Antiplatelets for Recurrent Ischemic Stroke

full update May 2025

The chart below provides dosing, cost, and other information to help you choose among options for recurrent ischemic stroke. **The information in the chart pertains to secondary stroke prevention in general and is not specific to patients who have a stroke while on aspirin.** Below the chart, find tips and clinical pearls about antiplatelet regimens.

Drug	Dose	Comments	Cost/30 days[a]
Preferred options[1,3,10]			
Aspirin	LD: see comments MD: usually 81 mg once daily (see comments)	• **Loading dose**, usually 160 to 300 mg daily, should be started within 24 to 48 hours of an acute ischemic stroke.[11] • **Maintenance dose**: ○ Guidelines recommend 80 to 325 mg (Canada), 75 to 100 mg (ACCP), and 50 to 325 mg (AHA/ASA) once daily.[1,3,10] ○ Limited data for doses <75 mg.[3] ○ Bleeding complications increase at doses >100 mg daily.[3]	US: <$1 Canada: <$2
Clopidogrel (Plavix, generics)	LD: see comments MD: 75 mg once daily[1,10]	• There are very limited data with loading doses of clopidogrel after an acute ischemic stroke (mostly limited to minor strokes or high-risk TIAs). However, loading doses of 300 to 600 mg rapidly inhibit platelets compared to platelet inhibition taking about five days with daily doses of 75 mg.[23] • Maintenance dosing efficacy similar to dipyridamole ER/aspirin (Aggrenox).[6] • May have lower GI bleed risk and stomach upset compared to aspirin.[7]	US: <$5 Canada: <$10
SHORT-TERM aspirin plus clopidogrel, followed by EITHER aspirin or clopidogrel alone	LD: see comments MD: Low-dose aspirin (usually 81 mg) plus clopidogrel 75 mg once daily usually for **21 days** (see comments), then continue EITHER aspirin or clopidogrel.[10,19,20]	• **Loading dose**: of the three major RCTs, POINT used clopidogrel 600 mg x 1 with aspirin 162 mg x 5 days, CHANCE used clopidogrel 300 mg x 1 with aspirin 75 to 300 mg x 1, and INSPIRES used clopidogrel 300 mg x 1 with aspirin 100 to 300 mg x 1.[2,8,22] Canadian guidelines recommend an aspirin LD of 160 to 300 mg.[10] • Start as soon as possible, ideally within 72 hours, or at least within seven days, of:[1,2,8,10,18,22] ○ **High-risk TIA** (e.g., ABCD^2 score[b] ≥4). ○ Minor ischemic stroke (e.g., NIHSS score[c] ≤3; INSPIRES used NIHSS score[c] ≤5). • Prevents stroke within three months better than aspirin alone (NNT ~53) [Evidence level A-1].[8,20] Significant impact on mortality or recurrent TIA has not been shown.[19,20,22] Safety/efficacy with thrombolysis or anticoagulation unknown.[8,20]	US: <$5 Canada: ~$10

Drug	Dose	Comments	Cost/30 days[a]
Preferred options, continued[1,3,10]			
SHORT-TERM aspirin plus clopidogrel, followed by EITHER aspirin or clopidogrel alone, continued		• May cause more major bleeding (e.g., bleeding requiring or prolonging hospital stay, death due to bleeding) or moderate-to-severe GUSTO bleeding compared to aspirin alone (NNH ~ 200) [Evidence Level A-1].[8,22,d] The risk of intracranial hemorrhage was increased (NNH ~ 333) in INSPIRES wherein the window for initiation was 72 hours.[8] • Generally, limit the combination of aspirin plus clopidogrel to **not more than 21 days** to maximize benefits and minimize risks.[10,19,20] o Can consider using **ten days** instead of 21 days for patients at higher bleeding risk (e.g., taking an NSAID or anticoagulant).[19,20] o Can consider combination therapy for **up to 90 days** after stroke or TIA attributable to severe stenosis (70% to 99%) of a major intracranial artery if bleeding risk is low (based on SAMMPRIS study).[1,10] • After 21 days of combination therapy, continue EITHER aspirin or clopidogrel as monotherapy (aspirin 81 mg/day generally preferred).[8,19,20] • Avoid combining aspirin and clopidogrel in patients who have a major stroke, due to increased risk for intracranial bleeding.[19] Also, there are no safety data for short-term aspirin plus clopidogrel in patients who received alteplase.[2,22]	
Dipyridamole ER/aspirin (US)	LD: none[1] MD: Dipyridamole ER 200 mg/aspirin 25 mg BID[1]	• May prevent one more event (vascular death, stroke, MI, major bleed) for every 100 patients treated/year vs aspirin.[4] • Bleeding risk similar to aspirin.[4] • Twice-daily dosing. Expensive. One in four patients discontinue due to headache.[4] • Do not substitute **immediate-release** dipyridamole plus aspirin for the combo ER product; no proof it's as effective.	US: ~$60
Non-preferred options[1,3,10]			
SHORT-TERM aspirin plus ticagrelor (Brilinta) *Continued…*	**LD**: **Aspirin**: 300 to 325 mg; **Ticagrelor**: 180 mg **MD**: **Aspirin**: 75 to 100 mg/day **Ticagrelor**: 90 mg BID for 30 days	• Aspirin plus ticagrelor for 30 days prevents one stroke or death within 30 days compared to aspirin alone, NNT = 91 [Evidence Level A-1].[17] However, there is no significant impact on mortality alone or disability scores.[17] In addition, use for 30 days may cause one episode of severe bleeding (e.g., fatal bleeding, intracranial hemorrhage [most common], or other bleeding that caused hemodynamic compromise requiring intervention) compared to aspirin alone (NNH = 263) [Evidence Level A-1].[17]	US: ~$140 Canada: ~$25

Drug	Dose	Comments	Cost/30 days[a]
Non-preferred options, continued[1,3]			
SHORT-TERM aspirin plus ticagrelor, continued		○ Based on subgroup analysis of this study, ticagrelor could be added to aspirin for up to 30 days for patients with minor stroke or high-risk TIA with ≥30% stenosis of a major intracranial artery on the same side as the event.[1,10] ○ Note that ticagrelor ALONE (180 mg LD, followed by MD of 90 mg BID) for 90 days is NOT superior to aspirin (300 mg LD, followed by 100 mg daily) in preventing the combined endpoint of stroke, myocardial infarction (MI), or death within 90 days in minor stroke (NIHSS score[c] ≤5) or high-risk TIA (ABCD[2] score[b] ≥4) [Evidence Level A-1].[16] • There are no safety data for short-term aspirin plus ticagrelor in patients who received alteplase.[17] • If using aspirin plus ticagrelor, don't exceed 30 days and ideally start within 24 hours of:[17] ○ **High-risk TIA** (e.g., ABCD[2] score[b] ≥6). ○ **Minor ischemic stroke** (e.g., NIHSS score[c] ≤5). • May cause dyspnea.[17] • Twice-daily dosing. Expensive.	
Cilostazol (US only)	LD: none[3] MD: 100 mg BID[3]	• Better than no antiplatelet at all if patient cannot take aspirin or clopidogrel.[3]	~$35
Cilostazol plus aspirin or clopidogrel	LD: none MD: cilostazol 100 mg BID added to aspirin or clopidogrel (see comments)[1]	• Can consider adding cilostazol to aspirin or clopidogrel for patients with stroke or TIA due to 50% to 99% stenosis of a major intracranial artery.[1] ○ This recommendation is based on Level B-1 evidence in mostly Asian populations (TOSS-1, TOSS-2, CATHARSIS, CSPS).[1] • The role of cilostazol for secondary prevention after stroke due to small vessel disease needs more study.[1]	~$40

a. Pricing based on wholesale acquisition cost (WAC). US medication pricing by Elsevier, accessed May 2025.
b. See https://www.mdcalc.com/abcd2-score-tia.
c. See https://www.ninds.nih.gov/health-information/stroke/assess-and-treat/nih-stroke-scale.
d. NNH of 200 represents 90 days of aspirin plus clopidogrel. Risk may be lower with only ten to 21 days of dual-antiplatelet therapy.

Abbreviations: ACCP = American College of Chest Physicians; AHA = American Heart Association; ASA = American Stroke Association; BID = twice daily; ER = extended-release; GUSTO = Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries; LD = loading dose; MD = maintenance dose; NIHSS = National Institutes of Health Stroke Scale; TIA = transient ischemic attack.

Tips and Clinical Pearls about Antiplatelet Regimens

- About 5% of patients who have a minor ischemic stroke or transient ischemic attack will have another stroke within a year.[21] The risk is especially high in the first week.[10]
- The choice among aspirin, clopidogrel, or dipyridamole/aspirin should be individualized.[10]
- Dual antiplatelet therapy can be considered for certain patients, but only short-term.[1]
- If a patient has had a stroke or TIA despite aspirin therapy, switching to another antiplatelet agent can be considered.[10]
  - The risk of a recurrent stroke may be lower if these patients are switched to a different long-term antiplatelet, **especially in the first few days** after a stroke or TIA [Evidence Level B-2].[12] However, there is no proof that any agent is more effective than aspirin in these patients.[1,10]
  - There is no evidence that increasing the aspirin dose improves efficacy.[1]
  - Check adherence, screen for drug interactions that might reduce antiplatelet efficacy, consider atrial fibrillation, and optimize statin dose, blood pressure, and glycemic control.[9]
- For most patients who receive intravenous thrombolysis for stroke (e.g., alteplase), generally delay aspirin therapy for at least 24 hours, but consider comorbidities.[11]
- Prasugrel (Effient) is contraindicated in patients with a history of stroke or TIA due to increased risk of intracranial bleeding.[14,15]
- If a patient has a gastrointestinal (GI) bleed on aspirin, stop the aspirin and add a proton pump inhibitor (PPI).[13,24] Post-endoscopy, once hemostasis is acceptable, restart aspirin within seven days (ideally within three days, and immediately if rebleeding risk is low).[5,13,24]
- Do not use anticoagulants unless the patient has another indication for one (e.g., atrial fibrillation).[10]

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician 2004;69:548-56. https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html.]

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HIV Pre-Exposure Prophylaxis (PrEP)

Updated May 2025

Use this checklist to identify high-risk patients and safely prescribe and monitor HIV PrEP therapy.

1 Identify potential candidates.

- Talk about HIV PrEP with ALL sexually active adults and adolescents.[3] About 14% of people with HIV in the US and Canada are unaware that they are infected.[2,11]
- Be aware of high-risk activities (realizing that not all patients will openly share this information), including:[2,14,23]
  - having condomless sexual activity with multiple partners, especially men who have sex with men.
  - having condomless sexual activity with an HIV positive person (or whose HIV status is unknown) who is not on treatment or has a high viral load.
  - recent (within the previous six months) IV drug use, especially if sharing needles.
  - recent (within the previous six months) STIs (e.g., chlamydia, syphilis, gonorrhea).
  - having medical procedures in regions where HIV is endemic.

2 Screen potential candidates.

- Look for signs and symptoms of acute HIV infection (e.g., fever, night sweats).[1,14]
- Document a negative laboratory (preferred) antibody/antigen plasma HIV test and/or HIV-1 RNA assay.[1,14,15]
  - If suspicion is high for an acute HIV infection, repeat the HIV test in about a month to confirm a negative result before prescribing PrEP.[1]
  - All formulations used for PrEP carry boxed warnings for the development of drug-resistant HIV when used in HIV-positive patients.[1,8,9,20,27]
  - Note that testing recommendations differ if patients have recently been on PrEP or post-exposure prophylaxis (PEP) (three months for oral PrEP or PEP and twelve months for injectable cabotegravir).[15]
- Determine pregnancy and breastfeeding status and discuss risks and benefits.
- Screen for STIs, hepatitis B in all patients, and hepatitis C in high-risk patients.[1] (Note: data unavailable for PrEP with cabotegravir if coinfected with hepatitis B or C.[20,27])
- Complete other appropriate baseline monitoring (e.g., serum creatinine, lipids)

3 Be familiar with possible HIV **PrEP regimens**.

- Approved PrEP options for adults and adolescents ≥35 kg include:
  - **Truvada**, generics (emtricitabine [FTC] 200 mg/tenofovir disoproxil fumarate [TDF] 300 mg) orally once daily.[3,5,8,9] (In Canada, Truvada is only approved for use as PrEP in adults.[9])
  - **Descovy** (emtricitabine 200 mg/tenofovir alafenamide [TAF] 25 mg) orally once daily (select patient groups, see row "Consider high-risk behaviors").[3,19]
  - **cabotegravir** (Apretude) 600 mg IM (first two doses separated by four weeks, then continued every eight weeks; injected by a healthcare professional).[3](Note there is an optional four-week oral lead-in).[15,20,a]
- Usually consider an oral option as first-line PrEP (See considerations in the rows below).[15]
- Think of long-acting IM cabotegravir PrEP for patients who:[15]
  - have difficulty taking oral PrEP options.
  - prefer getting a shot every two months over taking daily oral PrEP.
  - have severe kidney impairment (CrCl <30 mL/min) (see row "Consider kidney function").

4 Consider **high-risk behaviors** when choosing a PrEP regimen.

- Truvada is a recommended PrEP option regardless of high-risk behaviors due to extensive experience, proven efficacy, and tolerability.[21]
- **Males or transgender females who have sex with males**:
  - IM cabotegravir has been shown to be more effective than Truvada in males, females, and transgender females who have sex with males.[4,26] Note that this difference in efficacy may be due to lack of adherence with oral regimens.[21]
- **Receptive vaginal sex**: Descovy is NOT approved for PrEP in this group due to lack of data.[17,18]
- **IV drug use**: Truvada is the preferred PrEP regimen, due to lack of data with Descovy and IM cabotegravier.[21]

5 Consider **kidney function** when choosing regimen.

- Ensure CrCl is:[5,8,9,15,17,18]
  - ≥60 mL/min (Truvada, when used for PrEP) OR ≥30 mL/min (Descovy)
- Consider IM cabotegravir in non-dialysis patients with severely impaired kidney function (CrCl ≥15 to <30 mL/min).[15,20,27]

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6 Consider **pregnancy and breastfeeding** status.

- Experts recommend use of Truvada as PrEP in pregnant or breastfeeding patients at high risk of HIV who have receptive vaginal sex, due to known safety and efficacy.[24]
- Human data are lacking to evaluate the dosing, efficacy, and safety of Descovy or IM cabotegravir in patients who are pregnant or breastfeeding and their use is not recommended.[17,18,24]
  - If patients taking IM cabotegravir become pregnant, the limited safety data and long half-life should be discussed during shared decision making with the patient to determine options. Expert consultation should be considered. Patients should be registered with the Antiretroviral Pregnancy Registry (US).[24]

7 **Consider** drug-drug **interactions**.

- Consider using the Liverpool HIV Drug Interactions website (https://www.hiv-druginteractions.org/checker) or HIV/HCV Drug Therapy Guide website (https://hivclinic.ca/app/#drugInt) to screen for drug-drug interactions.
- There may be an increase in tenofovir levels (and therefore adverse effects) when **Truvada** is used with certain hepatitis C meds (e.g., ledipasvir/sofosbuvir [Harvoni], velpatasvir formulations [Epclusa, Vosevi]).[8,9]
- Drugs that significantly induce uridine diphosphate glucuronosyltransferase (UGT) 1A1 (e.g., carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine) are **contraindicated with cabotegravir** due to decreased levels of cabotegravir.[20,27]
- Several meds (e.g., tipranavir/ritonavir, carbamazepine, phenobarbital, rifampin, St. John's wort) can decrease **tenofovir alafenamide** levels, possibly reducing PrEP effectiveness. Coadministration with Descovy is not recommended.[17,18]
- Emtricitabine and tenofovir are both excreted by the kidneys by (in part) active tubular secretion. Interactions with other meds excreted via active tubular secretion (e.g., acyclovir, cidofovir, gentamicin, high-dose or multiple nonsteroidal anti-inflammatory drugs [NSAIDs]) have not been observed; however, there is a risk of increased adverse effects with emtricitabine, tenofovir, or the interacting med, when used together, especially if there is kidney dysfunction.[8,9,17,18,22]

8 Consider **cost**. (See step 13, "Help patients afford PrEP.")

- Without insurance, PrEP costs:[b]
  - Truvada: US ~ $1,840 (brand) or ~ $30 (generic); Canada ~ $915 (brand) or ~ $475 (generic) for one month.
  - Descovy: ~ $2,200 (US); ~ $845 (Canada) for one month.
  - Apretude: ~$4,025 (US); ~$1,850 (Canada) per dose.

9 Determine if **on-demand oral PrEP** is an option.

- Non-daily PrEP or on-demand PrEP may also be referred to as "event-driven" or "intermittent" PrEP.[15]
- On-demand Truvada (not an FDA- or Health Canada-approved indication) may be considered for men who have sex with men.[5,12,13,15] (No data for on-demand Descovy.[13])
- On-demand Truvada (200 mg/300 mg) can be complicated. Use "2-1-1" to help patients with on-demand dosing:[5,12,13,15]
  - 2: take two tablets two to 24 hours prior to sexual exposure (closer to 24 hours is preferred).
  - 1: take one tablet 24 hours after the first dose.
  - 1: take one tablet 48 hours after the first dose.
- If the interval between the last dose of a 2-1-1 regimen and the next sexual encounter is:[13]
  - <7 days: take one tablet daily (every 24 hours) until 48 hours after the last sexual encounter.
  - ≥7 days: use the 2-1-1 regimen as described above.

10 **Monitor** patients receiving **oral** PrEP.

- Patients receiving oral PrEP should be seen at least every 90 days. Recommended monitoring includes:
  - Every three months:[15]
    - check HIV status.
    - screen for bacterial STI in men and transgender women who have sex with men with certain risk factors (e.g., multiple sex partners) (screen all patients per Canadian guidelines.[5])
    - test sexually active patients with signs or symptoms of STIs.
    - assess medication adherence and drug-drug interactions (See the row above "Consider drug-drug interactions").
    - provide access to clean needles and drug treatment services (patients who inject IV drugs).
    - check pregnancy status (patients with potential to become pregnant).[24]

Continued...

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10 **Monitor** patients receiving **oral** PrEP (continued).

- Every six months:[15]
  - assess kidney function for patients ≥50 years or with a CrCl <90 mL/min when PrEP was started (no specific recommendations in Canadian guidelines.[5]). Assess kidney function more often if there are additional risk factors.
  - screen for bacterial STI in all sexually active patients (every three months per Canadian guidelines.[5]).
- Every 12 months:[15]
  - assess kidney function for all patients (no specific recommendations in Canadian guidelines.[5])
  - screen for chlamydia in heterosexually active patients (not specifically addressed in Canadian guidelines.[5])
  - monitor weight, triglycerides, and cholesterol for patients taking Descovy PrEP (US).
  - screen for hepatitis C in patients at high-risk (e.g., patients who inject drugs, men who have sex with men).
- Bone mineral density decreases have been associated with tenofovir; however, monitoring is not necessary for most patients taking PrEP.[8,9,17,18]
  - Bone mineral density assessment may be considered for patients on Truvada with a history of fracture or with risk factors for osteoporosis.[8,9]
- Monitor liver function tests if patients become HIV positive and are coinfected with hepatitis B.
  - Stopping Descovy or Truvada in patients coinfected with hepatitis B and HIV can lead to acute hepatitis B exacerbations.[8,9,17,18]

11 **Monitor** patients receiving **IM cabotegravir** for PrEP.

- One month after the first injection: check HIV status.[15]
- Every two months (starting with the third injection [i.e., month 3 of therapy]):[15]
  - check HIV status
  - provide access to clean needles and drug treatment services for people who inject IV drugs
- Every four months (starting with the third injection [i.e., month 3 of therapy]):[15]
  - screen for bacterial STIs in men and transgender women who have sex with men.
- Every six months (starting with the fifth injection [i.e., month 7 of therapy]):[15]
  - screen for bacterial STIs in all heterosexually active patients.
- Every 12 months (starting one year after the first injection [i.e., month 13 of therapy]):[15]
  - evaluate patient's desire to continue cabotegravir for PrEP.
  - screen for chlamydia in heterosexually active men and women.
- When stopping IM cabotegravir, continue to check HIV status every three months for 12 months AND:[15]
  - discuss HIV prevention plans.
  - educate patients about the "tail" effect (i.e., slowly declining cabotegravir levels over many months) and the risk of developing drug-resistant HIV if the patient becomes infected with HIV during this time period.
  - start oral PrEP (if ongoing risk of HIV exposure) within eight weeks after the last cabotegravir injection.

12 **Counsel** patients.

- Tell patients who are initiating or restarting (e.g., after a hospital admission) oral PrEP how long it takes for drug levels to build up for maximal protection (i.e., ~7 days [rectal tissue], ~21 days [blood and vaginal tissue]).[1,3]
- Stress adherence. Missed doses are linked to reduced effectiveness.[1]
  - Oral Descovy or Truvada significantly reduce the risk of HIV [Evidence Level A-1] when taken on schedule.[1,12] For example, one case of HIV can be prevented by treating about 50 adults for four months to four years with emtricitabine/tenofovir disoproxil fumarate [Evidence Level B-2].[10]
  - There is a 14-day window for administering IM cabotegravir (i.e., injections can be given up to seven days BEFORE or AFTER the due date).[20,27]
    - If a patient knows they will miss an IM cabotegravir dose (e.g., due to a vacation), patients can take oral cabotegravir 30 mg (Vocabria [US], Apretude [Canada]) once daily (starting two months after the last injection) for two months to replace one missed dose of IM cabotegravir (see footnote a).[20,27]
    - For recommendations on unintentional missed doses, consult the product labeling for detailed instructions based on which injection is missed and how long it has been since the last injection.[20,27]
- Tell patients about possible adverse effects including diarrhea, nausea, abdominal pain, flatulence, headache, and weight loss. Reassure patients that most adverse effects often go away within days to weeks.[1,6]
- Encourage acetaminophen if patients need something for pain. If possible, patients should avoid high dose or multiple NSAIDs, due to potential to reduce kidney function.[8,9,17,18]
- Encourage safe sex practices, including condoms. PrEP only protects against HIV, not other STIs (or pregnancy).[1,15]

HIV Pre-Exposure Prophylaxis (PrEP)

Updated May 2025

13 Help patients **afford PrEP**.

- In the US, the Affordable Care Act requires plans and insurers to completely cover PrEP for patients at high risk of acquiring HIV including screening and laboratory testing, at least one medication, necessary monitoring, adherence counseling, and associated office visits.[25]
  - For patients without insurance, see if patients qualify for assistance:
    - NASTAD PrEP and PEP Assistance Programs (https://nastad.org/prepcost-resources/prep-assistance-programs).
    - manufacturers: https://www.gileadadvancingaccess.com, https://www.viivconnect.com/.
    - Centers for Disease Control and Prevention (CDC): https://www.cdc.gov/hiv/prevention/prep.html#cdc_prevention_pre-paying-for-prep.
    - See our chart, Guide for Helping Patients Afford Their Medications, for other possible resources.
- In Canada, for specific provincial and territorial coverage see: https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/diseases-conditions/summary-hiv-antiretroviral-medication-coverage/phac-drugcoveragedoc.pdf.

Footnotes:
a. Oral cabotegravir (Vocabria [US], Apretude [Canada]) is approved for short-term PrEP as optional lead-in therapy prior to the first cabotegravir injection (to help assess tolerability) or as temporary coverage (up to two months) for patients receiving IM cabotegravir if an injection is to be intentionally missed.[16,20,27]
b. Pricing based on wholesale acquisition cost (WAC).US medication pricing by Elsevier, accessed April 2025.

Abbreviations:
BMD = bone mineral density; CrCl = creatinine clearance; FTC = emtricitabine; HIV = human immunodeficiency virus; IM = intramuscular; IV = intravenous; PrEP = pre-exposure prophylaxis; STI = sexually transmitted infection; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate.

Levels of Evidence:
In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).
[Adapted from Ebell MH, Siwek J, Weiss BD, et al.Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician 2004;69:548-56. https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html.]

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HIV Postexposure Prophylaxis (PEP)

Updated May 2025

Following a potential exposure to human immunodeficiency virus (HIV), postexposure prophylaxis (PEP, nPEP [non-occupational PEP], or oPEP [occupational PEP]) can be used to reduce the risk of developing HIV infection.[1-3] Use this checklist to identify when and how to safely use PEP in adults. See our *Pre-Exposure Prophylaxis (PrEP) Checklist*, for info on pre-emptive meds in patients at risk of HIV exposure. The National Clinician Consultation Center can be used by US healthcare providers for clinical advice.[1]

1 Identify the type of exposure.

- **Occupational**: percutaneous (i.e., needle stick); mucous membrane; or non-intact skin exposure to blood, body fluids, or tissue that may contain HIV as a part of work-related duties.[4]
  - Considered potentially infectious with HIV:[3] cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids.
  - Considered potentially infectious with HIV **if visibly bloody**:[3] feces, nasal secretions, saliva, sputum, sweat, tears, urine, or vomitus.
- **Non-occupational**: exposure to blood and/or semen or vaginal secretions that may contain HIV through sexual activity or contaminated needles (e.g., sharing needles for injection drug use).[4]

2 Determine the need for PEP.

- Follow workplace protocols after potential **occupational exposures**.
- After all possible exposures (occupational and non-occupational) consider the following:[2,3]
  - Determine the HIV status of the potentially exposed AND source patients, if possible.
  - **Do not delay starting PEP while waiting for HIV test results**. PEP can be discontinued if the source patient is found to be HIV-negative.
  - Assess risk of transmission based on type of exposure and the source to see if PEP is appropriate.

What is the likelihood the source patient has transmissible HIV?[1,2]	**Type of Non-Occupational Exposure**		
	High-risk (e.g., receptive anal sex, needle sharing)[1,2]	**Moderate-risk** (e.g., insertive anal sex, insertive or receptive vaginal sex)[1,2]	**Low-risk** (e.g., giving or receiving oral sex, oral-anal contact, biting, spitting **without visible blood**)[1,2]
Substantial (e.g., source patient: HIV positive without sustained viral suppression)	Offer/start PEP		PEP is not recommended
Low (e.g., source patient: unknown HIV status)	Can consider offering/starting PEP on a case-by-case basis		
Negligible (e.g., source patient: HIV negative)	PEP is not recommended		

3 Select a PEP regimen.

- For most patients with occupational or non-occupational exposure without contraindications, the preferred regimens are:
  - US:[1] tenofovir alafenamide (TAF) 25 mg, emtricitabine 200 mg, and bictegravir 50 mg (Biktarvy), all once daily. This is a single-tablet once daily regimen.[8,10]
  - US:[1] dolutegravir 50 mg and (tenofovir disoproxil fumarate [TDF] 300 mg OR TAF 25 mg) and (emtricitabine 200 mg OR lamivudine 300 mg), all once daily.
  - Canada:[2] TDF 300 mg plus emtricitabine 200 mg (e.g., Truvada) once daily and (dolutegravir 50 mg once daily OR raltegravir 400 mg twice daily) OR (darunavir 800 mg once daily plus ritonavir 100 mg once daily).
- There are multiple alternate regimens that can be considered based on various patient factors (e.g., kidney or liver function, pregnancy, concurrent medications, previous exposure to antivirals):
  - for CrCl 30 to 49 mL/min, TAF is generally preferred over TDF.[1] Adjust dose of TDF, if using.[1]
  - for CrCl <30 mL/min, generally avoid TDF. When using, dose adjustment is needed for TDF or lamivudine. Consider consultation with an infectious disease expert.
  - for pregnant patients, the above (US) preferred regimens can be used.[1] Despite a previous report (2018) of an increased risk of neural tube defects with dolutegravir, current evidence does not support this association.[1,6,9]
  - see CDC guidelines for additional alternative regimens.[1]

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HIV Postexposure Prophylaxis (PEP)

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3 Select a PEP regimen (continued).

- Address possible drug-drug interactions.[3] To assess drug-drug interactions, use the Liverpool interaction checker (https://www.hiv-druginteractions.org) or HIV/HCV Drug Therapy Guide website (https://hivclinic.ca/app/#drugInt).
- Consider consulting an infectious disease expert (e.g., https://nccc.ucsf.edu/clinician-consultation/pep-post-exposure-prophylaxis/ or 888-448-4911), especially when selecting a PEP regimen for infants or children, pregnant patients, reduced kidney function, or concomitant medications, and to discuss alternative PEP options.[1] However, keep in mind that PEP must be started promptly and can be adjusted if necessary following consultation.[1]

4 Promptly start PEP in appropriate patients.

- Start PEP as early as possible after the exposure (ideally within 24 hours).[1] Initiation of PEP is not recommended more than 72 hours after exposure.[1] Do not delay the first dose awaiting test results.[1] Continue PEP for a total of 28 days.[1-3]

5 Counsel patients.

- Counsel ALL patients to avoid condomless sex, blood/tissue donations, pregnancy, and if possible, breastfeeding, especially during the first six to 12 weeks postexposure.[3]
- Counsel and refer appropriate patients to local resources to assist with avoiding high-risk behaviors (e.g., unprotected sex, sharing needles).[3]
- Stress adherence to PEP for the full 28 days of therapy and adherence to appropriate follow-up.[1-3]
- Counsel about potential PEP side effects (e.g., rash, insomnia, gastrointestinal upset).[1-3]
- Ask patients not to add new meds or supplements without checking with a pharmacist or prescriber.[3]

6 Evaluate patients and assess laboratory tests.

- Get BASELINE TESTS in all exposed patients, and if possible, from source patients including HIV antigen/antibody test, hepatitis B serology, and (for exposed patient only) kidney and liver function and pregnancy test (if applicable). If exposure was sexual/non-occupational, test exposed and source patients for hepatitis C, syphilis, gonorrhea, and chlamydia.[1-3]
  - HIV rapid (point-of-care) test should be done, if available, at baseline.
  - If the source patient is determined to be HIV-negative, PEP can be discontinued and no follow-up HIV testing for the exposed patient is needed.[3]
- Conduct follow-up tests in all exposed patients after exposure:[1-3] four to six weeks:(US only): HIV, kidney and liver function, and pregnancy and if exposure was sexual, syphilis, gonorrhea, and chlamydia; 12 weeks: HIV, hepatitis A and C (Canada only); six months: HIV (six-month HIV testing is only necessary if combination antigen/antibody testing is not used, or if patients acquire hepatitis C during exposure).
- Refer patients who test positive for HIV at baseline or during follow-up to an HIV specialist.[1-3]

7 Monitor patients.

- Follow monitoring recommendations as specified in product labeling for PEP regimen.
- Promptly evaluate patients who develop acute symptoms (e.g., rash, fever, hematuria, jaundice).[3]
- Assess the appropriateness of patients for PIP (PEP-in-pocket), where PEP is prescribed in advance for patients to have on hand in case of an unexpected HIV exposure. Consider PIP for patients with infrequent exposures (zero to four per year), the potential for unanticipated HIV exposures (e.g., patients at risk of nonconsensual sex [e.g., sex workers]), or limited access to urgent care. Patients should see their prescriber within one week of self-initiating PIP for HIV and STI testing.[8]
- Offer PrEP to patients who require frequent or recurrent courses of PEP, due to high-risk behaviors. PrEP can be started immediately after completing PEP.[1]

8 Help patients afford PEP.

- In the US, 28 days of PEP can range in cost ~$2,140 to $4,700, depending on the regimen chosen.[5]Insurance often covers PEP.Options to help with costs include:
  - Sexual assault patients may qualify to have some or all of their medicines and care covered.[7]See the CDC PEP site and US Department of Justice's resource directory for more information (https://www.justice.gov/ovw/resources-for-survivors).
  - PEP after occupational exposure is often covered by insurance or worker's compensation.
  - Patients may qualify for manufacturer assistance programs (i.e., Truvada [https://www.gileadadvancingaccess.com/financial-support/uninsured], Tivicay [https://www.viivconnect.com/patient/get-savings-information/tivicay/], or Isentress [https://www.merckhelps.com/isentress]).

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8 Help patients afford PEP (continued).

- In Canada, 28 days of PEP costs up to ~$1,200. For provincial and territorial coverage see https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/diseases-conditions/summary-hiv-antiretroviral-medication-coverage/phac-drugcoveragedoc.pdf.

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