Cabotegravir (Apretude)

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Cabotegravir (Apretude) for HIV PrEP

**Oral Cabotegravir (Optional)**

- Oral Cabotegravir
  - 30 mg
  - INSTI

**Cabotegravir Injectable (IM)**

- Cabotegravir (200 mg/mL)
  - 600 mg (3 mL)
  - INSTI

December 2021: FDA Approved for PrEP At-risk adults and adolescents weighing ≥35 kilograms (77 pounds)
Dosing with Renal or Hepatic Impairment

- **Dosing with Renal Insufficiency**
  - Mild (CrCl ≥60 to <90 mL/min): no adjustment
  - Moderate (CrCl ≥30 to <60 mL/min): no adjustment
  - Severe (CrCl 15 to <30 mL/min) or ESRD (<15 mL/min): increased monitoring for adverse effects is recommended
  - Dialysis: not expected to alter cabotegravir levels

- **Dosing with Hepatic Impairment**
  - Mild-to-Moderate (Child A or B): no dose adjustment
  - Severe (Child C): unknown
Cabotegravir for HIV PrEP: Prescribing Information*

**Lead-In**

|  ≥28 days | 4 Weeks | 8 Weeks | 8 Weeks | 8 Weeks | 8 Weeks.. |

**Cabotegravir Injections**

- Cabotegravir 30 mg daily
- Cabotegravir 600 mg (3 mL) IM

*Source: Apretude Prescribing Information*
Cabotegravir for HIV PrEP: Prescribing Information*

- Consider alternative forms of PrEP after stopping cabotegravir if at continuing risk of acquiring HIV-1
- Start within 2 months of the final cabotegravir injection

*Source: Apretude Prescribing Information
**2021 CDC PrEP Guidelines**

**Cabotegravir for HIV PrEP: Monitoring**

- **Lead-In**
  - Cabotegravir 30 mg daily
  - OPTIONAL
  - ≥28 days

- **Cabotegravir Injections**
  - 4 Weeks
  - 8 Weeks
  - 8 Weeks
  - 8 Weeks...

- **Tail Phase**
  - ? Duration

**Cabotegravir**

- 600 mg (3 mL) IM

- TDF-FTC = tenofovir DF-emtricitabine
- TAF-FTC = tenofovir alafenamide-emtricitabine

- If PrEP indicated prescribe TDF-FTC or TAF-FTC within 8 weeks of stopping cabotegravir
- Continue follow-up visits quarterly for 12 months

Source: CDC Preexposure Prophylaxis for the Prevention of HIV Infection in the U.S.—2021 Update Clinical Practice Guideline
Cabotegravir Toxicity Monitoring

• **Not indicated** before starting or monitoring:
  - Creatinine, eCrCl
  - Hepatitis B serology
  - Lipid panels
  - Liver function tests.
2021 CDC PrEP Guidelines

Cabotegravir for HIV PrEP: Monitoring

Cabotegravir Injections

- 4 Weeks: HIV Ag/Ab
- 8 Weeks: HIV Ag/Ab, HIV RNA
- 8 Weeks: HIV Ag/Ab, HIV RNA, STI Screen*
- 8 Weeks: HIV Ag/Ab, HIV RNA
- 8 Weeks: HIV Ag/Ab, HIV RNA
- 8 Weeks+: HIV Ag/Ab, HIV RNA

*Bacterial STI screening for MSM and TGW who have sex with men (every 3 months)
^Bacterial STI screening for heterosexually active men and women (every 6 months)

Source: CDC Preexposure Prophylaxis for the Prevention of HIV Infection in the U.S.– 2021 Update Clinical Practice Guideline
Figure 2: Estimated plasma cabotegravir concentration (A) and reduction in per-act probability of HIV transmission (B), by time since last injection. Percentage reduction in per-act HIV transmission after a final long-acting cabotegravir injection was estimated on the basis of half-life values reported by Markowitz and colleagues.
IM Cabotegravir vs. TDF-FTC for HIV PrEP in MSM and TGW

HPTN 083
IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW
HPTN 083: Study Design

• **Background:** Phase 2b/3, double-blind, randomized, multinational, trial to assess efficacy of long-acting IM cabotegravir (CAB) compared to daily oral tenofovir DF-emtricitabine (TDF-FTC) for HIV PrEP in men who have sex with men (MSM) and transgender women

• **Setting**
  - 43 global sites

• **Inclusion Criteria**
  - Adult (≥18 years) cisgender MSM and transgender women who have sex with men age
  - Substantial HIV risk*
  - Negative HIV serologic test at enrollment and negative HIV RNA ≤14 days before trial entry
  - Generally good health and CrCl 60 mL/min
  - HBsAg negative and HCV antibody negative
  - No contraindications to gluteal injections
  - No injection drug use within 90 days of trial entry

*Condomless receptive anal intercourse; >5 sex partners, stimulant use, rectal/urthral STI or syphilis ≤6 months; SexPro Score <16 (U.S. only)

IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW
HPTN 083: Study Design

Participants Randomized n = 4,570

**Step 1**
- Oral CAB 30 mg Daily
- Oral TDF-FTC Placebo Daily

**Step 2**
- Oral TDF-FTC Placebo Daily
- **IM CAB 600 mg** Weeks 5, 9, and every 8 weeks thereafter

**Step 3**
- Oral TDF-FTC Daily
- Oral TDF-FTC Placebo Daily
- Oral CAB Placebo Daily
- IM CAB Placebo Weeks 5, 9, and every 8 weeks thereafter

IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW
HPTN 083: Study Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n = 4,566)</th>
<th>CAB (n = 2,282)</th>
<th>TDF-FTC (n = 2,284)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisgender MSM</td>
<td>3,992 (87.4)</td>
<td>2,013 (88.2)</td>
<td>1,979 (86.6)</td>
</tr>
<tr>
<td>Transgender Women</td>
<td>570 (12.5)</td>
<td>266 (11.7)</td>
<td>304 (13.3)</td>
</tr>
<tr>
<td>Median Age (IQR) Years</td>
<td>26 (22-32)</td>
<td>26 (22-32)</td>
<td>26 (22-32)</td>
</tr>
<tr>
<td>Black Race, United States</td>
<td>845 (49.8)</td>
<td>411 (48.4)</td>
<td>434 (51.1)</td>
</tr>
<tr>
<td>Geographic Region</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>United States</td>
<td>1,698 (37.2)</td>
<td>849 (37.2)</td>
<td>849 (37.2)</td>
</tr>
<tr>
<td>Latin America</td>
<td>1,964 (43.0)</td>
<td>980 (42.9)</td>
<td>984 (43.2)</td>
</tr>
<tr>
<td>Asia</td>
<td>752 (16.5)</td>
<td>375 (16.5)</td>
<td>377 (16.5)</td>
</tr>
<tr>
<td>Africa</td>
<td>152 (3.3)</td>
<td>78 (3.4)</td>
<td>74 (3.2)</td>
</tr>
</tbody>
</table>

*Abbreviations: MSM = men who have sex with men; IQR = interquartile range

IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW
HPTN 083: Acquisition of HIV After Enrollment

IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW  
HPTN 083: Results

IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW
HPTN 083: Results

• **When did incident HIV infections occur in CAB arm?**
  - 3 during oral lead-in
  - 5 after “prolonged hiatus” from IM CAB
  - 5 during continuous CAB administration

• **Were drug levels adequate in TDF-FTC arm?**
  - Random sample of 372 participants:
    - 87% detectable plasma tenofovir level
    - 75% levels correlated with high-level protection
    - ≈70% levels suggestive of >4 doses/week (by dried blood spot)

IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW HPTN 083: Cabotegravir Injection Site Reactions

• **Type and Severity of Injection-Site Reactions**
  – Most common pain and tenderness
  – 2.4% chose to discontinue study due to injection reaction

• **Onset**
  – Reactions typically began 1 day after injection

• **Duration**
  – Reactions typically lasted 3-4 days 1 day after injection

IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW HPTN 083: Results: Resistance with Cabotegravir

• INSTI Resistance in Cabotegravir Group
  – 1 at baseline; 4 with incident HIV infections
  – No resistance documented after last injection during “tail phase”

IM Cabotegravir versus TDF-FTC for PrEP in MSM and TGW
HPTN 083: Weight Gain

Conclusions: Long-acting cabotegravir was superior to daily oral Tenofovir DF–emtricitabine in preventing HIV infection among men who have sex with men and transgender women.

IM Cabotegravir vs. TDF-FTC for PrEP in Cisgender Women

HPTN 084
IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Study Design

• **Background:** Phase 3, double blind, randomized, multinational, trial to assess efficacy of long-acting IM cabotegravir (CAB) compared to daily oral tenofovir DF-emtricitabine (TDF-FTC) for HIV PrEP in cisgender women

• **Setting**
  - 20 sites in Sub-Saharan Africa, including 7 in South Africa

• **Inclusion Criteria**
  - Cisgender women (born female) 18-45 years of age
  - Sexually active (e.g. vaginal sex on ≥2 separate days in the 30 days prior to screening)
  - HBsAg-negative and willing to receive hepatitis B vaccination
  - HCV antibody negative
  - No contraindications to gluteal injections
  - Creatinine clearance of greater than or equal to 60 mL/min
  - ALT <2 x upper limit of normal (ULN) and total bilirubin ≤ 2.5 x ULN
  - Excluded if pregnant or breastfeeding

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Study Design

Participants
n = 3,224

Step 1
- 5 Weeks
- Oral TDF-FTC Placebo Daily
- Oral CAB Placebo Daily

Step 2
- Up to 185 weeks (3.5 Years)
- IM CAB 600 mg
  - Weeks 5, 9, and every 8 weeks thereafter
- Oral TDF-FTC Placebo Daily
- Oral TDF-FTC Daily

Step 3
- 48 weeks
- Oral TDF-FTC Daily
- IM CAB Placebo
  - Weeks 5, 9, and every 8 weeks thereafter

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Baseline Characteristics

• **Age**
  - Average age of 26 years
  - 57% were ≤25 years of age

• **Partners**
  - 87% lived with partner
  - 55% reported ≥2 partners in past month
  - 34% had partners that were HIV+ or had unknown status

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Results (n = 3,127 included in analysis)

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Results (n = 3,127 included in analysis)

**Investigator’s Conclusion:** Long-acting injectable cabotegravir was more effective than daily oral tenofovir DF-emtricitabine in preventing HIV infection in cisgender women.

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