, 4, 6 and 8. Any used or unused product remaining in a participant's possession at the time of study exit must be collected from the participant; and unused applicators should be returned to the pharmacy on the day of collection. For participants who do not bring their remaining product to their exit visits, arrangements should be made to collect the product as soon as possible and document all such efforts in the participants' study charts. For participants for whom all reasonable efforts fail, site staff should notify the MTN-011 PSRT.

When planning and scheduling study exit visits, clinic staff should instruct participants to bring all used applicators, and remaining unused product, to their follow-up visits. Clinic staff will provide participants with plastic bags in which to store their used and unused applicators.

**Appendix 7-1
MTN-011 PRESCRIPTION: GROUP 1**

Instructions: All entries must be made in dark ink. Press firmly when completing this form. Corrections may be made by drawing a single line through incorrect entries, recording correct information, and initialing and dating the correction.

CRS Name:	Case CRS	DAIDS Site ID:	2501
CRS Location:	Cleveland, Ohio	Female Participant ID (PTID):	<input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> - <input type="text"/> 0

Did the couple provide written informed consent for enrollment into MTN-011? Yes No Clinic Staff Initials: _____

MTN-011 Tenofovir 1% Gel Group 1

Sig: Insert entire contents of one (1) applicator into vagina as directed.

Quantity: **Six prefilled applicators dispensed according to study visit. May be refilled as needed as per request by designated clinic staff on MTN-011 Study Product Request Slip for the duration of participation in study.**

Authorized Prescriber Name (please print): _____

Authorized Prescriber Signature: _____

Date: - -
dd MMM vv

Clinic Staff Instructions: Complete all items on this form. Once form is complete, white copy (pharmacy) remains in the pharmacy; the yellow copy (clinic) is retained in the participant study book.

Pharmacy: Dispense one (1) pre-filled applicators of study gel at Visits 3a (visit code 03.0), 4a (visit code 04.0), 5a (visit code 05.0) and 6a (visit code 07.0). Dispense two (2) pre-filled applicators at Visit 7a (visit code 09.0).

Clinic Staff Initials: _____ Date: - -
dd MMM vv

Appendix 7-2
MTN-011 PRESCRIPTION: GROUP 2

Instructions: All entries must be made in dark ink. Press firmly when completing this form. Corrections may be made by drawing a single line through incorrect entries, recording correct information, and initialing and dating the correction.

CRS Name:	Pitt CRS	DAIDS Site ID:	1001								
CRS Location:	Pittsburgh, Pennsylvania	Female Participant ID (PTID):	<table border="1"> <tr> <td> </td><td> </td><td> </td> <td> </td><td> </td><td> </td> <td> </td> <td> </td> </tr> </table>								

Did the couple provide written informed consent for enrollment into MTN-011? Yes No Clinic Staff Initials: _____

MTN-011 Tenofovir 1% Gel Group 1

Sig: Insert entire contents of one (1) applicator into vagina as directed.

Quantity: **32 prefilled applicators dispensed according to study visit. May be refilled as needed as per request by designated clinic staff on MTN-011 Study Product Request Slip for the duration of participation in study.**

Authorized Prescriber Name (please print): _____

Authorized Prescriber Signature: _____

Date:

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dd MMM vv

Clinic Staff Instructions: Complete all items on this form. Once form is complete, white copy (pharmacy) remains in the pharmacy; the yellow copy (clinic) is retained in the participant study book.

Pharmacy: Dispense pre-filled applicators of study gel as follows:

<u>Visit</u>	<u>Visit Code</u>	<u>Quantity</u>
2	02.0	7
3a	23.0	1
4	24.0	7
5	25.0	1
6	26.0	8
8	28.0	8

Clinic Staff Initials: _____ Date:

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dd MMM vv

**Appendix 7-3
MTN-011 STUDY GEL REQUEST SLIP**

Instructions: All entries must be made in dark ink. Press firmly when completing this form. Corrections may be made by drawing a single line through incorrect entries, recording correct information, and initialing and dating the correction.

Mark whether this is a request for study product resupply, hold, resumption (after clinical hold), or permanent discontinuation. Sign and date the slip. Once form is complete, the white copy (pharmacy) must be delivered to and stored in the pharmacy; the yellow copy (clinic) must be retained in the participant study notebook.

CRS Name:	Case CRS	DAIDS Site ID:	2501
CRS Location:	Cleveland, Ohio	Female Participant ID (PTID):	<input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> - <input type="text"/> <input type="text"/>
Visit Number:		Visit Code:	<input type="text"/> <input type="text"/> . <input type="text"/>

<input type="checkbox"/> RESUPPLY Group (circle one): 1 2 Pharmacy dispense <input type="checkbox"/> pre-filled applicators Reason for resupply if not a scheduled visit: _____
<input type="checkbox"/> HOLD Reason for hold: _____ Pharmacy Staff Instructions: Do not dispense any further MTN-011 study product to the participant until another MTN-011 Study Product Request Slip marked "Resume" is received.
<input type="checkbox"/> RESUME Pharmacy dispense <input type="checkbox"/> pre-filled applicators
<input type="checkbox"/> PERMANENTLY DISCONTINUE Reason for permanent discontinuation: _____ Pharmacy Staff Instructions: Do not dispense any further MTN-011 study product to the participant.

Clinic Staff Name (please print): _____

Clinic Staff Signature: _____

Date: - -
 dd *MMM* *vv*

**Appendix 7-5
Product-Use Instructions**



1. After washing your hands, tear open the wrapper. Remove the applicator and plunger.

2. Place the small end of the plunger in the hole at the back end of the applicator (opposite the blue cap).

3. Unscrew the blue cap.

4. Hold the applicator with your thumb and middle finger at the grooves on the applicator.



5. Choose a comfortable position for inserting the applicator, for example standing with one leg raised, squatting with your feet apart, or lying on your back with your knees apart.

6. Fold back the skin that covers the opening of your vagina with your other hand. Gently slide the applicator into your vagina as far as it will go comfortably or until your fingers touch your body. The plunger should stay outside your body.

7. While holding the applicator in place with one hand, push the plunger all the way into the applicator with the other hand. Or, while holding the applicator in place, use your forefinger to push the plunger all the way into the applicator.

8. After the plunger has been pushed all the way into the applicator, gently slide the applicator out of the vagina. Discard the wrapper and blue cap. Place the used applicator in the bag provided to you by the study staff and return all used and unused applicators to clinic at your next visit.

Appendix 7-6 Product-Related Scenarios

1. What if the research study staff and/or authorized clinician think there is something wrong with the applicator?

A: If there seems to be something wrong with an applicator (for example, it is difficult to push the study gel out of the applicator, if study gel has leaked out, if the applicator appears to be empty or there is some other problem), do not use the applicator and notify the pharmacy. The unused applicator should be returned to the pharmacy when and if a new applicator is dispensed. The MTN Pharmacist should be notified as soon as possible by the Pharmacist of Record.

2. What is the best position to insert the gel?

A: Any position that is comfortable can be used to insert the gel. The positions that are recommended include sitting, standing, and lying down.

3. What should I do if it hurts when I use the applicator to insert the gel?

A: Inserting the gel should not be painful. If you have pain when inserting the gel, try another position (sitting, standing, or lying down). If you still have pain in the new position, perhaps you need to change the angle of the applicator. The applicator should be angled slightly upward, towards your back, when you insert it. If you try to change the angle, and you still feel pain on insertion, please contact the study clinic.

4. Where does the gel go to after I put it inside?

A: The gel will come out of the vagina (through the same opening where it was inserted) over the next day. Sometimes when the gel comes out it looks clear. Sometimes it has a white color, and sometimes it has white clumps. This has been seen in other studies of the gels and it is normal. It is not normal to see a yellow or green discharge from the vagina, or a discharge with a bad odor, or with pain or itching. If this happens, it could mean you have an infection, in which case you should contact the study clinic.

5. Can the applicator get lost inside me?

A: No, the applicator cannot get lost inside you. When you use the applicator, hold it with your fingers about half-way along the barrel, and insert it until your fingers touch your body. Half of the barrel of the applicator should go inside your body. The other half should stay outside the body.

6. What should I do if I have trouble applying the gel with the applicator?
- A: The applicators should be easy to use. If you have difficulty using the applicators, please contact the study clinic, as the clinic staff may be able to show you different ways that you can insert the gel, which might make it easier.
7. What happens if I press the plunger too early and most of the gel comes out on my outside? Can I put more in?
- A: Yes. If most of the gel comes out on your outside, discard that applicator and use a new applicator to insert another dose of gel.
8. If I have my period, should I use the gel?
- A: Yes. You should use the gel daily, even during your period.
9. What happens if the applicators get wet before I use them?
- A: If only the wrapper gets wet, the applicator can still be used. Dry the wrapper off before taking out the applicator. If the applicator itself gets wet, it should not be used, but this might only happen if the wrapper is already open.
10. What should I do if the wrapper is already open when I want to use the gel?
- A: You should only use applicators with sealed wrappers, so you should always open the wrapper right before inserting the gel. If you notice an applicator with a wrapper that is not sealed, do not use that applicator. Use a different applicator with a sealed wrapper instead. Discard the applicator with the open wrapper. When you return for the next scheduled visit and you should inform the study staff of any applicators you had to discard because the wrapper was not sealed. If you find that more than one wrapper is not sealed, please contact the clinic immediately to discuss obtaining a resupply of study product.
11. What should I do if I forget to use the gel?
- A: If you miss a dose you should insert the missed dose as soon as possible, unless the next dose is estimated to be due within 6 hours. If the next dose is estimated to be due within six hours, you should skip the missed dose. The next dose should be inserted as originally scheduled.
12. Is the gel a contraceptive?
- A: No, the gel will not prevent pregnancy during sex acts. If you wish to avoid pregnancy, you should continue to use known reliable method of contraception (such as pills, injections) while you are in this study.
13. Will the gel affect my partner's ability to father children?
- A: No. The ingredients in the gel are not known to have any effect on male fertility.

14. What should I do if my partner has a reaction to the gel?
- A: Contact the study clinic and ask their advice. They might ask your partner to go to the clinic to be assessed and receive treatment if needed.
15. What should I do if I have a reaction to the gel (e.g., unusual itching, stinging)?
- A: Contact the study clinic.
16. Can I use tampons at the same time as the gel?
- A: You should not use tampons when using gel at home, or 72 hours prior to follow-up visits. If you happen to be on your menses during your at-home gel use period, you may use tampons but please notify clinic staff at your next appointment.
17. How do I store the gel?
- A: Store the gel in a cool, dry place.
18. Can I have sex after inserting gel, or do I need to wait?
- A: For group 2 participants who are inserting gel at home, you should not have sex during the at-home gel use stage. For all participants during coital visits, you will be instructed to insert gel approximately 1 hour before having sex with your partner. More information will be given to you by study staff.
19. What should I do if the gel leaks out?
- A: It is likely that some gel will leak out. This is normal and you don't need to do anything about it. You should always apply the full amount contained in the applicator. It may be helpful to wipe yourself on the outside with a dry cloth/tissue if you have been standing for a minute or two after you applied the gel, if you find that a small amount leaks out. The study staff will give you panty liners to help catch the gel if it leaks out.
20. Can my partner insert the gel for me?
- A: It is preferable that you insert the gel yourself, but if you are happy that your partner knows how to do it in a way that won't cause you discomfort, then this is acceptable. It is better for your partner to insert the gel for you than not to use the gel at all.
21. Can I continue to take my birth control pills?
- A: You are requested as part of this study to continue your oral contraception as discussed with the study staff.