CME OUTFITTERS

COMPARING PrEP CHOICES

Efficacy, Safety, and What's New

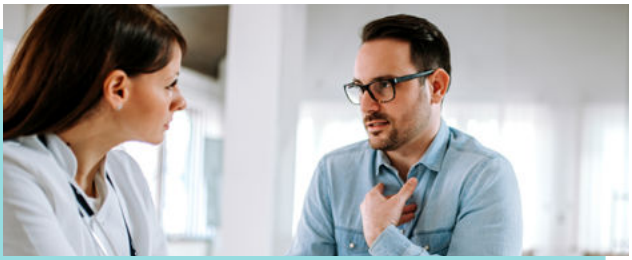
A clinical reference to support healthcare professionals in comparing oral and long-acting PrEP options and aligning evidence, guidelines, and patient preferences in routine practice.

Scope and Use Statement

Regulatory approval, labeled indications, and implementation guidance for HIV pre-exposure prophylaxis (PrEP) vary by country and region. This resource summarizes available clinical evidence and guideline-informed considerations to support healthcare professionals in evaluating PrEP options. Clinicians should consult **local product labels, national guidelines, and regulatory authorities** when making prescribing decisions.

Before initiating any PrEP regimen, clinicians should confirm eligibility:

- HIV-negative status
  - Preferably using a **4th-generation HIV antigen/antibody assay**
  - **HIV RNA testing** is recommended when acute HIV infection is suspected
- Clinical factors
  - Renal function
  - Bone health
  - Pregnancy status and reproductive plans
  - Age and adolescent considerations
  - Hepatitis B virus status, when relevant
- Structural and contextual factors
  - Local availability and regulatory approval of PrEP options
  - Insurance or public program coverage
  - Clinic capacity to deliver injectable PrEP
  - Patient ability and willingness to adhere to follow-up and monitoring requirements



Patient Eligibility and Clinical Considerations

	Oral Options			Injectable Options	
	F/TDF		F/TAF	Cabotegravir	Lenacapavir
	Daily	On-Demand	Daily	Every 2 Months	Every 6 Months
MSM	**FDA On-Label** Guideline Recommended (DHHS, IAS-USA, WHO)	**FDA Off-Label** Guideline Recommended (IAS-USA, WHO)	**FDA On-Label** Guideline Recommended (DHHS, IAS-USA, WHO)	**FDA On-Label*** Guideline Recommended (DHHS, IAS-USA, WHO)	**FDA On-Label*** Guideline Recommended (IAS-USA, WHO)
Transgender women		**FDA Off-Label** Not Recommended			
Heterosexual men					
Hetereosexual women			**FDA Off-Label** Not Recommended		
Transgender men					

People who inject drugs: assess and consider sexual risk.

CDC indicates that people who inject drugs are likely to benefit from any FDA-approved PrEP option with or without a sexual risk indication.

Except pregnancy: insufficient human data to adequately assess a drug-associated risk of birth defects and miscarriage.

CDC = Centers for Disease Control and Prevention

FDA = U.S. Food and Drug Administration

F/TDF = emtricitabine / tenofovir disoproxil fumarate

F/TAF = emtricitabine / tenofovir alafenamide

MSM = men who have sex with men

WHO = World Health Organization

Overview of Current PrEP Options

PrEP Option	Route	Maintenance dosing	Initiation considerations	Key clinical considerations
Emtricitabine/tenofovir disoproxil fumarate (TDF/FTC)	Oral	Daily	Initiate after con-firmed HIV-negative status	Renal and bone monitoring; HBV considerations
Emtricitabine/tenofovir alafenamide (TAF/FTC)	Oral	Daily	Initiate after con-firmed HIV-negative status	Not indicated for receptive vaginal sex per label
Cabotegravir long-acting (CAB-LA)	Intramuscular	Every 2 months	Requires loading phase; optional oral lead-in	Injection visit adherence; re-sistance risk with delayed dosing
Lenacapavir long-acting	Subcutaneous	Every 6 months	Oral + injectable initiation phase	Long dosing interval; evolving implementation data

FTC = emtricitabine; HBV = hepatitis B virus.

Initiation and Maintenance: Key Practical Differences

Cabotegravir Long-Acting (CAB-LA)

INITIATION

- Involves a **loading phase** prior to maintenance dosing
- An **oral lead-in** may be used to assess tolerability but is optional, depending on local guidance
- Loading doses are administered during the initiation phase prior to transitioning to every-2-month maintenance dosing

MAINTENANCE

- Intramuscular injection administered **every 2 months**

CLINICAL EVIDENCE

- Demonstrated superior efficacy compared with daily oral PrEP in randomized trials and sustained effectiveness in longer-term follow-up

Lenacapavir

INITIATION

- Requires an oral and injectable initiation phase to rapidly achieve protective drug concentrations
- The initiation phase includes oral dosing in combination with injection before transitioning to twice-yearly maintenance

MAINTENANCE

- Subcutaneous injection administered every 6 months

CLINICAL EVIDENCE

- Phase 3 trials demonstrate high efficacy and support the potential role of twice-yearly dosing for selected populations

Overall Efficacy, Safety, and Special Populations

- Efficacy
  - All approved PrEP options demonstrate high effectiveness when used as directed across studied populations
- Safety
  - Favorable safety profiles overall, with growing data in pregnancy and diverse populations
- Guideline perspectives
  - World Health Organization (WHO), Centers for Disease Control and Prevention (CDC), European AIDS Clinical Society (EACS), and International Antiviral Society–USA (IAS–USA) guidelines consistently emphasize shared decision-making, adherence support, and regular HIV testing as core components of PrEP delivery, although specific eligibility and implementation recommendations vary by region and population. See references and resources for specific details

(Guideline References: WHO, 2025; CDC, 2025; EACS, 2025)

PrEP Options: Consensus and Different Perspectives on Eligibility

Clinicians need to consider FDA labeling alongside recommendations from major guideline bodies, Department of Health and Human Services (DHHS), International Antiviral Society–USA (IAS-USA), and World Health Organization (WHO), highlighting areas of both agreement and divergence across populations and PrEP modalities.

Clinical Implications

- Eligibility decisions should be integrated with patient preferences, adherence considerations, and access realities
- Shared decision-making is essential when multiple appropriate options exist

Investigational and Emerging PrEP Approaches

Several long-acting and novel PrEP formulations are under investigation, including:

- Once-yearly injectable formulations
- Additional capsid inhibitors with oral and injectable delivery pathways

These agents are not **FDA-approved for PrEP** at this time but reflect continued innovation aimed at reducing adherence barriers and expanding prevention choices in the future.

KEY TAKEAWAYS FOR CLINICAL PRACTICE

1. All FDA-approved PrEP options are highly effective when used appropriately
2. Differences in dosing frequency, administration route, and safety profiles matter in real-world care
3. Long-acting injectable PrEP options may reduce adherence challenges for some patients
4. Eligibility should be guided by evidence, guidelines, and patient context, not assumptions
5. PrEP selection is dynamic and should be revisited as patient needs and circumstances change

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