ASPIRE Product Use Management: HIV Infection

START

HIV rapid tests

no rapid test(s) positive → CONTINUE product.

one or more rapid tests positive → HOLD product pending confirmatory testing.

status after confirmatory testing = HIV infected → PERMANENTLY DISCONTINUE product.

status after confirmatory testing = HIV uninfected → RESUME product.

If confirmatory HIV testing is unclear; contact the Network Laboratory for guidance.

Protocol Reference: Section 9.3 and 9.6
ASPIRE Product Use Management: Allergic Reaction to the Vaginal Ring

PERMANENTLY DISCONTINUE product.
**ASPIRE Product Use Management: Pregnant**

**HOLD**
product until negative pregnancy test AND pelvic exam confirms absence of findings that contraindicate resumption.

* Only resume if not breastfeeding. After a pregnancy hold, VR use should not be resumed earlier than 2 weeks after a 1st trimester loss, or earlier than 4 weeks after 2nd trimester (or later) pregnancy loss or delivery. Product restart timelines should begin when the pregnancy is lost (i.e., bleeding, elective termination, etc). This restart timeline should only be based off a negative pregnancy test if the date of pregnancy loss is completely unknown.

*Protocol Reference: Sections 9.3 and 9.7*
HOLD product until participant reports complete cessation of breastfeeding.
HOLD product until participant reports completion of PEP AND she is confirmed HIV-negative at the study site per protocol Appendix III.
ASPIRE Product Use Management: Grade 1 and Grade 2 Adverse Events

**Flowchart:**

- **Question:** AE addressed in protocol section 9.5?
  - **Yes:** Follow relevant protocol section
  - **No:** CONTINUE product.

*Protocol Reference: Section 9.4*
ASPIRE Product Use Management: Grade 3 Adverse Events

- **START**
  - AE addressed in protocol section 9.5?
    - yes: Follow relevant protocol section
    - no: Assess AE relationship to product
      - related: HOLD product. Re-evaluate at least weekly for up to 2 weeks. If grade ≤2 within 2 weeks after initiating hold: RESUME product. If grade >2 after 2 weeks of hold: Consult PSRT.
      - not related: CONTINUE product.

Protocol Reference: Section 9.4
ASPIRE Product Use Management: Grade 4 Adverse Events

- **AE addressed in protocol section 9.5?**
  - **no** → HOLD product. CONSULT PSRT.
  - **yes** → Follow relevant protocol section

*Temporary product hold must continue until a recommendation is received from the PSRT.*

Protocol Reference: Section 9.4
CONTINUE product, unless other product hold guidelines apply. Consult the PSRT if a temporary hold is deemed necessary and instituted by the IoR/designee.

Vaginally applied medications should not be used whenever possible, and oral or parenteral medications should be used instead.

*Treat per local guidelines, using observed single dose regimens whenever possible.
ASPIRE Product Use Management: Superficial epithelial disruption (abrasion/peeling)

CONTINUE product

Re-evaluate by speculum exam 3-5 days

Has condition worsened?

If condition worsens, temporarily HOLD product and consult the PSRT

CONTINUE product.
ASPIRE Product Use Management: Deep epithelial disruption (ulceration)

Remove vaginal ring and if confirmed deep epithelial disruption by IoR/designee HOLD product.

Re-evaluate in 3-5 days.

Has the AE resolved?

Re-evaluate within 2-3 days.

Has the AE resolved?

no

no

yes

RESUME product.

Has the AE resolved?

no

CONTINUE product.

yes

RESUME product.

Has the AE recurred?

no

HOLD product. CONSULT PSRT.

yes

CONTINUE product.

Continue to HOLD product. CONSULT PSRT. Treat per local standard of care.

Protocol Reference: Section 9.4
ASPIRE Product Use Management: Localized erythema or edema (area < 50% of vulvar surface or combined vaginal and cervical surface)

CONTINUE product

Is the participant asymptomatic?

no

Re-evaluate by speculum in 3-5 days.

Has condition worsened?

no

CONTINUE product.

yes

yes

HOLD product. CONSULT PSRT. Treat per local standard of care.

no

Re-evaluate at next scheduled visit

Protocol Reference: Section 9.4
ASPIRE Product Use Management: Generalized erythema or severe edema (area > 50% of vulvar surface or combined vaginal and cervical surface affected by erythema)

1. HOLD product and perform naked eye exam.
   - Re-evaluate in 3-5 days.
   - Has the AE resolved?
2. If no, re-evaluate within 2-3 days.
3. Has the AE resolved?
   - Yes: RESUME product.
   - No: CONSULT PSRT. Treat per local standard of care.
4. If yes, continue to HOLD product.

Protocol Reference: Section 9.4
ASPIRE Product Use Management: Unexpected genital bleeding

CONTINUE product and perform naked eye exam

*If determined to be due to deep epithelial disruption, refer to those guidelines; otherwise continue study product use

*VR may be held in presence of Grade 3 related or Grade 4 unexpected genital bleeding per clinician discretion (protocol section 9.4)
ASPIRE Product Use Management: Cervicitis (including findings on exam)

- **HOLD product and evaluate for GC/CT**
  - Positive for GC/CT?
    - yes: Provide treatment and CONSULT PSRT.
    - no: Re-evaluate 3 days after exam.
    - All signs and symptoms resolved?
      - yes: RESUME product.
      - no: CONSULT PSRT.

*Consider syndromic management pending results of testing and per clinician discretion.*
ASPIRE Product Use Management: Genital petechia(e), genital ecchymosis

CONTINUE product and perform naked eye exam
ASPIRE Product Use Management: Participant Non-compliance or other safety concerns

- HOLD product if a participant is unable or unwilling to comply with required study procedures, or otherwise might be put at undue risk to her safety and well-being by continuing product use, according to the judgment of the IoR/ designee.

- CONSULT the PSRT on all product holds instituted for this reason for further guidance on resuming product use, continuing the temporary hold, or progressing to permanent discontinuation.

- If the underlying reason for the product hold resolves, CONSULT the PSRT to resume study product at that time.
ASPIRE Product Use Management: CO-ENROLLMENT

- If co-enrollment in another study is identified, obtain as much information as possible about the other study from the participant and the other study team.

- HOLD product upon identification of co-enrollment unless the other study is known to not involve a study product and/or confirmation is available from the other study team that the participant is not using another study product.

- CONSULT the PSRT on further management of the participant.

- Schedule the participant to return when a response from the PSRT is expected.