Antiretroviral (ARV) Regimens

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SK HIV COLLABORATIVE

Regina Qu'Appelle HEALTH REGION

Acknowledgements

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Updated and reviewed annually and on an as needed basis to reflect current guidelines and information.

Abbreviations

NRTIs - Nucleoside Reverse Transcriptase Inhibitors

- **TDF** - Tenofovir disoproxil fumarate
- **TAF** - Tenofovir alafenamide
- **ABC** - Abacavir
- **3TC** - Lamivudine
- **FTC** - Emtricitabine

Not an exhaustive list of available ARVs

NNRTIs - Non-Nucleoside Reverse Transcriptase Inhibitors

- **RPV** - Rilpivirine
- **EFV** - Efavirenz

PIs - Protease Inhibitors

- **DRV** - Darunavir
- **ATV** - Atazanavir

Boosters

- **c** - Cobicistat
- **r** - Ritonavir

INSTIs - Integrase Strand Transfer Inhibitors ("Integrase Inhibitors")

- **RAL** - Raltegravir
- **EVG** - Elvitegravir
- **DTG** - Dolutegravir

Considerations

- This tool is not intended to replace sound clinical judgement
- Decisions about particular medical treatments should be made in consultation with an HIV pharmacist or ID specialist
- This tool reviews drug products that are available as components of an HIV treatment regimen. **Products are NOT necessarily a complete regimen on their own.**
    - Ensure regimens are complete by checking “Regimen Building Guidelines” or the DHHS Guidelines: https://aidsinfo.nih.gov/guidelines
- Saskatchewan Provincial Drug Plan (SPDP) requires antiretrovirals (ARVs) be used under in consultation with infectious diseases specialist for coverage
- Prices are taken from the Saskatchewan Online Formulary Database (does not include markup, dispensing fee, etc.): http://formulary.drugplan.health.gov.sk.ca/
- Drug interactions are not listed here. Consult HIV drug interaction databases:
    - http://app.hivclinic.ca/
    - http://hivinsite.ucsf.edu/insite?page=ar-00-02
- All drugs should be stored at room temperature **unless otherwise indicated**
- This tool does not contain an exhaustive list of available antiretroviral medications
    - Clinical use of ARVs may deviate from recommendations reflected here

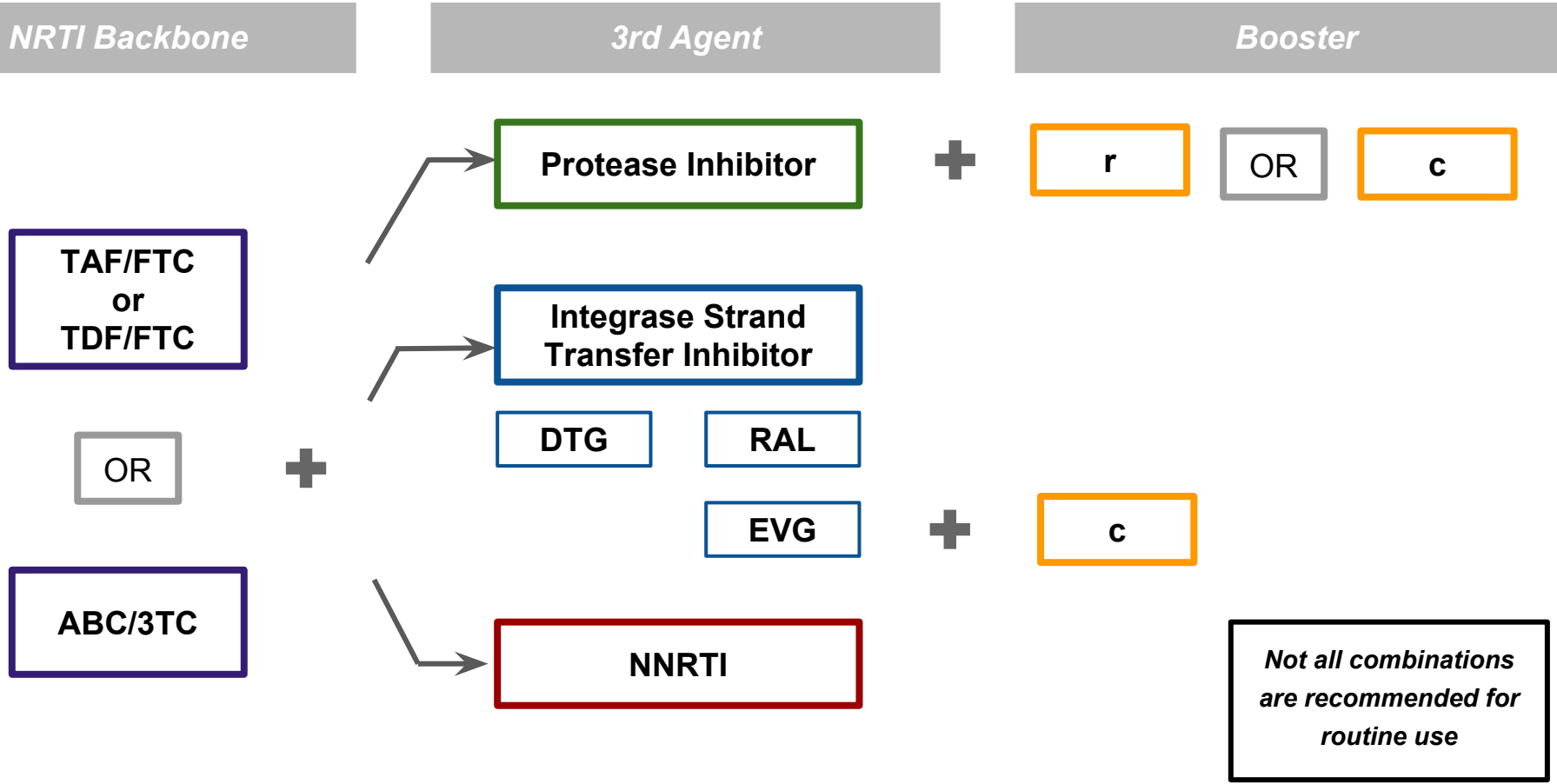
Considerations - Drug Coverage

- **Saskatchewan Provincial Drug Plan (SPDP)**: this tool includes EDS criteria for HIV positive, SPDP beneficiaries
  - Visit SPDP exeption drug status page for most current information: http://formulary.drugplan.health.gov.sk.ca/EDStProg.aspx
  - SPDP beneficiaries must enrol in the Special Support Program:
    - Income-tested program that provides a deductible/co-pay on an annual basis
    - Initial applicants and beneficiaries whose income or medication cost changes must apply for a reassessment with documentation of income changes. For more information and forms to apply visit: https://www.saskatchewan.ca/residents/health/prescription-drug-plans-and-health-coverage/extended-benefits-and-drug-plan/special-support-program

Considerations - Drug Coverage

- **Non-Insured Health Benefits (NIHB)**: this tool includes eligibility criteria for registered First Nations and recognized Inuit HIV patients
  - **Open Benefits**: do not have restriction criteria
  - **Limited Use Benefits**: have specific criteria for use; may require prior approval
  - **Prior Approvals**: require approval before coverage is applied
    - Contacting the Drug Exception Centre; require details about the prescription, the prescriber, the client and the pharmacy.
    - To complete Prior Approval process, the DEC may also fax an Exception or Limited Use Drugs Request Form to the prescriber for completion stating the medical need for the drug.
  - For moreinformation, visit the NIHB Drug Benefit List website: http://www.hc-sc.gc.ca/fniah-spnia/pubs/nihb-ssna/_drug-med/2016-prov-fourn-guide/index-eng.php#a23

Regimen Building Overview



DHHS Recommended Regimen Options

Demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.

INSTI + 2 NRTI Regimen:

- DTG/ABC/3TC - *if HLA-B*5701 negative*
- DTG + either TDF/FTC *or* TAF/FTC
- EVG/c/TAF/FTC *or* EVG/c/TDF/FTC
- RAL + either TDF/FTC *or* TAF/FTC

Boosted PI + 2 NRTIs:

- DRV/r + either TDF/FTC *or* TAF/FTC

Legend:

- NRTIs
- NNRTIs
- Protease Inhibitors
- Integrase Inhibitors
- Boosters
- Take on empty stomach
- Separate from antacids
- Not a complete regimen

DHHS Alternative Regimen Options

Effective and tolerable, but have potential disadvantages when compared with Recommended regimens, have limitations for use in certain patient populations, or have less supporting data from randomized clinical trials. However, an Alternative regimen may be the preferred regimen for some patients.

NNRI + 2 NRTIs:

- EFV/TDF/FTC
- EFV + TAF/FTC
- RPV/TDF/FTC *or* RPV/TAF/FTC - *if HIV RNA <100,000 copies/mL and CD4 >200 cells/mm^3*

Boosted PI + 2 NRTIs:

- (ATV/c** *or* ATV/r) + either TDF/FTC *or* TAF/FTC
- DRV/c *or* DRV/r + ABC/3TC - *if HLA-B*5701 negative*
- DRV/c + either TDF/FTC *or* TAF/FTC

** Not available in Canada

NRTI Backbone Options

*All adult DHHS-recommended regimens are built with a dual-NRTI backbone - one of **TDF/FTC**, **TAF/FTC**, or **ABC/3TC** should be included in all regimens**

*some exceptions apply, but should only be considered under the guidance of an HIV specialist

Ingredients	Trade Name/ Manufacturer (Strength)	Dosing	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Emtricitabine /Tenofovir **disoproxil fumarate** (FTC/**TDF**) 	**Truvada®** Gilead Sciences Canada Inc (200mg/300mg)	1 tablet ONCE daily Renal dysfunction: 30-49 mL/min = 1 tab Q 48 H Less than 30 mL/min = do not use Liver dysfunction: No adjustment required Refer to PrEP section for prophylaxis dosing	$27.70 ($831.09)	+/- food May split tablets or crush & stir into water or juice.	Common (>10%): Headache, insomnia Rash ↑lipids N/V/D ↓bone density 1-10%: Fatigue ↑SCr, renal failure	Severe exacerbations of HBV can occur if therapy interrupted Drug interaction potential: Inhibitor: TDF: CYP1A2 (weak) FTC: N/A Inducer: TDF: N/A FTC: N/A Substrate: TDF:P-gp FTC:N/A	**SPDP**: EDS (HIV treatment or post-exposure prophylaxis) **NIHB**: Open Benefit *Coverage available through* ***manufacturer co-pay assistance program***

Not a complete regimen - must be prescribed with a third agent +/- booster

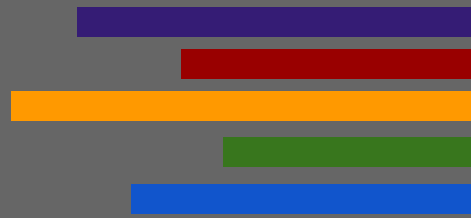
Ingredients	Trade Name/ Manufacturer (Strength)	Dosing	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Emtricitabine/ Tenofovir **alafenamide** (FTC/**TAF**) 	**Descovy®** Gilead Sciences Canada Inc (200mg/25mg) in regimens **NOT containing** ritonavir or cobicistat* (200mg/10mg) in regimens **containing** ritonavir or cobicistat* *200/25mg is safe, when coadministered *with* booster; Potential error risk for 200/10mg to be given *without* booster	1 tablet ONCE daily Renal dysfunction: Less than 30 mL/min = not recommended Liver dysfunction: Child-Pugh A&B = no adjustment Child-Pugh C = not recommended *Not indicated for PrEP*	Not yet listed on Sask Formulary	+/- food Do not crush (no data)	1-10%: Fatigue Nausea Less effect on bone density than TDF ↑lipids	Similar efficacy to TDF with less bone and renal toxicity Severe exacerbations of HBV if therapy interrupted Drug interaction potential:low Inhibitor: TAF:1A2 (weak) FTC:N/A Inducer: TAF:N/A FTC:N/A Substrate: TAF:P-gp FTC:N/A	**SPDP**: Not yet listed on Sask Formulary **NIHB**: Not covered *Coverage available through* ***manufacturer co-pay assistance program***

Not a complete regimen - must be prescribed with a third agent +/- booster

Ingredients	Trade Name/ Manufacturer (Strength)	Dosing	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Abacavir/ Lamivudine (ABC/3TC) 	**Kivexa®** ViiV Healthcare ***Generic Available*** (600mg/300mg)	1 tablet ONCE daily Renal dysfunction: Less than 50 mL/min = not recommended *(Use dose adjusted individual products:* *ABC = no adjustment required* *3TC = dose adjust based on estimated ClCr or dialysis)* Liver dysfunction: Child-Pugh B&C = contraindicated	Brand: $24.32 ($729.83) Generic: $5.98 ($179.63)	+/- food Tablet may be split or crushed and added to a small amount of food or water.	1-10%: Abnormal dreams, insomnia Migraine Fatigue Hypersensitivity reaction* - can be fatal (fever, rash, N/V/D, dyspnea, others)	*Risk increased if HLA-B*5701 gene present - must test before initiating ABC Severe exacerbations of HBV if therapy interrupted Drug interaction potential: low Inhibitor: ABC: N/A 3TC: N/A Inducer: ABC: N/A 3TC: N/A Substrate: ABC: N/A 3TC: N/A	**SPDP**: EDS (management of HIV) **NIHB**: Open Benefit

Not a complete regimen - must be prescribed with a third agent +/- booster

Recommended Regimens



INSTI + 2 *NRTI* Regimen

Boosted PI+ 2-*NRTI* Regimen

INSTI + 2 NRTI Regimen

Ingredients	Trade Name/ Manufacturer (Strength)	Dosing	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Dolutegravir (DTG) 	**Tivicay™** ViiV Healthcare (50mg)	1 tablet ONCE daily **Dosage adjustment for concomitant rifampin, carbamazepine, phenytoin, or phenobarbital:** Increase DTG dose to 50mg BID Renal dysfunction: No adjustment required in treatment-naive patients (caution in treatment-experienced as drug levels decreased with potential for viral breakthrough) Liver dysfunction: Child-Pugh C = not recommended	$18.87 ($566.10)	+/- food Tablets may be crushed and added to a small amount of food or liquid	Common (>10%): Hypeglycemia ↑liver enzymes 1-10%: Insomnia, depression, suicide ideation Frequency not defined: Benign ↑ SCr (not true decreases in GFR) - do not dose adjust other meds *Caution if SCr ↑ by 30µmol/L Well tolerated but higher rates of stopping for intolerance reported post-market than in clinical trials (arthralgia, CNS, depression, fatigue)	Separate from **antacids** - take 2 h before or 6h after medications containing Mg, Al, Fe, or Ca (if taken with food, can take at same time as calcium and iron supplements) Drug interaction potential:low Inhibitor: N/A Inducer: N/A Substrate: CYP3A4 (minor), P-gp	**SPDP**: EDS (HIV management in pts >12years old or post-exposure prophylaxis) **NIHB**: Open Benefit

Not a complete regimen - must be prescribed with 2 NRTIs (**TDF/FTC** or **TAF/FTC** or **ABC/3TC**)

Ingredients	Trade Name/ Manufacturer (Strength)	Dosing	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Dolutegravir / Abacavir/ Lamivudine (DTG/ABC/ 3TC) 	**Triumeq®** ViiV Healthcare (50mg/600mg/ 300mg)	1 tablet ONCE daily **Dosage adjustment for concomitant rifampin, carbamazepine, phenytoin, or phenobarbital:** Increase DTG dose to 50mg BID (ie: add Tivicay 50 mg) Less than 50 mL/min = not recommended *(Use dose adjusted individual products: DTG = no adjustment ABC = no adjustment 3TC = adjust < 50 mL/min)* Liver dysfunction: Child-Pugh B&C = contraindicated	$42.50 ($1275.02)	+/- food Tablets may be crushed and added to a small amount of food or liquid Separate from **antacids** - take 2 h before or 6h after medications containing Mg, Al, Fe, or Ca (if taken with food, can take at same time as calcium and iron supplements)	Common (>10%): Hyperglycemia (≥7 mmol/L) ↑serum lipase, ↑CK 1-10%: Insomnia, Abnormal dreams Depression, suicide ideation Migraine Fatigue **Hypersensitivity reaction* - can be fatal** (fever, rash, N/V/D, dyspnea, others) Benign ↑ SCr (not true decreases in GFR) - do not dose adjust other meds *Caution if SCr ↑ by 30µmol/L	*Risk increased if HLA-B*5701 gene present - must test before initiating ABC Severe exacerbations of HBV if therapy interrupted Drug interaction potential:low Inhibitor: N/A Inducer: N/A Substrate: Not metabolized by CYP enzymes	**SPDP**: EDS (management of HIV in adults) **NIHB**: Prior Approval *Coverage available through **manufacturer co-pay assistance program***

- Some patients may choose to take **DTG** (Tivicay™) with **ABC/3TC** separately to save on costs
  - **Cost of Triumeq®/day**: $42.5007 ($1275.02)
  - Cost of Tivicay™ + Kivexa®/day: $43.1977 ($1295.91)
  - **Cost of Tivicay™ + generic ABC/3TC/day**: $24.8575 ($745.73) - *least costly option*

Ingredients	Trade Name/ Manufacturer (Strength)	Dosing	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Elvitegravir/ cobicistat/ **Tenofovir disoproxil fumarate**/ Emtricitabine (EVG/c/**TDF**/ FTC) 	**Stribild®** Gilead Sciences Canada Inc (150mg/150mg / 300mg/200mg)	1 tablet ONCE daily Renal dysfunction: Less than 70 mL/min = do not initiate Less than 50 mL/min = discontinue Liver dysfunction: Child-Pugh C = not recommended	$45.52 ($1365.60)	Take with food Do not crush	Common (>10%): Nausea/diarrhea Proteinuria Benign ↑ SCr (not true decreases in GFR) - do not dose adjust other meds but caution if SCr ↑ by 30µmol/L 1-10%: Fatigue Headache Abnormal dreams Rash ↑lipids ↑CK ↓bone density	Separate from **antacids** by at least 2 hours Severe exacerbations of HBV if therapy interrupted Drug interaction potential:high Inhibitor: EVG:N/A C:3A4 (strong), 2D6 (weak) TDF:1A2 (weak) FTC:N/A Inducer: EVG:2C9 (weak-mod) C:N/A TDF:N/A FTC:N/A Substrate: EVG:3A4 (major) C:3A4 (major) TDF:P-gp FTC:N/A	**SPDP**: EDS (as a complete regimen for antiretroviral treatment-naïve HIV-1 pts in whom efavirenz is not indicated) **NIHB**: Open Benefit *Coverage available through **manufacturer co-pay assistance program***

Ingredients	Trade Name/ Manufacturer (Strength)	Dosing	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Elvitegravir/ cobicistat/ **Tenofovir alafenamide**/ Emtricitabine (EVG/c/**TAF**/ FTC) 	**Genvoya®** Gilead Sciences Canada Inc (150mg/150mg/ 10mg/200mg)	1 tablet ONCE daily Renal dysfunction: Less than 30 mL/min = not recommended Liver dysfunction: Child-Pugh C = not recommended	Not yet listed on Sask Formulary	Take with food Do not split or crush	1-10%: Headache Fatigue Nausea, diarrhea Less effect on bone density than TDF ↑lipids Frequency not defined: Benign ↑ SCr (not true decreases in GFR) - do not dose adjust other meds *Caution if SCr ↑ by 30µmol/L	Severe exacerbations of HBV if therapy interrupted Separate from **antacids** by at least 2 hours Drug interaction potential:high Inhibitor: EVG:N/A C:3A4 (strong), 2D6 (weak) TAF:N/A FTC:N/A Inducer: EVG:2C9 (weak-mod) C:N/A TAF:N/A FTC:N/A Substrate: EVG:3A4 (major) C:3A4 (major) TAF:P-gp FTC:N/A	**SPDP**: Not yet listed on Sask Formulary **NIHB**: Prior Approval *Coverage available through **manufacturer co-pay assistance program***

Ingredients	Trade Name/ Manufacturer (Strength)	Dosing	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Raltegravir (RAL) 	**Isentress®** Merck Canada Inc. (400mg) 1200mg QD coming in 2017	1 tablet TWICE daily (ONCE daily tablet coming to market) **Dosage adjustment for concomitant rifampin**: Increase RAL dose to 800mg BID Renal dysfunction: No adjustment required Liver dysfunction: Child-Pugh C = not recommended	$27.81 ($834.30)	+/- food Do not crush (tablets)	Common (>10%): ↑ ALT (higher if HCV or HBV coinfection) 1-10%: Insomnia Headache ↑blood glucose ↑ALT, serum lipase Abnormal neutrophil count Thrombocytopenia	Separate from **antacids** containing Al or Mg (Ca -antacids are fine) Drug interaction potential:low Inhibitor: N/A Inducer: N/A Substrate: UGT	**SPDP**: EDS (treatment of HIV-1 in treatment-experienced pts resistant to 3 classes of HIV agent or for post-exposure prophylaxis) **NIHB**: Limited use benefit - Prior Approval required (HIV treatment in ARV-experienced pts and have virologic failure due to resistance to at least 1 NRTI, NNRTI, and PI or for HIV post-exposure prophylaxis in combination with Truvada)

Not a complete regimen - must be prescribed with 2 NRTIs (**TDF/FTC** or **TAF/FTC** or **ABC/3TC**)

Boosted PI+ 2-NRTI Regimen

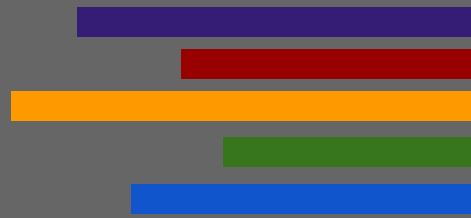
Ingredients	Trade Name/ Manufacturer (Strength)	Dosing	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Darunavir (DRV)   	**Prezista®** Janssen Inc. (600mg, **800**mg) Other doses available (not generally used): 75mg, 150mg, 400mg	800mg Prezista/100mg ritonavir ONCE daily DRV resistant mutations: 600mg Prezista/100mg ritonavir TWICE daily Renal dysfunction: No adjustment required Liver dysfunction: Child-Pugh C = not recommended	$21.7160 ($651.48) + $1.5037/day for ritonavir **= $23.2197 ($696.591)** BID dosing: $31.5698 ($947.094) + $1.5037/day for ritonavir **= $33.0735 ($992.205)**	Take with food (+ full glass of water or milk) Manufacturer says do not crush, but likely okay	Common (>10%): ↑ lipids N/V/D Rash 2-10%: Headache Fatigue ↑blood glucose ↑ALT/AST, serum lipase	Drug interaction potential:high Inhibitor: 3A4 (strong), 2D6 (mod) Inducer: N/A Substrate: 3A4 (major), P-gp	**SPDP**: EDS (HIV treatment or post-exposure prophylaxis) **NIHB**: Open Benefit

Not a complete regimen - must be prescribed with 2 NRTIs (**TDF/FTC** or **TAF/FTC**) and a booster (ritonavir)

Ingredients	Trade Name/ Manufacturer (Strength)	Dosing	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Darunavir/ Cobicistat (DRV/c) 	**Prezcobix®** Janssen Inc. (800mg/150mg)	1 tablet ONCE daily Renal dysfunction: No adjustment required Liver dysfunction: Child-Pugh C = not recommended	$23.867 ($716.01)	Take with food Do not crush or split	1-10%: Headache Fatigue N/V/D ↑blood glucose ↑liver enzymes Rash Frequency not defined: Benign ↑ SCr (not true decreases in GFR) - do not dose adjust other meds *Caution if SCr ↑ by 30µmol/L	Drug interaction potential:high Inhibitor: DRV:3A4 (strong), 2D6 (mod) c:3A4 (strong), 2D6 (weak) Inducer: DRV:N/A c:N/A Substrate: DRV:3A4 (major), P-gp c:3A4 (major)	**SPDP**: EDS (treatment of HIV in pts without darunavir resistance) **NIHB**: Open benefit

Not a complete regimen - must be prescribed with 2 NRTIs (**TDF/FTC**, **TAF/FTC**, or **ABC/3TC**)
Note: Although listed in the DHHS Guidelines as “Alternative Therapy”, Prezcobix (DRV/c) is commonly used first line in Saskatchewan due to lower pill burden than Prezista and Norvir (DRV/r)

Alternative Regimens



NNRTI+ 2-NRTI Regimen

Boosted PI+ 2-NRTI Regimen

NNRTI+ 2-NRTI Regimen

Ingredients	Trade Name/ Manufacturer (Strength)	Regimen	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Efavirenz (EFV) 	**Sustiva®** Bristol-Myers Squibb ***Generic Available*** (50mg, 200mg, **600**mg)	600 mg ONCE daily **Dosage adjustment for concomitant rifampin** (if patient weighs ≥50 kg): Increase efavirenz dose to 800 mg once daily. **Dosage adjustment for concomitant voriconazole**: Reduce efavirenz dose to 300 mg once daily and increase voriconazole to 400 mg every 12 hours Renal dysfunction: No adjustment required Liver dysfunction: Child-Pugh B&C = not recommended	**Brand (600mg)**: $15.21 ($456.37) **Generic (600mg)**: $3.80 ($114.09)	Take on empty stomach (1h before or 2h after meals) to avoid CNS adverse effects Dose at HS preferable to avoid CNS adverse effects Do not crush tablets, but can sprinkle contents of capsules	Common (>10%): Dizziness Fever Depression, insomnia ↑lipids Cough Rash 1-10%: Fatigue, ↓concentration, abnormal dreams ↑blood glucose ↑liver enzymes	Drug interaction potential:high Inhibitor: 2C9 (mod), 2B6 (mod) Inducer: 3A4 (mod), 2B6 (mod), 2C19 (weak) Substrate: 3A4 (major), 2B6 (major)	**SPDP**: EDS (management of HIV) **NIHB**: Open Benefit

Not a complete regimen - must be prescribed with 2 NRTIs (**TDF/FTC** or **TAF/FTC** or **ABC/3TC**)

Ingredients	Trade Name/ Manufacturer (Strength)	Dosing	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Efavirenz/ Emtricitabine /Tenofovir disoproxil fumarate (EFV/**TDF**/ FTC) 	**Atripla®** Bristol-Myers Squibb and Gilead Sciences Llc (600mg/ 200mg/ 300mg)	1 tablet ONCE daily **Dosage adjustment for concomitant rifampin** or **voriconazole**: see "Sustiva®" for dosing Renal dysfunction: Less than 50 mL/min = not recommended (*Use dose adjusted individual products:* *EFV = no adjustment* *TDF = adjust < 50 mL/min* *FTC = adjust < 50 mL/min)* Liver dysfunction: Child-Pugh B&C = not recommended	$42.92 ($1287.46)	Take on empty stomach (1h before or 2h after meals) preferably before bed to reduce incidence of adverse events. Do not split or crush - Bioequivalence not demonstrated	Common (>10%): ↑lipids 1-10%: Fatigue, abn dreams, insomnia Depression, ↓concentration, ↑blood glucose ↑liver enzymes Upper resp infection Rash	Severe exacerbations of HBV if therapy interrupted Drug interaction potential:high Inhibitor: EFV: 2C9 (mod), 2B6 (mod) TDF:1A2 (weak) FTC:N/A Inducer: EFV: 3A4 (mod), 2B6 (mod), 2C19 (weak) TDF:N/A FTC:N/A Substrate: EFV: 3A4 (major), 2B6 (major) TDF:P-gp FTC:N/A	**SPDP**: EDS (treatment of HIV-1 if: (a) replacing existing therapy with component drugs, or (b) patient is treatment naive, or (c) patient cannot tolerate other options) **NIHB**: Open Benefit

Ingredients	Trade Name/ Manufacturer (Strength)	Regimen	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Rilpivirine (RPV) 	**Edurant®** Janssen Inc. (25mg)	1 tablet ONCE daily **Dosage adjustment for concomitant rifabutin**: Increase rilpivirine dose to 50mg once daily. Renal dysfunction: No adjustment required Liver dysfunction: Child-Pugh C = not recommended	$15.02 ($450.46)	Take with normal to high calorie meal: absorption increased by ~40% Protein and liquid meal replacements not sufficient for absorption Do not crush or split	Common (>10%): Headache, insomnia Depression ↑liver enzymes Adrenal insufficiency 1-10%: Dizziness Abnormal dreams, fatigue	Contraindicated in naive patients with viral load **>100,000** due to increased risk of treatment failure Separate from antacids - take antacids 2h before or 4h after rilpivirine; Contraindicated with PPIs Drug interaction potential:high Inhibitor: N/A Inducer: N/A Substrate: RPV: 3A4 (major)	**SPDP**: EDS (management of HIV) **NIHB**: Open Benefit

Not a complete regimen - must be prescribed with 2 NRTIs (**TDF/FTC** or **TAF/FTC** or **ABC/3TC**)

Ingredients	Trade Name/ Manufacturer (Strength)	Dosing	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Rilpivirine/ Tenofovir disoproxil fumarate/ Emtricitabine (RPV/ **TDF**/ FTC) 	**Complera®** Gilead Sciences Canada Inc (200mg/25mg/ 300mg)	1 tablet ONCE daily **Dosage adjustment for concomitant rifabutin**: Increase rilpivirine dose to 50mg once daily Renal dysfunction: Less than 50 mL/min = not recommended Liver dysfunction: Child-Pugh C = not recommended	$41.91 ($1257.42)	Take with food Do not crush or split Protein and liquid meal replacements not sufficient for absorption	Common (>10%): ↑lipids ↑liver enzymes 1-10%: Headache, insomnia Depression, ↑serum creatinine	Contraindicated in naive patients with viral load **>100,000** due to increased risk of treatment failure Separate from antacids - take antacids 2h before or 4h after rilpivirine; Contraindicated with PPIs Drug interaction potential:high Inhibitor: RPV:N/A TDF:1A2 (weak) FTC:N/A Inducer: RPV: N/A TDF:N/A FTC:N/A Substrate: RPV: 3A4 (major) TDF:P-gp FTC:N/A	**SPDP**: EDS (treatment of HIV-1 in antiretroviral treatment-naïve patients, or to replace the 3 components given as dual or triple therapy) **NIHB**: Open Benefit

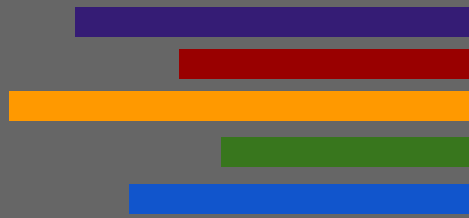
Ingredients	Trade Name/ Manufacturer (Strength)	Dosing	Cost/day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Rilpivirine/ Emtricitabine / Tenofovir alafenamide (RPV/ FTC/ **TAF**) 	**Odefsey®** Not available in Canada	1 tablet ONCE daily **Dosage adjustment for concomitant rifabutin**: Increase rilpivirine dose to 50mg once daily. Renal dysfunction: Less than 30 mL/min = not recommended Liver dysfunction: Child-Pugh C = not recommended	Awaiting pricing through pan-Canadian Pharmacuetical Alliance	Take with food Do not crush or split Protein and liquid meal replacements not sufficient for absorption	Common (>10%): Headache, insomnia Depression ↑liver enzymes Adrenal insufficiency 1-10%: Dizziness Abnormal dreams, fatigue ↑lipids	Contraindicated in naive patients with viral load **>100,000** due to increased risk of treatment failure Separate from antacids- take antacids 2h before or 4h after rilpivirine; Contraindicated with PPIs Drug interaction potential:high Inhibitor: RPV:N/A TAF:1A2 (weak) FTC:N/A Inducer: RPV:N/A TAF:N/A FTC:N/A Substrate: RPV:3A4 (major) TAF:P-gp FTC:N/A	**SPDP**: Not yet listed **NIHB**: Not yet listed *Coverage available through **manufacturer co-pay assistance program***

Boosted PI+ 2-NRTI Regimen

Ingredients	Trade Name/ Manufacturer (Strength)	Dosing	Cost/Day (30 days)	Administration	Adverse Effects	Therapy Considerations	Coverage
Atazanavir (ATV) 	**Reyataz®** Bristol-Myers Squibb (150mg, 200mg, **300**mg)	300mg Reyataz/ 100mg ritonavir <u>ONCE</u> daily Alternative: 400 mg once daily in patients *unable to tolerate ritonavir* **Dosage adjustment for concomitant PPI**: increase ATV dose to 400mg with 100mg of ritonavir (if PPI is absolutely necessary) <u>Renal dysfunction:</u> No adjustment required in non-dialysis Dialysis, treatment naive = 300mg/100 mg daily Dialysis, treatment experienced = avoid <u>Liver dysfunction:</u> Child-Pugh C = not recommended	300mg: $22.433 ($672.99)	Take with food (enhances absorption) Capsule contents may be sprinkled into applesauce and taken with meal	<u>Common (>10%)</u>: Nausea Cough ↑ lipids, liver function tests Rash ↑ CK <u>1-10%</u>: Headache Fatigue N/V/D ↑blood glucose ↑liver enzymes Rash	Separate from antacids- take ATV 2h before or 1h after antacids Coadministration with PPIs not recommended Drug interaction potential:high <u>Inhibitor:</u> 3A4 (strong), 2C9 (weak), 1A2 (weak) <u>Inducer:</u> N/A <u>Substrate:</u> 3A4 (major)	**SPDP**: EDS (HIV treatment or post-exposure prophylaxis) **NIHB**: Open Benefit

Not a complete regimen - must be prescribed with 2 NRTIs (**TDF/FTC** or **TAF/FTC**) and a **booster** (ritonavir or cobicistat)

Prophylaxis



Pre-Exposure Prophylaxis (PrEP)
Post-Exposure Prophylaxis (PEP)

Considerations - *Pre-Exposure Prophylaxis* ***(PrEP)***

- PrEP should be part of a **combination prevention strategy** that includes behavioural interventions such as **condoms** and **risk reduction counseling** - Frequent screening for HIV and other STIs at baseline, one month and every three months
- Can be considered in: 1) HIV negative men who have sex with men (MSM) & transgender women (TGW): who report condomless anal sex (esp. non-closed relationships, sex with HIV positive individuals who have significant risk of transmission, report of bacterial STIs) 2) Serodiscordant heterosexual couples where HIV positive partner has significant risk of transmission 3) Injection drug users (preferably after other harm reduction strategies have been implemented)
- Consider adherence, toxicities, and other risk reduction strategies

Ingredients	Trade Name/ Manufacturer (Strength)	PrEP Regimen	Cost/Day (30 days)	Food/ Crush	Adverse Effects	Special Considerations	Coverage
Emtricitabine/ Tenofovir **disoproxil fumarate** (FTC/TDF) 	**Truvada®** Gilead Sciences Canada Inc (200 mg/300 mg)	**Scheduled**: 1 tablet ONCE daily or **On Demand**: start 2 tab STAT 2-24 hours before exposure, then continue 1 tab OD until 48h after exposure	$27.70 ($831.09)	+/- food May split tablets or crush & stir into water, or juice.	Common (>10%): Headache, insomnia Rash ↑lipids N/V/D ↓bone density 1-10%: Fatigue ↑SCr, renal failure	**See Truvada under "Recommended Regimens" for more information**	**SPDP**: Not covered for PrEP **NIHB**: Open Benefit

Considerations - *Post-Exposure Prophylaxis* ***(PEP)***

- PEP is combination antiretroviral therapy used for 28 days to reduce risk of HIV infection after a potential exposure
- PEP should be started in HIV-negative people who have had recent exposure that is moderate to high risk for HIV transmission where the source is believed to have significant risk of having transmissible HIV
- PEP should be initiated as soon as possible after exposure, up to a **maximum of 72 hours** afterwards
- Saskatchewan emergency rooms contain 'PEP Kits' containing a 72 hour supply. Individuals who are given kits must follow up with an infectious disease specialist within 72 hours for evaluation and follow up.
    - Kits contain Kaletra® (LPV/r) + Combivir® (AZT/3TC) and are dosed twice daily
- PEP is available to patients ***at no cost*** - EDS criteria should be indicated on prescription as follows: *"When prescribed by, or on the advice of an Infectious Disease specialist familiar with HIV treatment for post-exposure prophylaxis (PEP)."*
    - Please refer to the HIV PEP Treatment document on the Saskatchewan Formulary website.

NRTI Backbone	***3rd Agent*** (other regimens may be considered)
FTC/TDF (once daily) 	**RAL** (twice daily) 
or	**DRV/r** (once daily) [DRV/c may be used]  or []
AZT/3TC (twice daily) [alternative for renal impairment] 	**DTG** (once daily) 

Special Populations

Pregnancy
Renal impairment

Pregnancy

- **Pregnancy**:regimen of 2 **NRTIs** + **INSTI** or **ritonavir**-boosted **PI** is preferred
  - Women who are already on a fully suppressive regimen should generally continue

	NRTIs	NNRTIs	Boosted PIs	INSTIs
Preferred	**ABC/3TC** • Well tolerated in pregnancy **TDF + [FTC or 3TC]** • Claims of bone & growth abnormalities in exposed infants require further evaluation		**ATV/r** **DRV/r**	**RAL** • Benign elevation of liver transaminases in mother in late pregnancy, which seem to resolve after stopping drugs
Alternative	**AZT/3TC** • Higher rates of mild-mod adverse effects	**EFV** • Associated with dizziness, fatigue, vivid dreams/nightmares, increased suicide risk	**Lopinavir/r** • Extensive clinical experience, but BID dosing & causes nausea/diarrhea	
Insufficient Data		**RPV**		**DTG *[likely okay]*** **EVG/c**
Not Recommended		**Nevirapine** **Etravirine**		

Renal failure

- **Renal failure (ClCr <60 mL/min):**
  - NRTI backbone: avoid **TDF/FTC,** use **TAF/FTC** or **ABC/3TC**

Estimated ClCr	NRTIs	INSTIs	Boosted PIs	NNRTIs
30-49 mL/min	**TDF** • 300 mg q48h **TAF** • No adjustment required **FTC** • 200 mg q48h **ABC** • No adjustment required **3TC** • 150 mg q24h	**DTG** • No adjustment required in treatment-naive • Caution in treatment-experienced **EVG** • No adjustment required **RAL** • No adjustment required	**ATV/r** • No adjustment required **DRV/r** • No adjustment required • Not recommended < 70 mL/min if used with TDF	**EFV** • No adjustment required **NVR** • No adjustment required **RPV** • No adjustment required
	Truvada = CI < 50 mL/min **Kivexa = CI < 50 mL/min**	**Triumeq = CI < 50 mL/min** **Stribild = CI < 50 mL/min**		**Atripla = CI < 50 mL/min** **Complera = CI < 50 mL/min**
15-29 mL/min	**TDF** • 300 mg twice weekly **TAF** • Do not use (limited data) **FTC** • 200 mg q72h **ABC** • No adjustment required	**DTG** • No adjustment required in treatment-naive • Caution in treatment-experienced **EVG** • No adjustment required **RAL** • No adjustment required	**ATV/r** • No adjustment required **DRV/r** • No adjustment required	**EFV** • No adjustment required **NVR** • No adjustment required **RPV** • No adjustment required
	Descovy = CI <30 mL/min	**Genvoya = CI < 30 mL/min**		**Odefsey = CI < 30 mL/min**

Renal failure - continued

- **Renal failure (ClCr <60 mL/min):**
  - NRTI backbone: avoid **TDF/FTC,** use **TAF/FTC** or **ABC/3TC**

	NRTIs	INSTIs	Boosted PIs	NNRTIs
<15 mL/min	**TDF** • No clear recommendation **TAF** • Do not use **3TC** • 150 mg x 1 then 100 mg q24h **FTC** • 200 mg q96h **ABC** • No adjustment required	**DTG** • No adjustment required in treatment-naive • Caution in treatment-experienced **EVG** • No adjustment required **RAL** • No adjustment required	**ATV/r** • No adjustment required **DRV/r** • No adjustment required	**EFV** • No adjustment required **NVR** • No adjustment required **RPV** • No adjustment required
Hemodialysis	**TDF** • 300 mg once weekly **TAF** • Do not use **3TC** • 50 mg x 1 then 25 mg q24h **FTC** • 200 mg q96h **ABC** • No adjustment required		**ATV/r** • Treatment naive = 300 mg/100 mg • Treatment experienced = not recommended	**EFV** • No adjustment required **NVR** • Not recommended **RPV** • No adjustment required

References

- All “Manufacturers” taken from Health Canada: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/pm_saf_mp_innoc/lab_safety_rep_rap_eval_etiq-eng.php
- Pregnancy: https://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf

- Health Canada: https://hpr-rps.hres.ca/index.php?lang=en
- DHHS Guidelines: https://aidsinfo.nih.gov/drugs
- Sask Formulary: http://formulary.drugplan.health.gov.sk
- Antacids: http://hivclinic.ca/wp-content/uploads/2014/09/DDI-Tool_acid-suppressing-agents_Eng.pdf
- NIHB: http://www.healthycanadians.gc.ca/publications/health-system-systeme-sante/nihb-drug-list-2016-liste-medicaments-ssna/index-eng.php
- EDS: http://formulary.drugplan.health.gov.sk.ca/PDFs/APPENDIXA.pdf
- PrEP: IPERGAY trial, CATIE: http://www.catie.ca/sites/default/files/Canadian%20PrEP%20and%20nPEP%20Guidelines%20Executive%20Summary%20for%20circulation%20v0-5%20May%2012%202016.pdf