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STEPS

New Drug Reviews

Cabotegravir (Apretude) for Pre-exposure Prophylaxis for HIV Type 1 Infection

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Drug	Dosage	Dose form	Cost per dose*
Cabotegravir (Apretude)	Single 600-mg intramuscular injection First two doses given one month apart After initiation doses, subsequent injections given every two months†	Single-dose vial: 600 mg per 3 mL (200 mg per mL)	$4,000 (only available at select specialty pharmacies)

*—Estimated retail price of one injection based on information obtained at https://www.drugs.com (accessed March 22, 2023).
†—The physician may choose to use a lead-in of oral cabotegravir (Vocabria), 30 mg once daily for 28 days, with the injection given on the final day of oral medication or within three days of completion of the oral regimen.

Cabotegravir (Apretude) is an extended-release injectable HIV type 1 (HIV-1) antiretroviral integrase strand transfer inhibitor. Cabotegravir is labeled for use in adults and adolescents weighing at least 35 kg (77 lb) who are HIV-negative but at risk of HIV-1. It is used as pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection, the most common form of HIV.[1]

Safety

Cabotegravir is a safe form of PrEP medication.[1] It should be prescribed only after a patient has been confirmed HIV-negative immediately before each injection. This is to reduce the risk of developing drug resistance in patients with previously undetected HIV infection. Cabotegravir has not been evaluated in pregnant patients, although neural tube defects have been associated with dolutegravir (Tivicay), another integrase strand transfer inhibitor.[2] It is unknown if cabotegravir passes through breast milk. Cabotegravir has not been studied in patients younger than 12 years or weighing less than 35 kg. Data in patients 65 years and older are limited. Cabotegravir is safe to use when creatinine clearance is 30 mL per minute per 1.73 m^2 (0.50 mL per second per m^2) or more, but increased monitoring for adverse effects is advised when creatinine clearance is less than 30 mL per minute per 1.73 m^2. Significant elevation in liver function tests requiring discontinuation of cabotegravir occurs in less than 1% of patients.[1]

Tolerability

Cabotegravir is well tolerated. Discontinuation due to adverse effects occurred at a similar rate as with the other currently available PrEP therapy, emtricitabine/tenofovir (Truvada), ranging from 1% to 6%.[1] In two clinical trials, the most common adverse effect of cabotegravir was injection site reaction, which occurred in 38% of participants in one study and 85% in the other (compared with 11% and 35%, respectively, with emtricitabine/tenofovir; number needed to harm = 2 to 4). Injection site reactions in these studies did not result in medication discontinuation.[1] Other adverse effects that did not lead to discontinuation of cabotegravir occurred at a rate similar to that of emtricitabine/tenofovir (less than 1% to 5%) and included gastrointestinal symptoms, headache,

STEPS new drug reviews cover Safety, Tolerability, Effectiveness, Price, and Simplicity. Each independent review is provided by authors who have no financial association with the drug manufacturer.

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fever, and fatigue.[1] As with other integrase strand transfer inhibitors taken over time, cabotegravir is associated with weight gain, hyperglycemia, and dyslipidemia.[2] In clinical trials, cabotegravir was associated with a mean weight gain of 3.5 kg (7.7 lb) in cisgender men/transgender women vs. a mean weight gain of 2 kg (4.4 lb) with emtricitabine/tenofovir. In cisgender women, mean weight gain with cabotegravir was 7 kg (15.4 lb) compared with 5 kg (11 lb) in those taking emtricitabine/tenofovir. Significant weight gain (greater than 10% from baseline) occurred in 16% of cisgender men/transgender women and 28% of cisgender women taking cabotegravir compared with 11% and 24%, respectively, of those taking emtricitabine/tenofovir.

Effectiveness

Cabotegravir has been shown to be more effective at preventing HIV-1 infection than emtricitabine/tenofovir. It has been directly compared with emtricitabine/tenofovir in two studies of 7,790 uninfected people (3,224 cisgender women from sub-Saharan Africa in addition to 4,456 cisgender men and transgender women who have sex with men from the United States and 42 other international sites) over three years.[3,4] The investigators stopped the trials early due to demonstrated effectiveness. Compared with emtricitabine/tenofovir, cabotegravir reduced the risk of acquiring HIV-1 infection in cisgender men and transgender women who have sex with men by 69%; however, given the low incidence of HIV acquisition in patients taking any PrEP, the number needed to treat to prevent one additional HIV infection is high at 273 (95% CI, 145 to 523) over an average of three years of treatment.[4] In cisgender women in Africa who have sex with men, cabotegravir reduced the risk of acquiring HIV-1 infection by 90%; again, with a high number needed to treat of 482 (95% CI, 179 to 1,205).[3] As with other PrEP therapies, cabotegravir does not prevent sexually transmitted infections apart from HIV-1.

Price

In comparison, a 30-day supply of emtricitabine/tenofovir disoproxil (Truvada) costs about $2,000 for brand and $30 for generic. [corrected][5]

Simplicity

Cabotegravir is a 600-mg gluteal injection given on days 1 and 30 of treatment and then every two months thereafter. Some patients will opt for a lead-in period of one month of oral 30-mg cabotegravir (Vocabria) before the first injection to ensure tolerability of the medication.[2] Physicians should verify a negative HIV-1 test result before every cabotegravir injection due to the risk of drug resistance in those with preexisting HIV-1 infection. Cabotegravir therapy for PrEP requires a physician visit in months 1 and 2 and every two months thereafter to perform HIV testing and to receive the gluteal injection. Any missed doses require careful attention to detailed instructions. Cabotegravir is contraindicated in people taking anticonvulsants (carbamazepine, oxcarbazepine, phenobarbital, phenytoin) or antimycobacterials (rifampin, rifapentine) due to the potential for significant reduction in drug activity of cabotegravir.[1]

Bottom Line

Cabotegravir is a safe and highly effective injectable option for at-risk cisgender female, cisgender male, and transgender female adults and adolescents to reduce the risk of HIV infection. It is more effective at preventing HIV than the other oral PrEP medications (i.e., two forms of emtricitabine/tenofovir combination pills). Injectable cabotegravir also eliminates the need to take a daily oral medication if this is what the patient wants, which potentially improves adherence. However, cabotegravir requires gluteal injections at a physician's office and is significantly more expensive than other available treatment options. The choice of which PrEP regimen to use should ultimately be a shared decision with the patient; however, other forms of PrEP should be considered as first-line treatment due to the high cost of injectable cabotegravir.

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