REVIEW ARTICLE

Antiretroviral Therapy in India (2025): Drugs, Indications, Contraindications, Mechanisms, and Prophylaxis (PEP/PrEP)

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Abstract

Background: India has made major gains in HIV control, with nationwide scale-up of antiretroviral therapy (ART), routine viral load monitoring, and simplified dolutegravir-based regimens. Yet gaps persist in differentiated service delivery, drug-resistance surveillance, and prevention implementation (PEP/PrEP).

Objectives: To provide a comprehensive, India-focused review of currently available antiretroviral drugs and fixed-dose combinations (FDCs), indications and contraindications for ART initiation, core mechanisms of action by class, regimen selection and monitoring, and detailed, practical guidance on HIV postexposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP), with attention to 2024–2025 updates.

Methods: Narrative review of national guidance (NACO), WHO recommendations, and key implementation documents and peer-reviewed Indian literature (2018–2025), emphasizing policy-relevant updates and practical algorithms.

Key findings: (1) First-line ART in India is an FDC of tenofovir disoproxil fumarate/lamivudine/dolutegravir (TLD), with alternatives guided by renal, hepatic, pregnancy, TB cotreatment, and toxicity considerations. Viral load monitoring and "Treat All" remain policy cornerstones. (2) *PEP*: NACO's national PEP document continues to list a 28-day triple regimen with TDF + 3TC + EFV started as soon as possible (preferably ≤2 h; within 72 h). Several institutions have operationalized DTG-based PEP (TDF/3TC/DTG) in line with broader ART updates and WHO's 2024 PEP guidance favoring 3-drug regimens. (3) *PrEP in India*: DCGI approved TDF/FTC for PrEP; national technical guidance exists, but programmatic rollout remains uneven. Global prevention options expanded with FDA approval (June 2025) of twice-yearly injectable lenacapavir for PrEP. Indian availability will depend on future regulatory decisions and access arrangements.

Conclusion: India's ART platform is strong and increasingly INSTI-based. Scaling PrEP, standardizing DTG-aligned PEP, fortifying viral load and resistance monitoring, and integrating long-acting prevention as it becomes available are the next priorities.

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Introduction

India's National AIDS Control Program (NACP) has progressively simplified treatment, expanded access to FDCs, and strengthened routine viral load (VL) testing—core enablers of the "Treat All" policy (ART for all PLHIV regardless of CD4 count or clinical stage).[1–3] The 2021 NACO guidance established TLD as the preferred first-line regimen, aligned with global best practices, while subsequent testing/guideline updates emphasize differentiated service delivery and standardized VL monitoring.[1–3]

Despite these gains, India continues to face high TB coinfection rates, regional variability in service delivery, and prevention gaps among key populations.[1–3] Consolidated WHO guidance (2021–2024) underpins many national recommendations, including a public-health approach to ART, PEP, and PrEP.[3,4]

Scope

This review synthesizes Indian programmatic guidance and global recommendations to present (1) current ARV classes, mechanisms, and drugs available in India; (2) indications, contraindications, and regimen selection; (3) monitoring and switching; and (4) India-specific guidance and practical algorithms for PEP and PrEP, including 2024–2025 updates.[1–18]

Antiretroviral Drugs Available in India and Mechanisms of Action

Drug Classes and Core Mechanisms

NRTIs/NtRTIs (e.g., TDF, 3TC, FTC, ABC, AZT) are nucleoside analogs that, once phosphorylated (NRTIs), compete at reverse transcriptase and terminate viral DNA chain elongation.[1–3]

NNRTIs (e.g., EFV, NVP, ETR) bind an allosteric site on reverse transcriptase, inducing conformational changes and noncompetitive inhibition; resistance can emerge rapidly with low adherence.[1–3]

Integrase strand transfer inhibitors (INSTIs) (e.g., DTG, BIC, RAL) block the strand-transfer step of HIV integrase, preventing proviral DNA integration; DTG has a high barrier to resistance and excellent tolerability, driving its first-line selection in India.[1–3]

Protease inhibitors (PIs) (e.g., ATV, LPV/r) inhibit HIV protease, blocking polyprotein cleavage and producing immature, noninfectious virions; typically reserved for second-line therapy given metabolic effects and interactions.[1–3]

Entry/fusion inhibitors/CCR5 antagonists (e.g., enfuvirtide, maraviroc) target viral entry; not widely used programmatically in India due to cost, monitoring needs, and availability.[1–3]

Emerging classes include capsid inhibitors and maturation inhibitors. Of special note for prevention, the capsid inhibitor lenacapavir received FDA approval in June 2025 as twice-yearly PrEP in the US, with pending/ongoing submissions elsewhere; Indian regulatory status is awaited.[12–15]

Drugs and Fixed-Dose Combinations in Indian Practice

Preferred first-line FDC (adults/adolescents): TDF/3TC/DTG (TLD) once daily—programmatically favored for potency, tolerability, and high resistance barrier. Alternatives are chosen when TDF is contraindicated or when TB co-treatment, pregnancy, or organ dysfunction requires modification.[1–3]

Second-line options: Boosted PI-based regimens (e.g., LPV/r + two NRTIs not used in first-line) remain standard after confirmed virologic failure on first-line; DTG-based second/third-line constructs are increasingly used per updated national guidance.[1–3]

Pediatric regimens: Weight-band dosing with DTG-containing backbones is expanding, consistent with international

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pediatric recommendations (country adoption proceeds as formulations become available) (Table 1).[1–3]

Indications and Contraindications for ART

Treat-All: Initiation for Every PLHIV

India adopted treat-all in April 2017 and continues to recommend immediate ART initiation after diagnosis, once readiness and baseline labs are assessed.[1–3] Early ART improves survival, reduces OI risk, and underpins treatment-as-prevention.[1–3]

Priority groups (initiate without delay): pregnant/breastfeeding women; TB or HBV/HCV co-infection; advanced disease; serodiscordant partners; children/adolescents.[1–3]

Baseline Evaluation

Before starting ART: VL (if available), CD4 (for baseline status), creatinine/eGFR, hepatic panel, hemoglobin (AZT), pregnancy testing, HBV/HCV screening, TB screening (symptom screen ± GeneXpert per clinical context), STI screen as indicated, and adherence counseling.[1–3,17]

Contraindications and Cautions

Absolute contraindications are uncommon; regimen choice/adjustment is driven by:

- Hypersensitivity (e.g., abacavir).
- Renal impairment (avoid/adjust TDF).
- Hepatic dysfunction.
- Significant drug–drug interactions (e.g., rifampicin with DTG/PI—dose/timing adjustments).
- Pregnancy (safety-guided selection).
- Certain OIs (e.g., cryptococcal meningitis—time ART carefully to avoid severe IRIS).
- Adherence concerns (Fig. 1).[1–3,17]

Regimen Selection, Monitoring, and Switching

First-Line: TLD

TLD (TDF/3TC/DTG) is the national preferred first-line for adults/adolescents based on potency, tolerability, pill burden, and resistance barrier; AZT- or ABC-based alternatives are used when TDF is unsuitable.[1–3]

Special Situations

- *TB co-treatment*: Rifampicin induces DTG metabolism; dose DTG 50 mg twice daily during rifampicin or consider EFV-based alternatives if DTG BID is not feasible. Monitor hepatotoxicity when pairing ARVs with anti-TB therapy.[1–3]
- *HBV co-infection*: Choose TDF-containing regimens when possible; avoid abrupt discontinuation to prevent HBV flares[1–3,17]
- *Pregnancy*: DTG-based regimens are now widely accepted in pregnancy; follow the national protocol and document counseling.[1–3]
- *Renal impairment*: Avoid or adjust TDF if eGFR is < 50–60 mL/min (programmatic cutoffs vary); consider AZT/ABC backbones with appropriate monitoring.[1–3,17]

Monitoring

Virologic: VL at ~6 months after initiation and routinely thereafter; VL-driven management is the standard.[1–3,17]

Laboratory: Creatinine/eGFR (TDF), liver enzymes (NNRTIs/PIs/INSTIs), hematology (AZT), lipids/glucose (PIs/INSTIs), pregnancy tests as applicable.[1–3]

Clinical/adherence: At every visit, use differentiated models for stable patients.[1–3]

Defining and Managing Failure

Virologic failure:

- Persistent VL >1,000 copies/mL after ≥6 months on ART with good adherence.
- Confirm adherence and interactions; repeat VL.
- If confirmed, switch to second-line (often boosted PI-based with two NRTIs not previously used; DTG-based second/third-

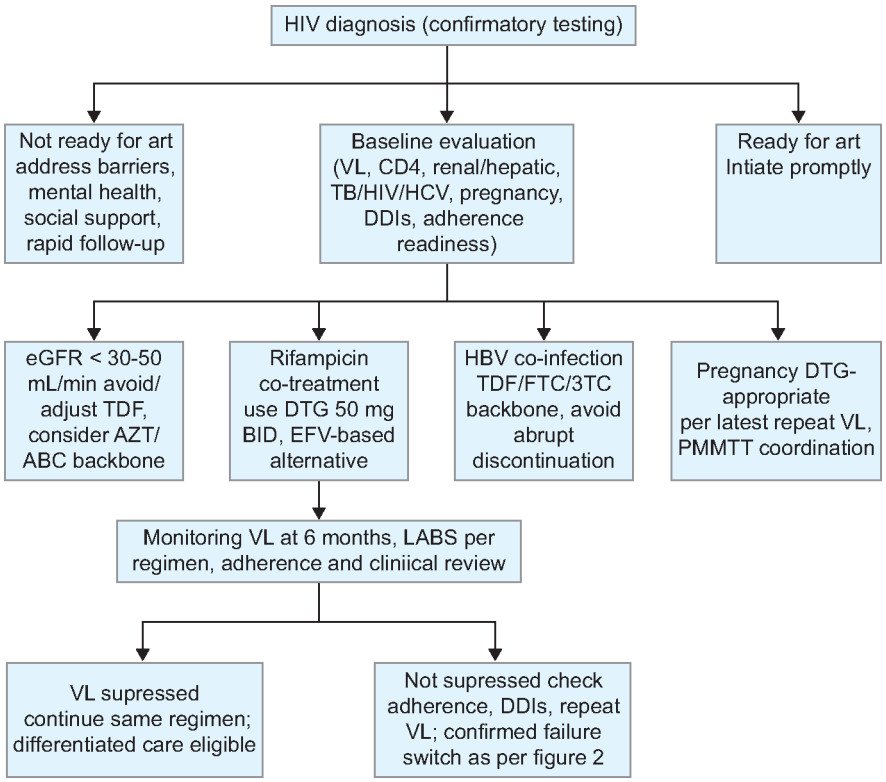

Fig. 1: ART initiation and selection (India, 2025)

Table 1: Antiretroviral classes, mechanisms, and common Indian agents

Class	*Core mechanism*	*Key agents in India*	*Typical programmatic role*
NRTIs/NtRTIs	Chain termination at RT	TDF, 3TC, FTC, ABC, AZT	Universal backbones; TDF/3TC commonly paired with DTG
NNRTIs	Allosteric RT inhibition	EFV, NVP, ETR	Legacy first-line; now alternatives
INSTIs	Block DNA strand transfer	DTG, RAL, (BIC limited availability)	Preferred first-line anchor
PIs (boosted)	Inhibit protease maturation	LPV/r, ATV/r	Second-line/salvage
Entry/fusion	Block entry/fusion	Maraviroc, enfuvirtide	Limited use

line per updated guidance and availability) (Fig. 2).[1–3,9,10]

Postexposure Prophylaxis (PEP) in India

Indications and Timing

Postexposure prophylaxis is indicated after occupational (e.g., needlestick) or nonoccupational high-risk exposures (e.g., condomless sex with a known positive partner, sexual assault, needle sharing), ideally as soon as possible—preferably within 2 hours and not later than 72 hours. Duration is 28 days.[4–6]

Recommended Regimens

National (NACO) PEP guidance: Lists TDF 300 mg + 3TC 300 mg + EFV 600 mg once daily for 28 days; use single-pill FDC where available.[5]

Evolving/operational practice in India: Several government facilities (e.g., ESIC circulars) have operationalized TDF/3TC/DTG (TLD) once daily as PEP, reflecting broader national ART shifts and simplicity/tolerability, while WHO's 2024 PEP guideline recommends 3-drug regimens and issuing a full 28-day prescription up front. Local protocols should be followed, with attention to pregnancy, renal function, and drug interactions (Fig. 3).[4–6]

Special Populations

- *Pregnancy*: PEP is safe and recommended after substantial exposure; choose pregnancy-appropriate regimens and counsel on risk/benefit.[4–6]
- *Renal impairment*: Avoid or adjust TDF; consider alternative NRTI backbones per renal function.[4–6]
- *Source unknown/not testable*: Base decision on exposure type, local prevalence, and patient preference after counseling[4–6]

Programmatic Challenges in India

Rapid access (especially after-hours), clarity of protocols across facilities, and ensuring full 28-day supply at first visit remain common issues; standardized training and stocking at EDs and casualty are recommended.[4–6]

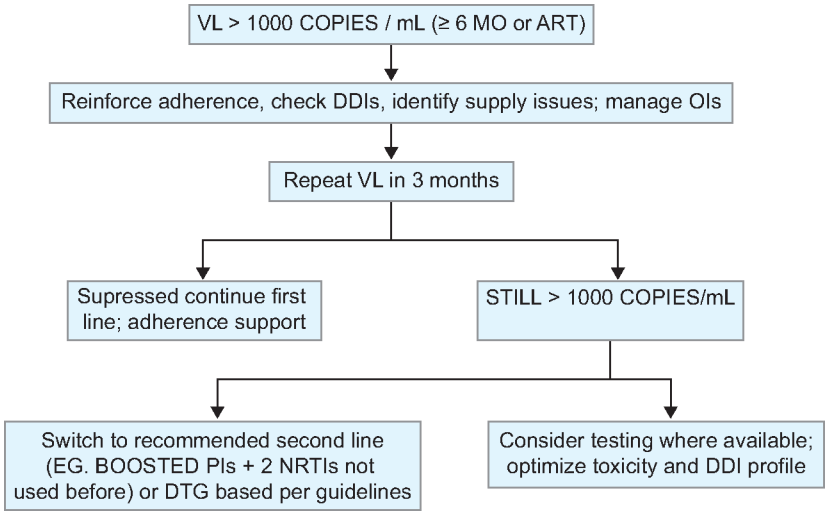

Fig. 2: Switching pathway (programmatic)

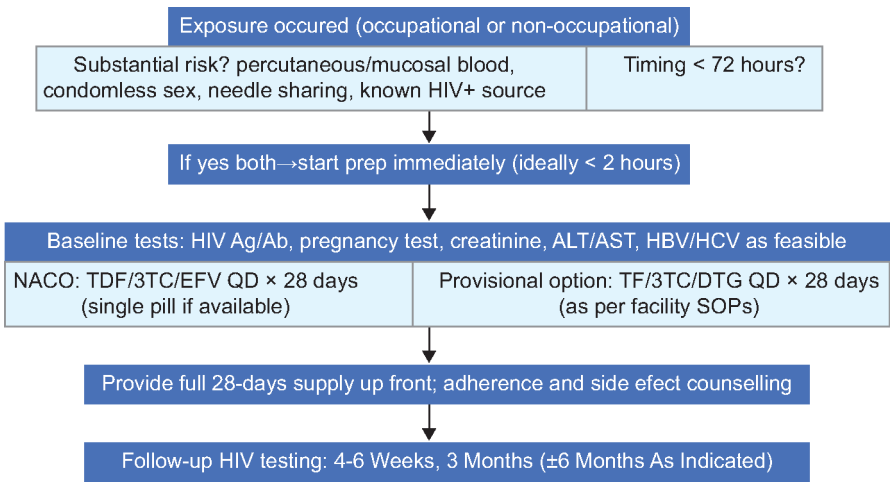

Fig. 3: PEP decision algorithm (adults/adolescents)

Pre-exposure Prophylaxis (PrEP) in India

Policy Status, Indications, and Candidates

Regulatory status: DCGI-approved TDF/FTC for PrEP; NACO released National Technical Guidelines for PrEP. National scale-up has been cautious, with pilots and targeted implementation discussed; rollout varies by state and service platform.[7,8,11]

Candidate groups: HIV-negative persons at substantial risk—MSM and transgender persons with condomless anal sex, serodiscordant partners without viral suppression, sex workers with inconsistent condom use, people who inject drugs (needle sharing), and individuals with recurrent STIs or PEP use. Baseline HIV testing is mandatory; assess renal function and HBV status (Table 2).[7,8,11]

PrEP Regimens and Dosing

Daily oral PrEP: TDF/FTC 300/200 mg once daily (preferred) or TDF/3TC where FTC is not available, with attention to evidence-based and local guidance.[7,8,11]

Event-driven (2-1-1) is an option in some populations (e.g., MSM) where supported; ensure clear counseling on dosing windows and contraindications.[7,8]

Long-acting options (global): Lenacapavir received US FDA approval (June 18, 2025) as a twice-yearly PrEP; WHO welcomed the approval. EMA issued a positive opinion later in 2025. Indian availability will depend on future regulatory submissions and access agreements. For now, India remains oriented to oral TDF-based PrEP (Fig. 4).[12–15]

Table 2: PrEP eligibility and baseline work-up (India)

Domain	*Recommendation*
Eligibility	HIV-negative, substantial ongoing risk; willing and able to adhere to and attend follow-up
Baseline	HIV Ag/Ab test, creatinine/eGFR, HBV serology (HBsAg/anti-HBc), pregnancy test if applicable, STI screen per risk
Counseling	Adherence, daily vs event-driven (where appropriate), condoms, harm reduction, symptoms of acute HIV, follow-up schedule
Follow-up	HIV test q3 months; renal function q6–12 months; STI screen per risk; adherence support

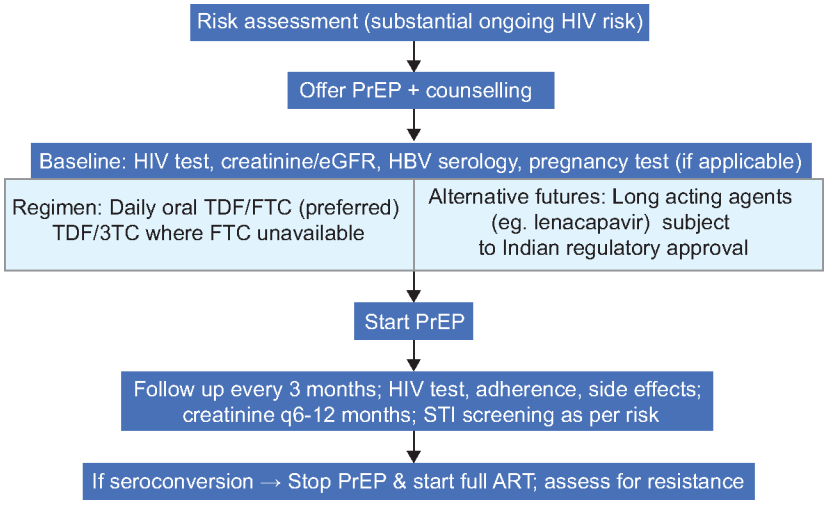

Fig. 4: PrEP workflow

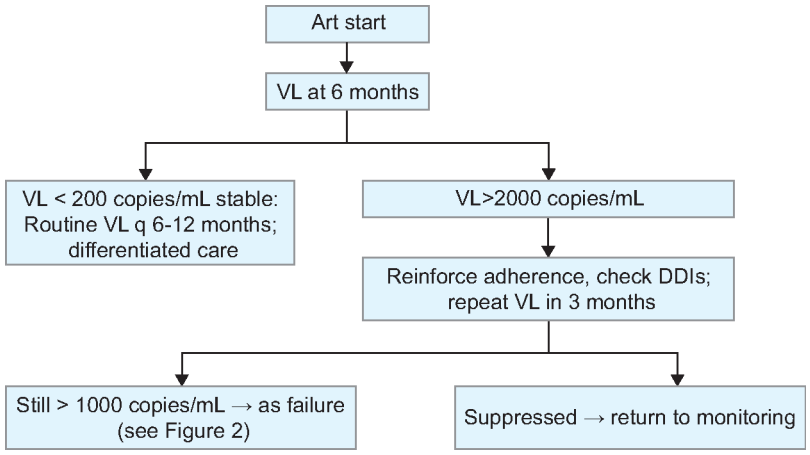

Fig. 5: VL-anchored monitoring cycle

Table 3: PEP quick checklist (adults/adolescents)

Step	*Action*
Exposure triage	Assess type, timing (≤72 h), source status
Baseline	HIV Ag/Ab, pregnancy test, creatinine, ALT/AST ± HBV/HCV
Start NOW	NACO 2021: TDF/3TC/EFV QD × 28 d; Institutional: TDF/3TC/DTG QD × 28 d where adopted (4–6).
Counseling	28-day supply up front (per WHO), adherence, side effects, risk reduction (4–6)
Follow-up	HIV test at 4–6 weeks and 3 months (± 6 months as indicated)

Table 4: PrEP quick checklist

Step	*Action*
Eligibility	HIV-negative, substantial ongoing risk; willing for quarterly follow-up
Baseline	HIV test, creatinine/eGFR, HBV serology, pregnancy test if applicable
Regimen	Daily TDF/FTC preferred (TDF/3TC acceptable where FTC unavailable per local guidance)
Counseling	Adherence, condoms/harm reduction, acute HIV symptoms, missed-dose plans
Follow-up	HIV test q3 months; creatinine q6–12 months; STI screen per risk

Contraindications and Safety

Do not start PrEP if HIV status is positive/uncertain (risk of resistance). Avoid or adjust TDF if eGFR <60 mL/min (per local policy). In HBV co-infection, TDF-based PrEP also treats HBV; avoid abrupt discontinuation to prevent flares. Pregnancy and breastfeeding: PrEP can be considered with counseling; follow current guidance.[7,8,11]

Implementation Considerations in India

Persistent barriers include awareness, stigma, logistics of quarterly HIV testing, renal monitoring, and linkage for key populations. Implementation science from India underscores the need for demand creation, community-engaged delivery models, and integration with STI and harm-reduction services.[7,8,11,17,18]

Drug–Drug Interactions, Toxicity, and Special Populations

Rifampicin

Induces UGT/CYP; DTG BID is recommended with rifampicin to maintain levels; monitor closely if EFV alternatives are used.[1–3,17]

Renal Disease

Favor AZT/ABC backbones when eGFR <30–50 mL/min; reassess dosing for TDF; consider TAF where available (programmatic availability may be limited).[1–3,17]

Metabolic Risk

PIs (and to a lesser extent INSTIs) affect lipids/glucose; periodic lipid/glucose monitoring is suggested in patients with NCD risk.[1–3,10]

Pregnancy

DTG-based regimens are acceptable; document counseling; coordinate with PMTCT services and newborn prophylaxis per national guidance.[1–3,17]

HBV/HCV

Choose TDF-containing backbones for HBV; comanage with DAAs for HCV; avoid discontinuations that precipitate HBV flares.[1–3,17]

Service Delivery: Monitoring, VL, and Differentiated Care

India is strengthening routine VL monitoring and differentiated service delivery (multimonth dispensing, fast-track refills for stable patie nts).[1–3,17,18] Continued investment in laboratory capacity and logistics is essential to maintain suppression and achieve 95-95-95 (Table 3 and Fig. 5).[1–3,17,18]

PEP and PrEP: Practical Checklists for Clinics

The practical checklists are presented in Tables 3 and 4.

Future Directions

Long-acting Prevention

Twice-yearly lenacapavir for PrEP in the US opens a path to improved adherence—India will need regulatory review, pricing/access strategies (e.g., voluntary licensing),

and delivery models capable of injection scheduling and follow-up (Table 4).[12–15]

Resistance Surveillance

As INSTI-based regimens dominate, systematic resistance monitoring (especially postfailure) should expand.[1–3,9,10]

PrEP Scale-up

Implement at-scale, culturally competent models in key populations; integrate with STI services and community networks.[7,8,11,16–18]

PEP Standardization

Align national PEP regimens with current programmatic ART (DTG-based) where feasible, while ensuring consistent availability and training; WHO now favors 3-drug PEP with full 28-day dispensing.[4–6]

Differentiated Care

Expand multimonth dispensing and community ART refills to reduce clinic burden and improve retention.

Conclusion

India's HIV program has successfully transitioned to simplified, potent TLD-based first-line ART with routine VL monitoring. To consolidate gains and accelerate incidence reduction, India should scale PrEP, harmonize PEP with contemporary regimens, and invest in laboratory systems and resistance surveillance, while preparing for long-acting prevention as regulatory and access pathways mature. With consistent policy attention and implementation science, the program can advance toward 95-95-95 and beyond.

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