Product Use Management

MTN Annual Meeting
16 March 2010
VOICE Product Use Management: Grade 3 Adverse Events

ORAL and VAGINAL Study Product

Under Letter of Amendment #02

START

AE addressed in protocol sections 9.5 – 9.13?

no

Has the AE resolved prior to the visit?

no

Assess AE relationship to product

related

HOLD product. Re-evaluate at least weekly for up to 2 weeks.

grade ≤2 within 2 weeks after initiating hold

grade >2 through 2 weeks after initiating hold

PERMANENTLY DISCONTINUE product.

Continues product use at the discretion of the investigator

Yes

Follow relevant protocol section (9.5 – 9.13)

No

CONTINUE product.

not related

RESUME product. If same grade 3 AE recurs, regardless of relationship to product, HOLD product and CONSULT PSRT.

Protocol Reference: Section 9.4

LoA #02
VOICE Product Use Management: Grade 4 Adverse Events
ORAL and VAGINAL Study Product
Under Letter of Amendment #02

If product is resumed and the same grade 4 AE recurs, PERMANENTLY DISCONTINUE product.

AE addressed in protocol sections 9.5 – 9.13?

Has the AE resolved prior to the visit?

Follow relevant protocol section (9.5 – 9.13)

Continue product use at the discretion of the investigator

HOLD product. CONSULT PSRT.

Protocol Reference: Section 9.4
LoA #02
VOICE Product Use Management: Nausea, Vomiting, and/or Diarrhea

VAGINAL Study Product

Under Letter of Amendment #02

Assess AE relationship to product

- Not related
  - CONTINUE product. Treat symptomatically.

- Compelling evidence that it’s related
  - HOLD product. Treat symptomatically. CONSULT PSRT.

Protocol Reference: Section 9.5.1
LoA #02
VOICE Product Use Management: AST or ALT Elevation
VAGINAL Study Product
Under Letter of Amendment #02

Assess AE relationship to product

Compelling evidence that it’s related

HOLD product. CONSULT PSRT.

not related

CONTINUE product.

Protocol Reference: Section 9.5.2
LoA #02
VOICE Product Use Management: Grade 4 AST or ALT Elevation

**ORAL** Study Product

Under Letter of Amendment #02

![PERMANENTLY DISCONTINUE

product and consult
the PSRT.
Re-test at least
weekly until both
AST and ALT are
grade ≤1.](image)

Protocol Reference: Section 9.5.2
LoA #02
Did any repeat and/or accompanying test result warrant product hold?

- No

Continue product use and repeat testing within one week accompanied by serum creatinine testing and urine dipstick for protein/glucose. If failure to return within one week, consult PSRT. Advise on intake of phosphate-rich food or fluid. May give oral supplementation at IoR discretion

- Yes

HOLD Study product, consult PSRT and follow relevant protocol section 9.5

Note: Product use guidance should be followed for creatinine clearance, serum creatinine, proteinuria and glycosuria

*Urine dipstick results of 1+ will be managed according to guidance in Sections 9.6 (for proteinuria) and 9.7 (for glycosuria). Findings of proteinuria and/or glycosuria of 2+ require consultation with the PSRT for the participant’s further testing and management.
VOICE Product Use Management: Grade 4 Hypophosphatemia

ORAL Study Product

Under Letter of Amendment #02

**grade 4 decreased phosphate**

- HOLD product and consult PSRT

**≤ Grade 2 on retest?**

- yes
  - Continue HOLD.

- no
  - Retest weekly until return to ≤ Grade 2, accompanied by serum creatinine testing and urine dipstick for protein/glucose*.
  - Advise on intake of phosphate-rich food or fluid.
  - May give oral supplementation at IoR discretion

**Did any accompanying test warrant a product hold?**

- yes
  - Continue Hold
  - Follow the management for the specific test that warrants a hold

- no
  - Resume study product after consultation with the PSRT

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*PSRT notification should occur for any results ≥ Grade 2 for protein or glucose measured by urine dipstick performed at the time of confirmatory draw for phosphate level

**Note:** Product use guidance should be followed for creatinine clearance, serum creatinine, proteinuria and glycosuria, per protocol section 9.5

**Protocol Reference:** Section 9.5.6

LoA #02
got questions?