Cabenuva (cabotegravir extended-release injectable suspension, rilpivirine extended-release injectable suspension)

NEW PRODUCT SLIDESHOW

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Introduction

- **Brand name:** Cabenuva
- **Generic name:** Cabotegravir, rilpivirine
- **Pharmacologic class:** HIV-1 integrase strand transfer inhibitor (INSTI) + non-nucleoside reverse transcriptase inhibitor (NNRTI)
- **Strength and Formulation:** 200mg/mL, 300mg/mL; suspension for intramuscular injection
- **Manufacturer:** ViiV Healthcare
- **How supplied:** Kit—Cabenuva 400mg/600mg (single dose vial of 400mg/2mL cabotegravir + single dose vial of 600mg/2mL rilpivirine); Cabenuva 600mg/900mg (single dose vial of 600mg/3mL cabotegravir + single-dose vial of 900mg/3mL rilpivirine)
- **Legal Classification:** Rx

Cabenuva

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Indication

- As a complete regimen for **HIV-1 infection** in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine.

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Dosage and Administration

- Must be administered by a healthcare professional.
- **Prior to initiation**, assess tolerability using oral lead-in daily dose: Vocabria 30mg and Edurant 25mg for approx. 1 month (at least 28 days).
- **At month 2 (on last day of oral lead-in)**: administer initial IM injections of cabotegravir 600mg and rilpivirine 900mg.
- Administer at separate gluteal injection sites (on opposite sides or 2 cm apart) during same visit.
- **Month 3 onwards**: administer cabotegravir 400mg IM and rilpivirine 600mg IM at each visit once monthly (may be given up to 7 days before or after the scheduled date).

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Dosage and Administration

Missed Injections

- Adherence strongly recommended.
- Refer to oral dosing recommendations if patient plans to miss a scheduled injection visit.
- **Less than or equal to 2 months**: resume with cabotegravir 400mg IM and rilpivirine 600mg IM monthly as soon as possible.
- **Greater than 2 months**: reinitiate with cabotegravir 600mg IM and rilpivirine 900mg IM then continue to follow the cabotegravir 400mg IM and rilpivirine 600mg IM monthly injection dosing schedule.

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Considerations for Specific Populations

- **Pregnancy:** Insufficient human data to assess drug-associated risk of birth defects and miscarriage.
- **Nursing mothers:** Not recommended while breastfeeding.
- **Pediatric**: Not established.
- **Geriatrics**: Use caution; clinical trials did not include sufficient numbers of patients aged ≥65yrs.
- **Renal impairment**: Increased monitoring for adverse effects is recommended in patients with severe renal impairment (CrCL 15 to <30mL/min/1.73 m^2) or ESRD (CrCL <15mL/min). Unknown effects in patients with ESRD not on dialysis.
- **Hepatic impairment**: Unknown effects in patients with severe hepatic impairment.

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Contraindications

- Concomitant carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, systemic dexamethasone (more than 1 dose), St. John's wort.

Warnings and Precautions

- Discontinue immediately if signs or symptoms of hypersensitivity reactions are suspected or develop; monitor clinical status, including liver transaminases.
- Monitor for post-injection reactions (approx. 10 minutes after injection); treat appropriately if occur.
- Increased risk for worsening or development of transaminase elevations in patients with underlying liver disease or marked elevation in transaminases.
- Monitor liver function; discontinue if hepatotoxicity is suspected.

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Warnings and Precautions

- Promptly evaluate if depressive symptoms occur to determine whether the risks of continued therapy outweigh the benefits.
- Long-acting properties: residual concentrations of both cabotegravir and rilpivirine may remain for prolonged periods (up to 12 months or longer).
- Switch to an alternative regimen if virologic failure is suspected.

Interactions

- See Contraindications.
- Concomitant use with other antiretroviral drugs: not recommended.
- Cabotegravir: antagonized by strong UGT1A1 or 1A9 inducers.
- Rilpivirine: antagonized by CYP3A inducers or may be potentiated by CYP3A inhibitors.
- Concomitant drugs with a known risk for torsade de pointes (eg, azithromycin, clarithromycin, erythromycin); caution; consider alternatives.
- Concomitant methadone; monitor; may need dose adjustment for methadone.

Adverse Reactions

- **Most common (grades 1 to 4 observed in ≥2%)**: Injection site reactions, pyrexia, fatigue, headache, musculoskeletal pain, nausea, sleep disorders, dizziness, rash.
- **Others**: Hepatotoxicity, depressive disorders, hypersensitivity reactions, increased weight, abdominal pain, gastritis, dyspepsia.

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Mechanism of Action

- **Cabotegravir** inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of retroviral deoxyribonucleic acid (DNA) integration which is essential for the HIV replication cycle.
- **Rilpivirine** inhibits HIV-1 replication by non-competitive inhibition of HIV-1 reverse transcriptase. It does not inhibit the human cellular DNA polymerases α, β and γ.

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Pharmacokinetics

	Cabotegravir	Rilpivirine
Absorption Tmax (days), median	7	3 to 4
Distribution % bound to human plasma proteins	>99.8	99.7
Metabolism Metabolic pathways	UGT1A1 UGT1A9 (minor)	CYP3A
Elimination		
Half-life (weeks), mean	5.6 to 11.5	13 to 28
% of dose excreted in urine/feces	27% / 59%	6% / 85%

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Clinical Trials

- Approval was based on 2 randomized, multicenter, active-controlled, parallel-arm, open-label, non-inferiority phase 3 trials (FLAIR [NCT02938520] and ATLAS [NCT02951052]) that evaluated the efficacy and safety of Cabenuva in 1182 HIV-infected adults who were virologically suppressed (HIV-1 RNA <50 copies/mL) prior to initiation.
- Patients were randomly assigned to receive either a cabotegravir plus rilpivirine regimen or remain on their current antiretroviral regimen.

Clinical Trials

- Patients assigned to receive cabotegravir plus rilpivirine initiated treatment with daily oral lead-in dosing with Vocabria 30mg plus Edurant 25mg for at least 4 weeks, followed by monthly injections with Cabenuva for an additional 44 weeks.
- The primary endpoint of both trials was the proportion of patients with plasma HIV-1 RNA ≥50 copies/mL at week 48.

Clinical Trials

- At week 48, results showed that treatment with Cabenuva was noninferior to the current antiretroviral regimen (ART).
- Virologic suppression rates (HIV-1 RNA <50 copies/mL):
  - **FLAIR:** 94% for Cabenuva vs 93% for current ART (treatment difference: -0.4%; 95% CI, -2.8%, 2.1%).
  - **ATLAS:** 93% for Cabenuva vs 95% for current ART (treatment difference: 0.7%; 95% CI, -1.2%, 2.5%).
- Adjusted for study and randomization stratification factors, the treatment difference of HIV-1 RNA ≥50 copies/mL for the pooled data was 0.2% (95% CI, -1.4, 1.7).

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New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/cabenuva/