MTN-036 Clinical Considerations

Site Specific Training | 11 Sept 2017

Overview

Medical and Menstrual History
Physical and Pelvic Exams
STI/RTI/UTIs
Con Meds
Conraception
Prohibited Meds and Practices
Product Use Management

Medical History

Baseline Medical History
Starting at the Screening Visit and reviewed/updated at enrollment visit, prior to randomization

- Hospitalizations
- Abnormal screening labs
- Abnormal physical and pelvic findings

Follow-up Medical History
Medical history must be updated at all follow-up visits

- Are previously reports conditions ongoing?
- Are there new or worsening symptoms?

Medical History Documentation

Baseline Medical History

- BMHQ Sheet
- Baseline Medical History Summary/Log CRF

Follow-up Medical History

- Chart notes, or
- Site specific tool
- All newly-identified symptoms and conditions will be documented on the AE Log CRF
- NOTE: the Baseline Medical History Log CRF is not updated

Special Case: Genital Bleeding

Baseline Menstrual History

- Collected at Screening and Enrollment
- Documented on Baseline Medical History Questions sheet
- Moving away from strict ranges for menses
- Moving towards FGGT definitions of bleeding abnormalities
- Changes in bleeding patterns will be assessed during follow-up

Follow-up Menstrual History

- Collected at all follow-up visits
- Expected bleeding is not considered an AE
- Bleeding associated with speculum insertion and/or specimen collection is not an adverse event.
- Bleeding to also be documented within 7 days of PK collection, to interpret results if needed.

UTERINE BLEEDING AND PREGNANCY COMPLICATIONS					
PARAMETER	**GRADE 0 NORMAL**	**GRADE 1 MILD**	**GRADE 2 MODERATE**	**GRADE 3 SEVERE**	**GRADE 4 POTENTIALLY LIFE-THREATENING**
ABNORMAL UTERINE BLEEDING UNRELATED TO PREGNANCY					
Menorrhagia [2] (prolonged and/or heavy menstrual bleeding)	Participant report of normal bleeding relative to her baseline	Increase from usual with no or minimal interference with usual social & functional activities (including sexual functioning)	Increase from usual with moderate interference with usual social & functional activities (including sexual)	Incapacitating or severe interference with usual social & functional activities (including sexual functioning), transfusion indicated	Life threatening hemorrhage with or without shock
Metrorrhagia [2] (intermenstrual or frequent bleeding)	None or any expected nonmenstrual bleeding	Increase from usual with no or minimal interference with usual social & functional activities (including sexual functioning)	Increase from usual with moderate interference with usual social & functional activities (including sexual)	Incapacitating or severe interference with usual social & functional activities (including sexual functioning), transfusion indicated	Life threatening hemorrhage with or without shock
Unexplained infrequent bleeding (excludes expected absence of menses due to hormonal contraception or pregnancy/postpartum)	Participant report of normal or expected bleeding frequency	No menses for 1-3 months (missed menses)	No menses for > 3 months (oligomenorrhea/ amenorrhea)	NA	NA
Postcoital bleeding	None	Occasional (< 25% of coital acts) OR Increase from usual with no or minimal interference with usual social functioning (including sexual functioning)	Frequent (25-75% of coital acts) OR Increase from usual with moderate interference with usual social functioning (including sexual)	Consistent (> 75% of coital acts) OR Incapacitating or severe interference with usual social functioning (including sexual functioning), transfusion indicated	Life threatening hemorrhage with or without shock

Phyical Exam

When

- Full exam required at Screening
- Targeted exam at Enrollment
- Targeted at any other time, if indicated

Cross Reference

Con Meds Log – if participant reports medication, check to see if connected to a physical exam finding or vice versa

Document

- Physical Exam CRF is recommended source document
- Transcribe abnormal findings at Screening or Enrollment onto Baseline Medical History Log CRF
- During follow-up, transcribe abnormalities onto AE eCRF as needed

Physical Exam Components

	Full Exam	Targeted Exam
General appearance	X	X
Vital Signs	X	X
Weight, Height	X	*
Lympth nodes, neck, HEENT	X	*
Heart, lungs, abdomen, extremeties, skin, neurological	X	*

NOTE: Respirations as component of vital signs only required at screening visit

Pelvic Exam

When

- Required at all visits, except Final Contact (Visit 11)
- Careful attention needed for order of procedures
  (follow pelvic exam checklist)
- Performed with ring in place
- Avoid during menses

Reminder
Use terms from the Pelvic Exam CRF or FGGT

Document

- Pelvic Exam CRF is recommended source document
- Transcribe abnormal findings at Screening or Enrollment onto Baseline Medical History eCRF
- During follow-up, transcribe abnormalities onto AE eCRF as needed

STI/RTI/UTI Management

- Manage per CDC guidelines
- Provide observed single dose regimens when possible
- Document all treatments taken on Con Meds Log CRF

STI/RTI/UTI Management, con't

If diagnosed with **RTI/UTI** during screening
→
enroll after treatment is complete

If diagnosed with **STI** during screening
→
exclusionary, may not be enrolled

If diagnosed with **RTI/UTI/STI** during follow-up (**AE**)
→
must be documented and followed to resolution

Contraception

Must use effective method 30 days prior to enrollment with intention to continue use:

- Hormonal methods (not contraceptive ring)
- IUD
- Sterilization
- Sex exclusively with cis-women
- Abstinent from PVI for 90 days prior and intending to continue

Prohibited Meds

Prohibited during study participation

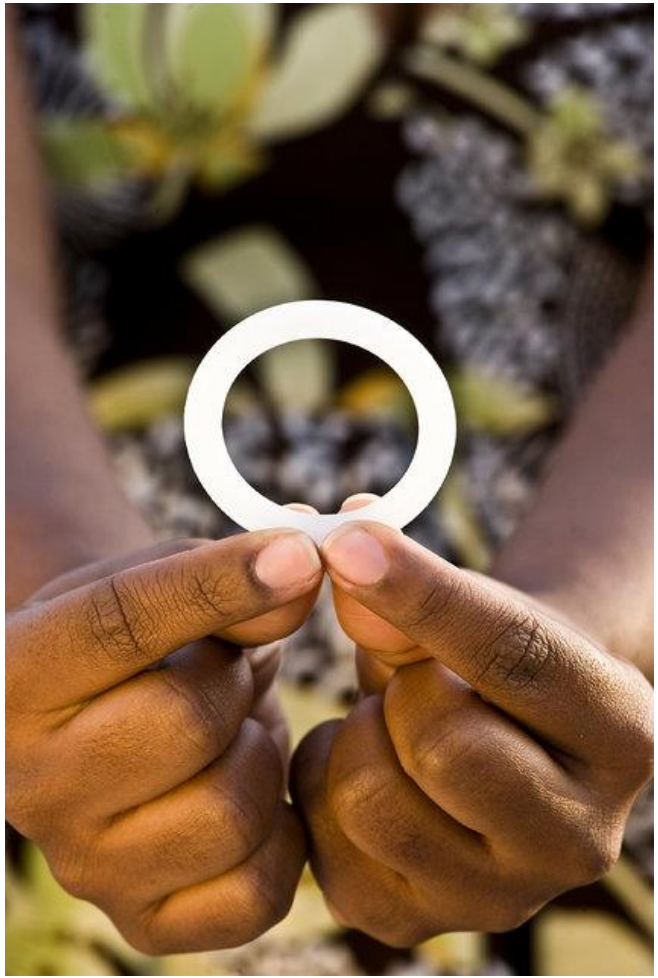
- PEP and PrEP
- Anticoagulants or blood thinners

Participants to abstain from aspirin 72 hrs before and after biopsies (Visit 8 and PUEV)

Product Use Management

Identify the conditions that would require a product hold or discontinuation

Review conditions that require follow-up per protocol before product resumed



Permanent Discontinuation

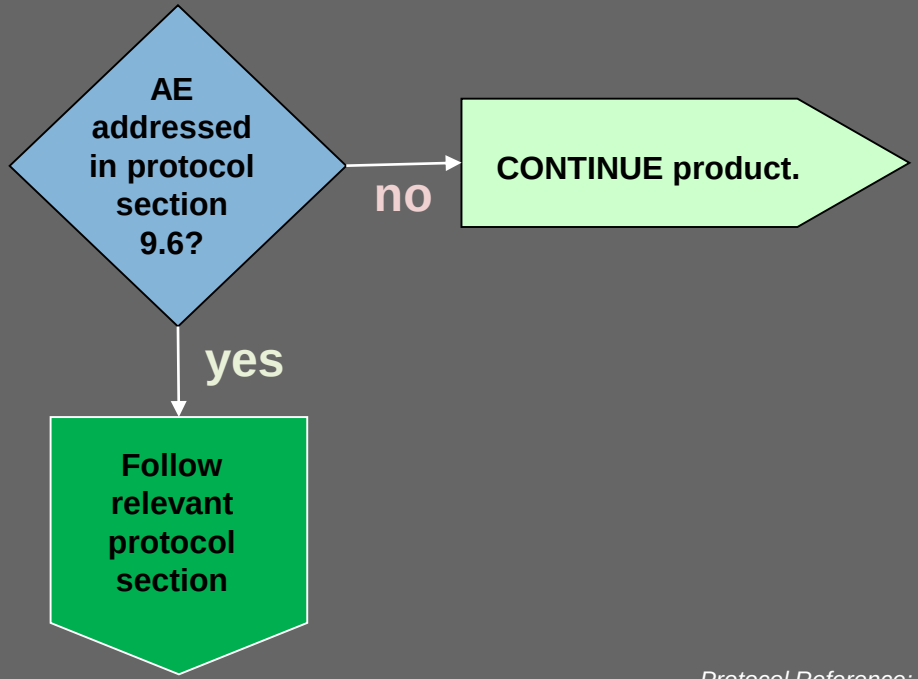
- Acquisition of HIV-1 infection
- Allergic reaction to VR
- Pregnancy
- Breastfeeding
- Non therapeutic injection drug use

Temporary Discontinuation

- Reported PEP use
- Reported PrEP use
- Use of heparin, Lovenox, warfarin, Plavix, or other anticoagulant
- Product hold for more than 7 days
- Participant unwilling to comply with procedures, etc.

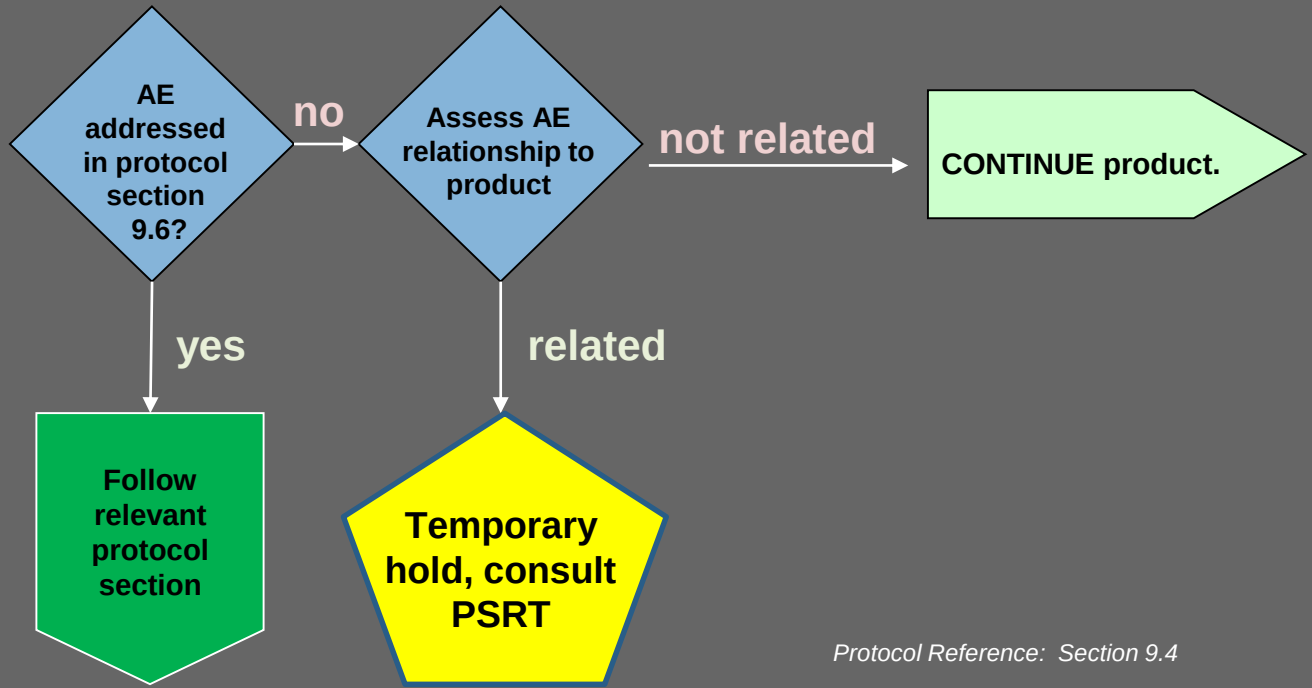
Submit PSRT query

Product Use Management:
Grade 1 and Grade 2 AEs



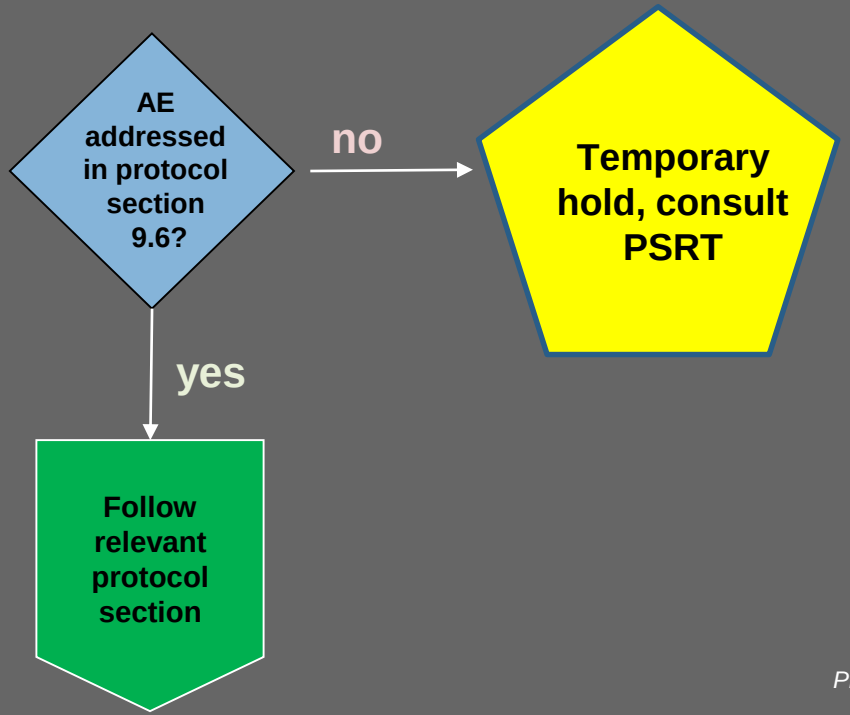
Protocol Reference: Section 9.4

Product Use Management: Grade 3 AEs



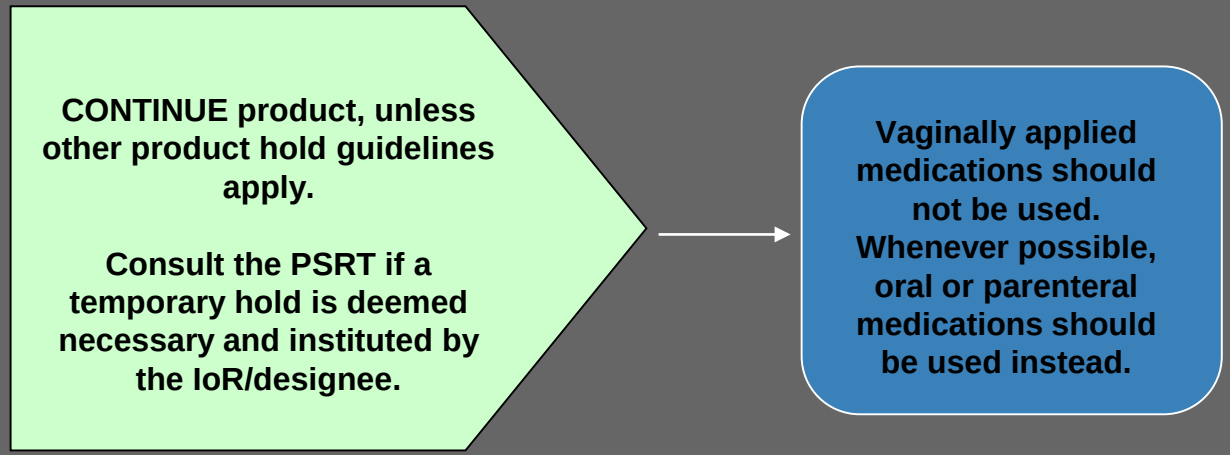
Protocol Reference: Section 9.4

Product Use Management: Grade 4 AEs



Protocol Reference: Section 9.4

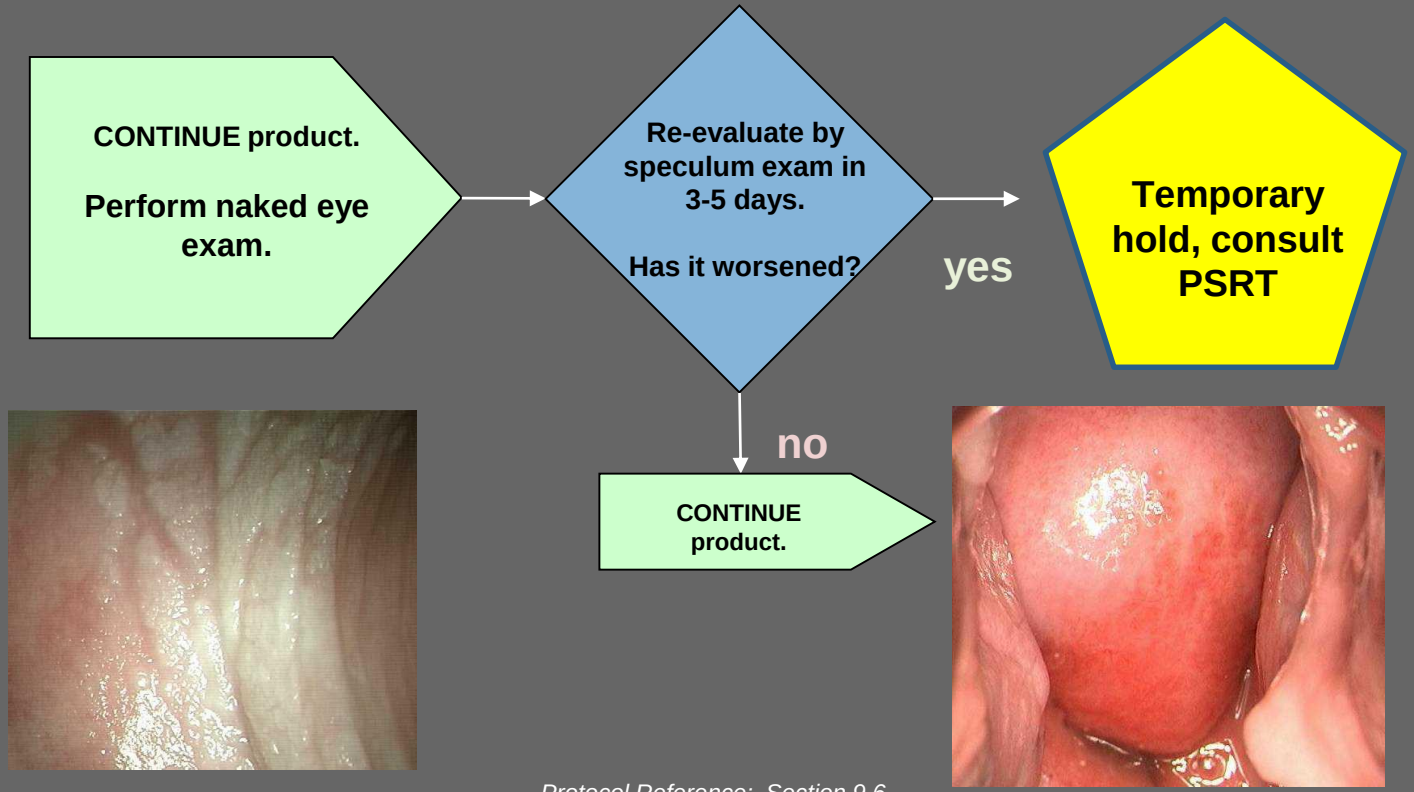
Product Use Management: STI/RTIs



Protocol Reference: Section 9.4

Product Use Management:

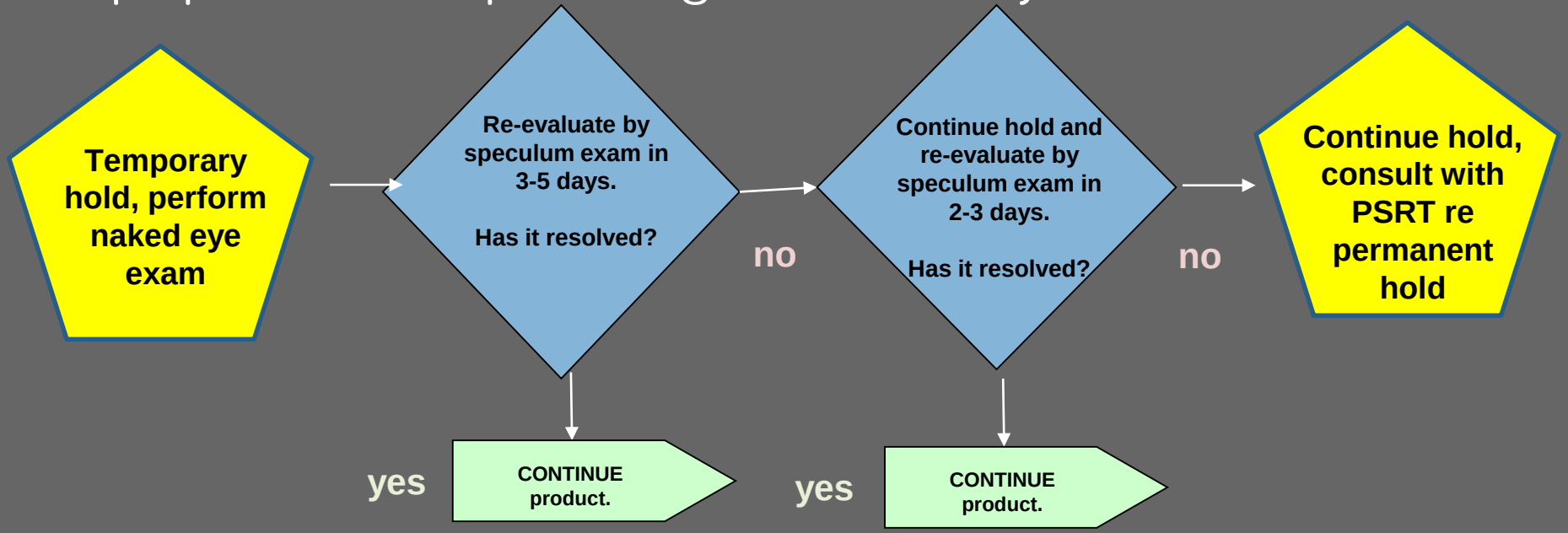
Superficial epithilial disruption or localized erythema/edema



Protocol Reference: Section 9.6

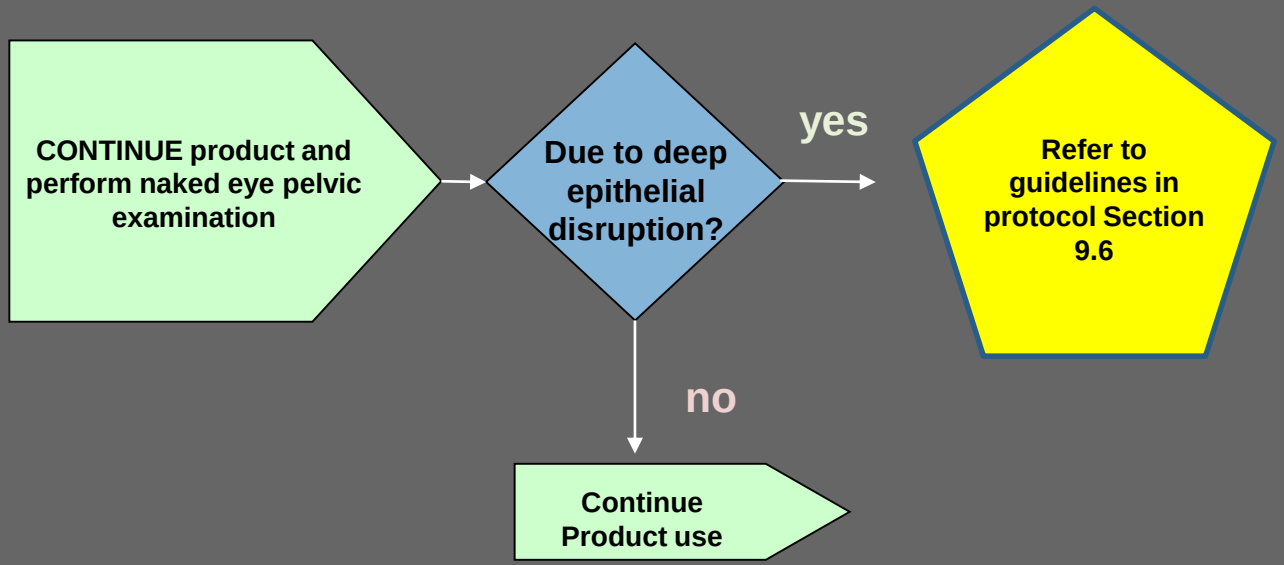
Product Use Management:

Deep epithilial disruption or generalized erythema/edema



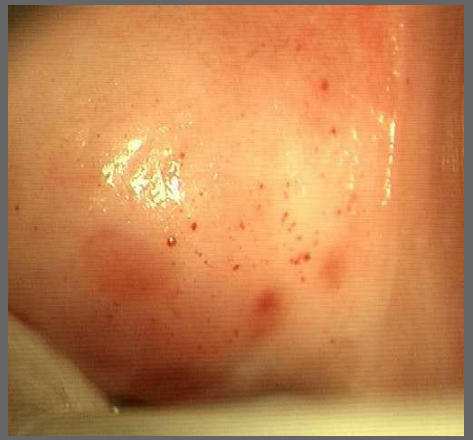
Protocol Reference: Section 9.6

Product Use Management: Unexpected genital bleeding

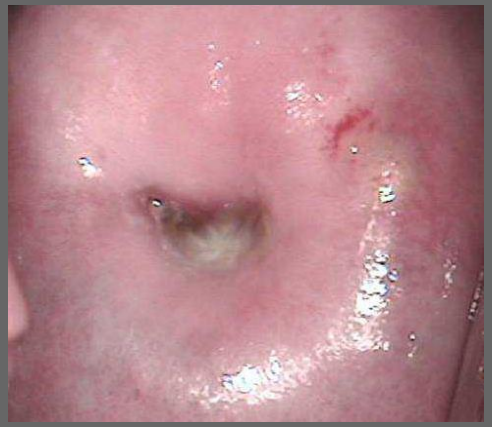


Protocol Reference: Section 9.6

Product Use Management: Genital petechia and ecchymosis



CONTINUE product and perform naked eye exam



Protocol Reference: Section 9.6

THANKS!

Any questions?