Australian Government

Department of Home Affairs

Notes for guidance for Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency syndrome (AIDS)

Deals with financial implications and consideration of prejudice of access to services associated with human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS)

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Information provided in this document, including the estimated financial considerations within a specified framework for treatment, are based on accurate, available resources at the time of development/review. It is the end user's responsibility to re-confirm the details before using the information for any binding purposes.

This includes consideration of the current eligibility criteria and cost of medications set out in the Pharmaceutical Benefits Scheme (PBS) tables, where there have been significant changes that would affect the outcome (for which archived tables can be accessed via the following link: www.pbs.gov.au/info/publication/schedule/archive).

Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS)

Definition and brief description of HIV/AIDS

HIV is the human immunodeficiency virus. AIDS is the acquired immune deficiency syndrome that is caused by HIV. A person is described as having AIDS when they experience at least 1 of several defined opportunistic infections and cancers that can occur after being infected with HIV. Sometimes, the public will use the terms 'HIV' and 'AIDS' synonymously; however, while all persons with AIDS have HIV infection, not all those with HIV infection will go on to develop AIDS. The distinction has less prognostic significance than it had in the past and is not particularly helpful from a costing point of view.

Since the introduction of effective antiretroviral (ARV) treatments, the accumulated evidence strongly suggests that HIV/AIDS in developed countries has changed from a fatal illness to a chronic, manageable condition. In Australia, the number of HIV diagnoses declined by 23% during 2014–2018, following implementation of pre-exposure prophylaxis (PrEP).[10] Following a landmark study that proved combination Active Antiretroviral Therapy (ART) can prevent transmission, in 2016 the World Health Organization (WHO) recommended that rapid ART initiation be offered to all individuals living with HIV who have uninfected partners to reduce HIV transmission.[15, 37] Most people who receive ART, and who adhere to their prescribed therapy, maintain an undetectable viral load, experience immune reconstitution and, therefore, may be expected to live a normal or near-normal lifespan.

In recent years, ART combinations have become better tolerated by patients, with fewer side effects, and require fewer tablets to be taken less frequently. While there are now more than 20 different antiretroviral agents available for prescription, some have been superseded and others are rarely used due to intolerable adverse effects. The continued development of better-tolerated combinations is likely to lead to further improvement in prognoses. In addition, clinicians may switch medications to avoid toxicities in individual patients.

A 2017 study analysis of large HIV cohorts found the 3-year life expectancy of male and female patients starting ART between 1996 and 2013 increased during the second and third years of ART. Patients who started ART during 2008–2010 whose CD4 counts exceeded 350 cells/microlitre 1 year after ART initiation have an estimated life expectancy (78 years of age) approaching that of the general population. Patients who start ART before becoming severely immunodeficient and achieving restoration of CD4+ T-cell counts can expect good longevity.[1]

Globally, access to ART is improving, although it continues to vary within and between countries and regions.[30] In Australia the number of people diagnosed with HIV has declined over the last 5 years and the main route of HIV transmission in 2017 was sexual contact between men.[11, 28] The pattern of the epidemic varies worldwide, including high-income countries. In some countries the number of cases related to injecting drug use is high; the sexual pattern of disease transmission also varies, for example in sub-Saharan Africa HIV is predominantly spread through heterosexual contact.

Prognosis and factors affecting progression, including rate of progression

When initiating ART, it is important to educate patients on strategies to optimise adherence to taking the medications.[4]

All coinfections may have an impact on outcomes in HIV infection, although chronic coinfections with hepatitis viruses are generally associated with worse overall outcomes. It should be noted that some

treatments for HIV (e.g. lamivudine, tenofovir and emtricitabine) also are used in the treatment of infection with hepatitis B virus (HBV), leading to potential cost savings.

Resistance to antiretroviral drugs can be acquired at the infection stage, or may be secondary to inadequate adherence to ART. Resistance to antiretroviral agents depends on changes in the RNA of HIV, which allows the virus to replicate in the presence of particular antiretroviral drugs.

The prevalence of primary or transmitted resistance to 1 or more antiretroviral agents has been reported to be as low as 4% of newly diagnosed Australian patients,[2] with research in the US finding it as low as 1% in the contemporary treatment era.[24] Primary resistance varies worldwide depending on the availability of different medications in the HIV-infected population.

Resistance does not develop in the presence of fully suppressive combination ART that is taken regularly, without missed doses. The likelihood of developing resistance depends on the combination. WHO data suggest most (~84%) patients who commence therapy with 1 of the current first-line drug regimens will achieve and maintain viral suppression.[22] In patients in low- and middle-income countries, factors associated with resistance have included the need to pay for medications and employment status.

Most clinicians order a genotyping test to look for resistance at the time of diagnosis and in instances of virological treatment failure. This assists in the choice of a new antiretroviral therapy combination. Genotyping may not be possible if the viral load is <1,000 copies/mL as the amplification success rate is low. Resistance testing is funded by the Medicare Benefits Schedule (MBS) under Item 69380 when the viral load exceeds 1,000 copies/mL.[12]

It is unlikely that people living with HIV will require admission to hospital for treatment. Admission would generally only be necessary for the management of AIDS-defining illnesses, including opportunistic infections and HIV-related cancers, in addition to comorbidities including liver disease and substance dependency.[26] The rate of disease progression is highly variable between individuals, ranging from 6 months to more than 20 years.[23] Median survival following AIDS in the absence of ART is dependent on the CD4+ T-cell count at AIDS diagnosis: 3.7 years if less than 200 cells/microlitre and 1.3 years if the count is less than 70 cells/microlitre.[17]

Information required for diagnosis

Screening for HIV is usually undertaken with an enzyme-linked immunosorbent assay (ELISA) antibody test. The fourth-generation test is now routine in Australia as a highly specific and sensitive combined HIV antibody-antigen ELISA.

If the ELISA result is seropositive or close to the positive cut-off value, this is confirmed by a Western blot test (another, more specific antibody test). A seropositive Western blot test result is analogous to infection with HIV. An indeterminate test result may imply infection with HIV (particularly if around the time of HIV seroconversion), or may be a false-positive result. In such a case, the Western blot test should generally be repeated after 2 weeks and then again after 3 months. In some countries, 2 positive test results with 2 different enzyme immunoassays (EIA) or rapid test kits on the same sample of blood will be considered to represent HIV seropositivity without need for a further Western blot test.

HIV testing for immigration purposes is required for all permanent visa applicants aged above 15 years of age; all applicants who will be working or training in Australia as a doctor, dentist, nurse or paramedic; temporary applicants with clinical indications of AIDS (recurrent, severe, and occasionally life-threatening infections and/or opportunistic malignancies); all children seeking adoption; and children aged less than 15 years of age who are suspected of having HIV infection or whose mother is HIV positive. See Appendix A for details Australian HIV screening requirements.

For children aged <18 months of age: A virological assay (HIV RNA and DNA polymerase chain reaction [PCR] assays) is needed to diagnose HIV infection in non-breastfed infants with perinatal HIV exposure by 1–2 months of age and in almost all infants by 4–6 months of age. Antibody tests do not establish the presence of HIV in infants because of transplacental transfer of maternal HIV antibodies.[32]

In the case of infants with 'needle phobia', alternative testing may be provided. Finger-prick or more usually heel prick samples rather than venepuncture is permissible, and salivary-based tests are currently being trialled. The sensitivity and specificity of these samples depend on the assay used. Point of Care nucleic acid amplification (NAAT) tests which meet a sensitivity and specificity of at least 98% should be used to reduce the rate of false positive results and should always be confirmed by a second NAAT, especially in settings where the prevalence of HIV is <5% in the community. Rapid HIV serology tests performed in low prevalence populations can have a high false positive rate and should not be used to diagnose infants ≤18months. A positive test result should be confirmed as soon as possible through repeat virologic testing.

The presumptive exclusion of HIV infection in non-breastfed infants is based on:

- 2 negative virologic tests (1 obtained at ≥14 days of age and 1 obtained at ≥4 weeks of age), OR
- 1 negative virologic test at age ≥8 weeks of age, OR
- 1 negative HIV antibody test at age ≥6 months of age.

Definitive exclusion of HIV infection in non-breastfed infants is based on:

- 2 or more negative virologic tests (1 obtained at ≥1 month of age and 1 at ≥4 months of age), OR
- 2 negative antibody tests from separate specimens obtained at ≥6 months of age.

For both presumptive and definitive exclusion of HIV infection, a child must have no other laboratory evidence (such as, no positive virologic test results or low CD4 cell count) or clinical evidence of HIV infection and must not be breastfeeding.

In cases where any screening results are positive previous testing of applicants overseas may not be reliable for a variety of reasons, so it may be difficult to determine whether someone has seroconverted recently. Recent seroconversion often is associated with a glandular fever-type illness and may be associated with changing test results, especially a negative to positive ELISA test result and a negative or indeterminate Western blot test result that becomes seropositive. Risk factors for HIV may be useful in specific national or regional settings; however, in most countries with a high prevalence of HIV infection, the most common source of acquisition is heterosexual intercourse. There are few, if any, situations in which risk factor data would alter the understanding of an HIV test result.

In general, most practitioners would repeat HIV RNA testing every 6 months and the CD4+ T-cell count every 12 months. The exception is when CD4+ count is <200 cells/microlitre, in which case it should be repeated at every visit so that antimicrobial prophylaxis can be stopped once the CD4+ count is stable at a particular threshold (e.g. ≥200 cells/microlitre for at least 6 months). Together, the viral load test and CD4+ T-cell count determine:

- level of activity of the virus in the bloodstream
- level of damage to the immune system
- if current antiviral treatments are working and whether it may be necessary to change treatments
- when to initiate preventative drugs (prophylaxis) to decrease the chances of acquiring some of the more common opportunistic illnesses that are associated with AIDS.

Tests for coinfections/complications that are usually performed at diagnosis may include:

- hepatitis B serology
- hepatitis C serology
- syphilis serology (Venereal Disease Research Laboratory [VDRL] test or rapid plasma reagin [RPR] test)
- cytomegalovirus (CMV) antibody
- toxoplasma antibody
- QuantiFERON TB Gold assay

- chest x-rays image
- HIV genotype resistance assay (if available).

The CD4+ count is a measure of the current degree of immunodeficiency. The viral load is a measure of the risk of future damage to the immune system. Caution must be used in considering an individual CD4+ T-cell count. Factors that may impact a CD4+ T-cell count include the individual assay, diurnal variation and acute illness.

Usually, patients require 3 to 6-monthly medical reviews, with clinical assessment and monitoring of the CD4+ T-cell numbers and HIV viral load. In addition, a full blood examination (FBE) and renal and liver function tests are performed in all patients. Additional tests would be undertaken only if another condition, or new symptoms, are present. These reviews can be carried out by a specialist in infectious diseases, or a GP with a special interest in HIV, who holds section 100 prescribing rights for ART.

It is important to note that considerable individual variation occurs in the rate of decline for CD4+ T- cell counts; therefore, a series of readings over time is required to assess the future antiretroviral needs of a person living with HIV infection.

In those individuals receiving ART, responses to treatment generally are good.

While concerns have been expressed about the long-term toxicities of some antiretroviral drugs, clear overall clinical benefits can be seen in the decline in the frequency of deaths of all causes.

Currently accepted treatments

The recommended treatment guidelines in Australia are updated regularly in conjunction with international guidelines.[5] Since April 2014, all HIV-positive individuals in Australia are eligible under the Pharmaceutical Benefits Scheme (PBS) to receive subsidised ART. Patients no longer need to wait for their CD4 counts to fall, or for clinical symptoms to emerge, before they can be prescribed PBS-subsidised treatments.[13] The Strategic Timing of Antiretroviral Therapy (START) trial definitively showed that all people with HIV should be treated for HIV infection regardless of CD4 count at diagnosis and that ART should commence as soon as possible after diagnosis.[20]

The Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) Sub-Committee for Guidance on HIV Management, strongly recommends ART be initiated in all people with HIV, wherever possible, irrespective of CD4 count, to reduce the risk of disease progression and transmission.[5]

ART has significantly improved the prognosis of individuals who are infected with HIV. Although some types of antiretroviral drugs have been associated with various toxicities, these can usually be minimised with substitution of therapy. In some people, 'nucleoside-sparing' ART combination regimens may be preferred, although at this stage none are recommended as preferred treatment options. Factors included in the choice of a regimen include:

- comorbidities (e.g. liver disease, tuberculosis [TB], mental illness, diabetes, osteoporosis)
- cardiovascular risk
- chemical dependency
- pregnancy or pregnancy potential
- likely adherence
- dosing convenience
- possible adverse effects
- drug–drug interactions
- pre-treatment CD4+ T-cell counts

- sex and genotyping results (if available).

The 2019 ASHM Antiretroviral Guidelines: US Department of Health and Human Services (DHHS) Guidelines with Australian Commentary recommend ART regimens combine a 2-drug nucleoside reverse transcriptase inhibitor (NRTI) backbone with a third ARV from one of the following drug classes:

- an integrase strand transfer inhibitor (INSTI);
- a non-nucleoside reverse transcriptase inhibitor (NNRTI); or
- a protease inhibitor (PI) with a pharmacokinetic (PK) enhancer.

The December 2019 recommendations also include the use of bictegravir as first-line regimen, and the 2-drug regimen dolutegravir plus lamivudine for initial treatment.[5]

See Table 1 for the preferred antiretroviral component options for constructing a regimen for a treatment-naive patient, and Table 5 for PBS costs of regimens.

The selection of a regimen should be individualised based on virologic efficacy, toxicities, pill burden, dosing frequency, drug interaction potential, childbearing potential and use of effective contraception, resistant test results and comorbid conditions. Components are designated as preferred when clinical trial data suggest optimal and durable efficacy, with acceptable tolerability and ease of use. Alternative components are those in clinical trial data showing efficacy, but with disadvantages, such as antiviral activity or toxicities, when compared with the preferred agent. In some cases, for an individual patient, a component listed as an alternative may actually be the preferred component. When there is more than 1 component for a preferred or alternative option, the components are listed in alphabetical order.

The option to switch between regimens would depend on the reason; either because of adverse effects or a failure to control the virus as a result of resistance. Current guidelines suggest all patients complete baseline resistance testing before commencing treatment. Resistance testing should be repeated if the viral load becomes detectable, that is, in the advent of virologic failure. Since a certain amount of virus is required for amplification, this usually means the viral load needs to be ≥1,000 copies/mL. Viral replication in most patients initially is suppressed successfully with therapy and such suppression can be maintained over many years. Therefore, resistance testing is unlikely to be a significant cost in the management of individual patients who are newly commencing therapy, but may be more important in those who are receiving third- or fourth-line treatment.

Table 1: *Preferred regimens for antiretroviral therapy-naive patients*

Regimens	Comments
An ARV regimen for a treatment-naive patient generally consists of two nucleoside reverse transcriptase inhibitors (NRTIs) in combination with a third active ARV from one of 3 drug classes: an integrase strand transfer inhibitor (INSTI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a protease inhibitor (PI) with a pharmacokinetic (PK) enhancer (booster) (cobicistat or ritonavir). **The preferred regimens are arranged first by evidence rating, and when ratings are equal in alphabetical order.**	
INSTI-based regimen plus 2 NRTIs: • Bictegravir/tenofavir alafenamide† /emtricitabine (AI) • Dolutegravir/abacavir/lamivudine – only if HLA-B*5701-negative‡ and without chronic HBV coinfection (AI) • Dolutegravir plus emtricitabine (or lamivudine) plus tenofovir alafenamide (or tenofovir disoproxil fumarate)† (AI) • Raltegravir plus emtricitabine (or lamivudine) plus tenofovir alafenamide (BII) or tenofovir disoproxil fumarate†, (BI)	INSTI-based regimen plus 1 NRTI: • Dolutegravir/lamivudine – except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available (AI)
Rating of recommendations: A = strong; B = moderate; **Rating of evidence**: I = data from randomised controlled trials; II = data from well-designed non-randomised trials or observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies or regimen comparisons from randomised switch studies; III = expert opinion.	
† Tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF) are two forms of tenofovir. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost and access are among the factors to consider when choosing between these drugs. ‡ HLA-B*5701 screening test should be performed in patients before starting the abacavir-containing regimen. A positive HLA-B*5701 screening test is linked to hypersensitivity to abacavir and the abacavir-containing regimen is not recommended. (AI)	
Source: ASHM. Antiretroviral Guidelines: US DHHS Antiretroviral Guidelines with Australian Commentary. Recommended Antiretroviral Regimens for Initial Therapy.[5]	

Regimens	Comments
http://arv.ashm.org.au/what-to-start-initial-combination-regimens-for-the-antiretroviral-naive-patient/	

Treatment of pregnant women infected with HIV

Treatment recommendations listed in this document are based on the principle that therapies of known benefit to women should not be withheld during pregnancy unless there are known adverse effects on the mother, foetus or infant, and these adverse effects outweigh the benefit to the pregnant woman. Thus, pregnancy should not preclude the use of optimal drug regimens.[7, 35]

All pregnant and breastfeeding women with HIV should initiate a recommended ART regimen and continue lifelong with ART. HIV-infected pregnant women should receive regular monitoring for complications of pregnancy and for potential toxicities. Raltegravir is a first-generation INSTI and the only INSTI that has evidence for safety in pregnancy. A pregnancy test should be performed for women of childbearing potential prior to the initiation of ART.

Dolutegravir is not recommended for use in women who are pregnant and within 12 weeks post-conception or who are planning pregnancy, unless there are no alternative options. Early evidence shows that dolutegravir is associated with a slightly higher risk of neural tube defects in infants born to women who were receiving dolutegravir at the time of conception, compared to women taking other antiretrovirals.[7]

Prevention of mother-to-child transmission of HIV

ASHM recommends during pregnancy an additional goal of ART is to maintain a viral load below the limit of detection to reduce the risk of transmission to the foetus and newborn. If a pregnant woman does not commence an ART regimen, the rate of perinatal transmission is approximately 25–30%. This can be reduced to as low as 1–2% with appropriate management and prevention strategies. Risk factors that increase the likelihood of perinatal transmission include:[16]

- acute stage of the mother's illness
- high maternal viral load
- low CD4 (T-cell) count
- prolonged rupture of the membranes
- vaginal birth
- premature birth
- breastfeeding.

Perinatal strategies for the prevention of mother-to-child transmission of HIV require that an HIV-infected woman’s status is known during pregnancy, whether by testing before becoming pregnant or during the antenatal period.

Effective preventive strategies now include:[35]

- highly active ART (HAART) during pregnancy;
- 4–6 weeks of prophylactic ART (usually zidovudine alone) postnatally for the newborn child, initiated as close as possible to the time of birth, preferably within 6–12 hours of delivery;
- sulfamethoxazole/trimethoprim to prevent *Pneumocystis carinii (jiroveci)* pneumonia (PCP*).* If HIV testing shows the infant is not infected with HIV, the medication is stopped;
- elective caesarean section, particularly if HIV viral suppression has not been achieved with HAART; and
- formula feeding.

Early infant diagnosis of HIV

Australian recommendations are in line with the current *US DHHS guidelines for the use of antiretroviral agents in paediatric HIV infection.*[32]

In infants and children younger than 18 months with perinatal or postnatal HIV exposure

It is recommended virologic assays (e.g. HIV RNA and HIV DNA nucleic acid tests [NATs]) that directly detect HIV must be used to diagnose HIV infection in infants and children younger than 18 months with perinatal and postnatal HIV exposure. HIV antibody tests should not be used. HIV RNA or HIV DNA NATs are recommended.

An assay that detects HIV non-B subtype viruses or group O infections (such as an HIV RNA NAT or a dual-target total DNA/RNA test) is recommended for use in infants and children born to mothers with known or suspected non-B subtype virus or Group O infections. Virologic diagnostic testing is recommended for all infants with perinatal HIV exposure at the following ages:

- 14–21 days
- 1–2 months
- 4–6 months.

Additional virologic diagnostic testing at birth should be considered for infants at higher risk of perinatal HIV transmission. A positive virologic test should be confirmed as soon as possible by a repeat virologic test. Definitive exclusion of HIV infection in non-breastfed infants is based on 2 or more negative virologic tests:

- 1 obtained at age ≥1 month and 1 at age ≥4 months; or
- 2 negative HIV antibody tests from separate specimens obtained at age ≥6 months.

See Table 2 for recommended virologic testing schedules for infants.

For children with non-perinatal exposure only, or children with perinatal exposure aged >24 months

Diagnostic testing relies primarily on the use of HIV antibody (or antigen/antibody) tests. When acute HIV infection is suspected, additional testing with an HIV NAT may be necessary to diagnose HIV infection.

Definitive exclusion of HIV infection

Definitive exclusion in non-breastfed infants is based on 2 or more negative virologic tests, with 1 obtained at ≥1 month of age and 1 at ≥4 months of age, or 2 negative HIV antibody tests from separate specimens obtained at ≥6 months of age.

Since children aged 18–24 months with perinatal HIV exposure occasionally have residual maternal HIV antibodies, definitive exclusion or confirmation of HIV infection in children in this age group who are HIV antibody-positive should be based on an HIV NAT and antibody re-testing at age 24 months. When acute HIV infection is suspected, additional testing with an HIV NAT may be necessary to diagnose HIV infection.

If a baby is breast fed by a HIV positive mother a negative test more than 6 weeks after cessation of breast feeding definitively excludes HIV (negative NAAT if ≤18 months and negative Ab/Ag test if ≥18months). See Appendix B: algorithm for early infant diagnosis.

Table 2: *Recommended virologic testing schedules for infants*

Recommended virologic testing schedules for high- and low-risk infants	
Infants who were exposed to HIV and who are at higher risk of perinatal HIV transmission	
High-risk infants are born to mothers who:	• have HIV and did not receive prenatal care • did not receive antepartum or intrapartum ARV drugs • received intrapartum ARV drugs only • initiated ART late in pregnancy (during the late second or third trimester) • received a diagnosis of acute HIV infection during pregnancy • had detectable HIV viral loads close to the time of delivery, including those who received combination ARV drugs and did not have sustained viral suppression
Age at NAT testing	• Birth • 14–21 days • 1–2 months • 2–3 months* • 4–6 months
Infants who were exposed to HIV and who are at low risk of perinatal HIV transmission	
Low-risk infants are born to mothers who:	• have HIV who received standard ART during pregnancy • had sustained viral suppression with no concerns related to maternal adherence (usually defined as confirmed HIV RNA level below the lower limits of detection of an ultrasensitive assay)
Age at NAT testing	• 14–21 days • 1–2 months† • 4–6 months
Adapted from US DHHS guidelines for the use of antiretroviral agents in pediatric HIV infection. [32]	
* For higher risk infants, additional virologic diagnostic testing is recommended at birth and 2–6 weeks after cessation of ARV prophylaxis (i.e. at 8–12 weeks of life). † Test may be timed to occur at least 2 weeks after cessation of ARV prophylaxis.	

Treatment of HIV infection in paediatric patients

Treating children who are diagnosed HIV positive with antiretroviral drugs within their first 12 weeks of life reduces mortality by 75%. Without treatment, one-third of children living with HIV die before their first birthday, and half before their second birthday.[29]

Most children living with HIV become infected through mother-to-child transmission. Children born to mothers living with HIV need to be tested as soon as possible after birth to determine if they are infected with the virus and to commence ART.

Prophylactic ART should be given to all exposed infants for the first 6 weeks of life; if HIV infection is confirmed, then it should be changed to a full regimen of ART.

Since 2010, WHO has been recommending that ART should be initiated in all children living with HIV without delay, regardless of WHO clinical stage or their CD4 cell count, which includes:[38]

- infants diagnosed in the first year of life; and
- children living with HIV between 1 year of age to adolescents (i.e. 12 years of age).

In September 2019, the *US guidelines for the use of antiretroviral agents in paediatric HIV infection* updated recommendations on the use of the ARVs bictegravir/emtricitabine/tenofovir alafenamide and dolutegravir in children and adolescents.[34] The ART regimen for children should generally consist of 2 NRTIs plus an active drug from one of the following classes for initial therapy:

- INSTI-based regimen; or
- NNRTI-based regimen; or
- PI-based regimen.

For children >14 days of age, choice of ART regimen will be based on:

- age
- weight (preferred determinant)
- sexual maturity rating (SMR)
- results of viral resistance testing.

See Table 3 for the regimens recommended for initial therapy of ARV naive children. Preferred regimens are designated based on efficacy, ease of administration and acceptable toxicity. Alternative regimens have also demonstrated efficacy, but clinical experience with these regimens is limited and/or these regimens are more difficult to administer than the preferred regimens.[34]

ART has significantly impacted morbidity and mortality in children with HIV.[36] However, there are unique paediatric challenges with ART. These issues include the limited number of syrup or liquid preparations or chewable tablets for the majority of the antiretroviral drugs that are suitable for infants and children who are unable to swallow pills, or whose weight precludes the use of fixed tablet/capsule formulations (see Appendix C for ARV fixed-dose combination tablets [FDC]). Currently, raltegravir pills or chewable tablets are available for infants weighing 2 kg or more; granules can be administered to infants and children from birth to age 2 years.

The financial costs of the preferred paediatric regimens are shown in Table 4.

Table 3: *Antiretroviral regimens recommended for initial therapy for HIV infection in paediatric patients (preferred and alternative)*

Age	Weight	SMR	Preferred regimen	Alternative regimen
The ART regimen for children should generally consist of 2 NRTIs plus an active drug from one of the following classes for initial therapy: • **INSTI-based regimen; or** • **NNRTI-based regimen; or** • **PI-based regimen.** Regimens should be tailored to the individual patient age, SMR and weight recommendations.				
Infants (birth to <14 days old)	≤2 kg	n/a	2 NRTIs plus NVP	none
	≥2 kg	n/a	2 NRTIs plus RAL	
Children (≥14 days to <3 years)	n/a	n/a	2 NRTIs plus LPV/r*	2 NRTIs plus NVP
	≥2 kg	n/a	2 NRTIs plus RAL	
Children (≥3 months to <3 years)	≤25 kg	n/a		2 NRTIs plus ATV/r
Children ≥3 years	<25 kg	n/a	2 NRTIs plus ATV/r 2 NRTIs plus DRV/r 2 NRTIs plus RAL	2 NRTIs plus EFV 2 NRTIs plus LPV/r
	≥20 kg to <25 kg	n/a		2 NRTIs plus DTG†

Age	Weight	SMR	Preferred regimen	Alternative regimen
	≥25 kg	n/a	2 NRTIs plus DTG† 2 NRTIs plus EVG/COBI§	2 NRTIs plus ATV/r 2 NRTIs plus DRV/r 2 NRTIs plus RAL
Children (≥6 years <12 years)	≥25 kg	n/a		2 NRTIs plus BIC‡
Adolescents aged ≥12 years	≥25 kg	SMR 1–3	2 NRTIs plus BIC‡	none
		SMR 4 or 5	Refer to the ASHM antiretroviral guidelines for adolescents and young adults with HIV.[8]	
Adolescents aged ≥12 years	≥35 kg	SMR 1–3		2 NRTIs plus RPV 2 NRTIs plus ATV/c
	≥ 40 kg	SMR 1-3		2 NRTIs plus DRV/c
Adapted from: US DHHS guidelines for the use of antiretroviral agents in pediatric HIV infection.[34]				
* LPV/r should not be administered to neonates before a post-menstrual age of 42 weeks and postnatal age ≥14 days. † An FDC tablet containing ABC/DTG/3TC (Triumeq) is available for children weighing ≥25 kg. ‡ BIC is available only as part of a FDC tablet containing BIC/FTC/TAF (Biktarvy); however, it is not PBS-subsided for children under 18 years of age. § EVG/COBI/FTC/TAF FDC is recommended at this time. DRV should only be used in children aged ≥10 kg. Once-daily DRV should not be used in children aged <12 years or weighing <40 kg.				

Age	Weight	SMR	Preferred regimen	Alternative regimen
ABC, abacavir; ATV/r, atazanavir/ritonavir; ATV/c, atazanavir/cobicistat; BIC, bictegravir; COBI, cobicistat; DTG, dolutegravir; DRV/r, darunavir/ritonavir; DTG, dolutegravir; DRV/c, darunavir/cobicistat; EFV, efavirenz; EVG, elvitegravir; FDC, fixed dose combination; FTC, emtricitabine; INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; LPV/r, lopinavir/ritonavir; NVP, nevirapine; PI, protease inhibitor; RAL, raltegravir; RPV, rilpivirine; SMR, sexual maturity rating; TAF, tenofovir alafenamide; 3TC, lamivudine.				

Table 4: *Recommended dosages and formulations for paediatric patients' drug regimens as of April 2020*

Drug	PBS item no.	Usual dosage	Unit cost	Estimated annual cost
Nucleoside reverse transcriptase inhibitors (NRTIs)				
Zidovudine 50 mg/5 mL oral liquid, 200 mL (Retrovir)	10361H	10 mL three times daily	$38.41	$2,103
Lamivudine 10 mg/mL oral liquid, 240 mL	10320E	6 mL twice daily	$59.14	$1,079
Emtricitabine 200 mg + tenofovir alafenamide 25 mg tablet, 30 (Descovy)	11113X	Once daily	$723.76	$8,806
Lamivudine 150 mg + zidovudine 300 mg tablet, 60 (Combivir)	10284G	Once daily for children weighing >30 kg*	$108.75	$662
Abacavir 20 mg/mL oral liquid, 240 mL	10356C	6 mL twice daily	$70.31	$1,283
Integrase strand transfer inhibitors (INSTIs)				
Dolutegravir 50 mg tablet, 30	10283F	50 mg/once daily (children >25 kg)	$655.97	$7,981
Raltegravir 25 mg chewable tablet, 60	10299C	50–150 mg twice daily	$76.26	$5,567
Non-nucleoside reverse-transcriptase inhibitors (NNRTIs)				
Nevirapine 10 mg/mL oral liquid, 240 mL	10319D	5 mL daily	$139.74	$1,063
Efavirenz 30 mg/mL oral liquid, 180 mL	10275T	6.7 mL daily	$69.89	$949

Drug	PBS item no.	Usual dosage	Unit cost	Estimated annual cost
Protease-inhibitors (PIs)				
Lopinavir 400 mg/5 mL + ritonavir 100 mg/5 mL oral liquid, 60 mL (Kaletra)	10327M	1.9 mL twice daily	$130.89	$3,026
* For children weighing >9 kg and <30 kg, administer as separate components; 9 mg/kg zidovudine and 5 mg/kg lamivudine, given twice daily.				
Source of unit cost data: Schedule of Pharmaceutical Benefits, Effective 1–30 April 2020.[13] Available from: www.pbs.gov.au/info/publication/schedule/archive Unit cost of drug = Dispensed Price for Maximum Quantity (DPMQ)/Max qty packs. Unit values are presented up to 2 decimal places. Total costs have been computed on these unit values, and rounded to the nearest whole number.				

Maternal viral load

Infants born to mothers not on ART with detectable viral load, as well as those born to mothers on ART with an undetectable viral load in plasma require different management.

Infants of mothers on suppressive ART

The risk of HIV infection in infants born to women who had achieved viral suppression on ART, or who had been on regular ART for more than 4 weeks by the time of delivery is low. The recommended prophylaxis regimen for such infants is 6 weeks of daily nevirapine for those who are breastfeeding, and 4–6 weeks of daily nevirapine or twice-daily zidovudine for those who are receiving replacement feeding.[41]

Infants of mothers with detectable viral load

For these infants, the recommended prophylaxis regimen is daily nevirapine plus twice-daily zidovudine for the first 6 weeks of life depending on HIV NAT results.[34, 41] Breastfeeding infants should continue with an additional 6 weeks of prophylaxis with the same combination or with nevirapine alone. If the mother cannot tolerate or declines ART, then the infant should continue nevirapine prophylaxis throughout the duration of breastfeeding, until 1 week following breastfeeding cessation (if nevirapine is not tolerated, daily lamivudine can be used).[41]

Adolescents living with HIV

Adolescents living with HIV have either acquired HIV in infancy and are heavily ART-experienced or acquired HIV more recently during their teens. These adolescents should receive maximally suppressive ART, especially urgent for those who are sexually active, considering pregnancy or are pregnant. Adolescents should also be prepared for the transition into adult care settings.

The ASHM antiretroviral guidelines for adolescents and young adults with HIV recommend ART for ART-naive adolescents. The adolescent SMR can be helpful to guide regimen selection for initiation or changes in ART (i.e. adolescents with SMR of 4 or 5).[8]

Viral load monitoring is the most useful indicator of adherence and is a routine component of monitoring individuals on ART.[8] Regimens for adolescents should be simplified from the multiple pills or unpalatable liquids children are required to take. Consideration should be given to number of pills, volume of liquid and number of daily doses to improve medication adherence in adolescents.

Once-daily co-formulated options available for adolescents include:[33]

- For children and adolescents who weigh ≥25 kg, single tablet, once-daily regimens include Triumeq (ABC/DTG/3TC), Genvoya (EVG/COBI/FTC/TAF) and Biktarvy (BIC/FTC/TAF).
- For children and adolescents who weigh ≥20 kg, dolutegravir 50 mg is recommended. The PBS-recommended dose of 50 mg dolutegravir and 300 mg lamivudine (Dovato) for adolescents who weigh at least 40 kg is one tablet, once daily.
- For children who weigh ≥25 kg, dolutegravir 50 mg can be given as Triumeq (ABC/DTG/3TC) in 1 large pill, or as Descovy (FTC/TAF) plus DTG, which requires 2 small pills.
- Biktarvy (BIC/FTC/TAF) is PBS-subsidised for use in children and adolescents who weigh ≥25 kg.

See Appendix C for more weight-based fixed-dose combination tablets available for adolescents.

Coinfection with hepatitis C, hepatitis B and tuberculosis

All coinfections can impact outcomes in people with HIV infection, but coinfection with chronic hepatitis generally is associated with worse overall outcomes. Some treatments for HIV are also used in hepatitis B (e.g. lamivudine, emtricitabine and tenofovir); therefore, care should be taken to avoid double-counting of costs.

Hepatitis C

Approximately 10% of people living with HIV infection in Australia have coinfection with hepatitis C virus (HCV). In other parts of the world, rates depend on the mode of transmission of HIV and HCV.

People with HIV and HCV coinfection show a higher rate of chronic infection with HCV, a higher viral load of HCV and accelerated progression of liver disease. The ASHM antiretrorviral guidelines for HCV/HIV coinfection recommend all individuals with HIV to be screened for HCV infection. Furthermore, all individuals at high risk of HCV infection should be screened annually and whenever incident HCV infection is suspected.[3]

While accelerated progression of HIV disease in persons with HIV/HCV coinfection has been demonstrated in some studies, it has been refuted by others.

Testing for HCV usually takes place at the time of HIV diagnosis. Persons with a positive result for hepatitis C antibody are tested further by means of an HCV PCR assay. Persons with advanced immunodeficiency show lower sensitivity in antibody testing for HCV. HCV RNA testing can be performed in those with clinical suspicion of liver disease. In about 25% of people, HCV infection clears spontaneously.[19]

Baseline testing generally includes viral genotype and a quantitative HCV RNA (viral load) test as the efficacy of antiviral therapy against HCV is associated with both parameters. Unlike HIV viral load, the hepatitis C viral load has no prognostic value in terms of assessing disease progression and does not require regular monitoring. Newer 'pan-genotypic' direct acting antiviral (DAA) regimens (e.g. sofosbuvir/velpatasvir) will mean that response to therapy will not necessarily be dependent on HCV genotype.

Treatment of HCV

The staging of liver disease will remain an important tool for the determination of a prognosis and decision-making on treatment. ASHM recommends evaluating all persons who are co-infected with HCV/HIV by assessing their liver fibrosis stage to inform the length of their therapy and subsequent risk of hepatocellular carcinoma (HCC) and liver disease complications.[3] Elastography (FibroScan®) has taken over from biopsy as a way to identify the stage of liver diseases.[21] In addition, the AST to platelet ratio index (APRI) score is used to exclude cirrhosis, particularly where elastography is unavailable or not readily available.

ART may slow the progression of liver disease by preserving or restoring immune function and reducing HIV-related immune activation and inflammation in persons with HIV/HCV coinfection. For most persons with this coinfection, including those with cirrhosis, the benefits of ART outweigh concerns regarding drug-induced liver injury.

People with chronic HCV/HIV coinfection should be screened for active and prior HBV infection by testing for the presence of hepatitis B surface antigen (HBsAg), as well as hepatitis B surface antibody (HBsAb) and hepatitis B core antibody (HBcAb), and total or immunoglobulin G (IgG).

The ASHM guidelines on HCV/HIV coinfection recommend that all people:[3]

- who are not immune to HBV infection (HBsAb-negative) should receive anti-HBV vaccination; and
- with HCV/HIV coinfection and active HBV infection (HBsAg-positive) should receive ART that includes 2 agents with anti-HBV activity prior to initiating HCV therapy.

DAA regimens for co-infected patients are the same as those used for hepatitis C mono-infections, with due consideration to potential drug–drug interactions.

In ART-naive patients, HIV infection should be controlled and HIV-related opportunistic infections treated before initiation of hepatitis C treatment, particularly in those with advanced HIV immunosuppression (CD4+ count <200 cells/mm^3). Treatment of persons with a CD4+ cell count greater than 500 cells/mm^3 may be deferred until hepatitis C treatment is completed, to avoid drug–drug interactions. Tipranavir, in particular,

should be avoided in concurrent ART-DAA therapy. However, it is recommended that ART be initiated as soon as reasonable.

Initial ART regimens recommended for HCV/HIV coinfection are the same as those recommended for individuals without HCV infection. However, when treatment for both HIV and HCV is indicated, the ART and HCV treatment regimens should be selected with special consideration for potential DAA and overlapping toxicities. In all cases where HIV and HCV drugs are used concomitantly, patients should be closely monitored for HIV and HCV virologic efficacy and potential toxicities.

ART should not be switched for people who are on a stable regimen unless an unavoidable and unmanageable drug–drug interaction is identified, because switching ART in HIV virologically suppressed patients has a risk of HIV virological failure.

An important resource for assessing potential drug–drug interactions is the University of Liverpool's Hepatitis Drug Interactions website,[31] available from: www.hep-druginteractions.org

Monitoring of hepatitis C viral load at 12 weeks after the commencement of HCV treatment allows an assessment of response and the decision whether to persist with treatment.

For DAA treatment regimens, especially when metabolic pathway of drugs are unknown,[3] see https://arv.ashm.org.au/hepatitis-c-virus-hiv-coinfection/

It should be noted however HCV is not a complication of, nor directly related to, HIV infection and so if present would be assessed as a separate condition for visa purposes. As in most cases the total cost of treatment for HCV will now be below the significant cost threshold, in cases of coinfection it is likely the HIV infection alone is relevant for visa costing purposes. For further details on management of hepatitis C mono-infection, refer to *Financial Implications and Consideration of Prejudice of Access to Services Associated with Viral Hepatitis.*

Hepatitis B

HIV infection modifies the natural history of hepatitis B infection. Higher rates of progression to advanced liver disease occur among persons with coinfection with HIV and hepatitis B. The presence of HIV infection is associated with greater rates of progression to cirrhosis. The impact of hepatitis B infection on the natural history of HIV infection is less certain.

Persistent infection with HBV is more common in people with HIV. Studies among men who have sex with men (MSM) and exposed to HBV show evidence of chronic infection with HBV in almost 25% of these individuals, compared with 3–5% in those without HIV. Although it is rare, reactivation of HBV infection may occur in the setting of advanced immunodeficiency, in spite of seroconversion to HBsAb. Furthermore, in persons with HIV/HBV coinfection, hepatitis B DNA levels are substantially higher and rates of seroconversion from HBe antigen (HBeAg) to anti-HBeAg are lower than in persons with HBV alone.[9]

At diagnosis with hepatitis B infection, individuals undergo serology testing, including for HBeAg, hepatitis B viral load estimation, ultrasound examination and measurement of alpha-fetoprotein levels. Asymptomatic patients with HIV/HBV coinfection require a similar number of routine clinical consultations for monitoring as for mono-infected patients. Monitoring liver enzyme levels occurs as part of HIV care.

It is well established that hepatitis B infection markedly increases the risk of primary HCC. Although an increased rate of HCC has yet to be described in people with HIV, the known overall increased risk of malignancy in this population suggests a risk that is potentially higher. Screening every 6–12 months with triple-phase computed tomography (CT) scanning and for alpha-fetoprotein levels is strongly recommended.

Before initiation of ART, all patients who test positive for HBsAg should be tested for HBV DNA using a quantitative assay to determine the level of HBV replication.

In the case of people with HIV co-infected with HBV, ART should contain the NRTI tenofovir (either in TDF or TAF forms). In these instances, the use of emtricitabine would also be added as TDF and TAF are co-

formulated with emtricitabine (FTC). In this instance, the TDF or TAF plus emtricitabine offers excellent HBV suppressive therapy.[9] The use of the abacavir/lamivudine fixed-dose combination should not be used, as this offers only lamivudine monotherapy against HBV, which is suboptimal and leads to HBV lamivudine resistance and the risk of liver disease progression. Treatment costs for hepatitis B infection depend on the use of antiretroviral drugs for coinfection with HIV.

Due to lower dosing, TAF has a preferable side effect profile than TDF and appears to cause a more rapid viral suppression than TDF in trials. TAF may soon become first choice treatment for HBV. If it is not possible to obtain TAF/FTC or TDF/FTC then the anti-HBV drug entecavir should be administered to achieve adequate HBV control (as well as ART directed at the HIV infection).

Emtricitabine, lamivudine, TDF and TAF have antiviral activity and efficacy in children and should be considered for use in children with HBV/HIV coinfection.

Tuberculosis and HIV

The risk of reactivation of TB in HIV-infected individuals is approximately 14% during the 2 years after exposure to *Mycobacterium tuberculosis*, in contrast to the risk in HIV-negative persons of 10% over their lifetime. The development of TB in an HIV-infected person may accelerate the progression of HIV disease.[42]

Treatment of latent *Mycobacterium tuberculosis* infection (LTBI) is important to prevent the development of active disease in HIV-infected individuals. People at risk are those with a positive Mantoux test with a reaction of at least 5 mm in diameter, or known exposure to a person with infectious *Mycobacterium tuberculosis* disease.

The TEMPRANO trial has now shown clinical benefit (reduced mortality) for anergic people as an adjunct to ART initiation in people with HIV.[27] WHO has recommended the use of isoniazid preventive therapy (IPT) regardless of Mantoux test result in people with HIV. Generally, if someone is HIV-positive and from a country endemic for TB then they should be offered IPT (along with ART initiation and other standard prophylaxis as per guidelines).

Interferon-gamma release assays (IGRAs) have been available alternatives to Mantoux testing for some years. While the current consensus from Australia's National Tuberculosis Advisory Committee (NTAC) is that these assays do not offer a clear advantage in terms of assessing LTBI compared to Mantoux testing, the tests do not require people to return for a reading 3 days after the test.[25]

Before instituting prophylaxis for *Mycobacterium tuberculosis*, it is important to exclude TB infection. To reasonably exclude active TB, it is important to consider the presence of a cough of any duration, fever of any duration or night sweats lasting 3 or more weeks in the preceding 4 weeks.

Prophylaxis with a single agent during active infection with *Mycobacterium tuberculosis* will lead to drug resistance. Isoniazid given in a daily 300 mg dose for 9–12 months is effective, as is daily rifabutin and pyrazinamide, which are administered for 2 months.

Both regimens are associated with hepatotoxicity and should be used with caution in people with hepatic disease. Close monitoring of liver function is required during the administration of a rifamycin drug and pyrazinamide combination, and as a result of this higher rates of hepatotoxicity is recommended. Isoniazid is the preferred drug in this setting.

The management of *Mycobacterium tuberculosis* infection requires systemic combination antimicrobial therapy. If HAART is used in combination with the standard TB treatment regimen, then consideration of drug interactions between the antiretroviral agents and the rifamycin drug is paramount.

Initiating ART for HIV/TB coinfection

When isoniazid alone is used for LTBI treatment, any ART regimen can be used.

- Efavirenz 600 mg in combination with the abacavir/lamivudine or tenofovir disoproxil fumarate/emtricitabine with once-weekly isoniazid plus rifapentine; the doses of the NRTI backbone do not require adjustment.
- If rifampin or rifapentine is used to treat LTBI, the potential for drug–drug interactions among different ARV drugs and rifamycin antibiotics should be assessed.

The timing of antiretroviral and anti-tuberculous therapy is important ASHM recommends 'integrated ART', which is ART therapy within 2–8 weeks after initiating ATT. ART initialisation should not be delayed until the completion of TB treatment.[6]

- If CD4 count <50 cells/mm^3: initiate ATT first, and then ART within 2 weeks.
- If CD4 count ≥50 cells/mm^3: initiate ART within 8 weeks of starting TB treatment.
- During pregnancy, regardless of CD4 count: initiate ART as early as feasible for treatment of the mother with HIV and to prevent HIV transmission to the infant.
- For TB meningitis: when initiating ART early, patients should be closely monitored for adverse events.

HIV prevention

Pre-exposure prophylaxis (PrEP)

The annual number of new HIV diagnoses in Australia declined by 23% during 2014–2018, largely due to Pre-Exposure Prophylaxis (PrEP) implementation to prevent HIV acquisition among HIV-negative MSM.[10]

All the current PrEP trials are testing tenofovir-based regimens, which use an ARV containing tenofovir (TDF) and emtricitabine (FTC), sold under the brand name Truvada in Australia. On 1 April 2018, the PBS subsided brand and generic versions of Truvada, co-formulated tenofovir and emtricitabine for HIV PrEP. Daily PrEP used continuously, or for shorter periods of time, has been recommended by ASHM clinical guidelines as a key HIV prevention option.[39]

Patients should present with no signs or symptoms of HIV infection before commencing PrEP. A fourth-generation HIV antibody/antigen venous blood test should be performed within 7 days of the patient being evaluated for PrEP. HIV testing must be repeated every 3 months when patients attend for a repeat prescription.

Creatinine, estimated glomerular filtration rate (eGFR) and urinary PCR measurements should be evaluated at baseline, with eGFR repeated every 3 months after commencing PrEP and then 6-monthly thereafter.

With the increased risk of HIV transmission by over 2-fold for women who are pregnant, current evidence suggests PrEP can be used safely during pregnancy and breastfeeding.[10]

Daily PrEP

In September 2019, the ASHM PrEP Guidelines panel endorsed the WHO recommendation that daily PrEP regimen should be offered to all populations at risk of HIV infection who meet the following recommended criteria:[10]

- MSM
- transgender and gender-diverse people
- heterosexual men and women
- people who inject drugs.

On-demand PrEP

On-demand PrEP ('The 2 + 1 + 1' dosing of PrEP) involves taking 2 tablets of Truvada 2–24 hours before a potential sexual exposure to HIV, followed by a third tablet 24 hours after the first dose, and a fourth tablet 48 hours after the first dose. If sex continues for several days, patients should take 1 tablet of Truvada daily until the last sex act, followed by a final dose 24 hours later, and again at 48 hours after the last episode of sex.

The ASHM PrEP Guidelines panel endorsed the WHO recommendation on-demand PrEP should be offered to cisgender MSM. On-demand PrEP is contraindicated in people with chronic hepatitis B infection.[10]

Post-exposure prophylaxis (PEP)

Although non-occupational Post-Exposure Prophylaxis (nPEP) is still available, PrEP is now used for treatment rather than prevention. However, nPEP may be required before transitioning to PrEP. Patients who have had a recent high-risk exposure within 72 hours may also be assessed for nPEP.

Adolescent patients

Due to low evidence and issues with patient adherence to medication, the ASHM PrEP Guidelines panel recommend caution for on-demand and daily PrEP for adolescent MSM. PrEP use for prevention of HIV in adolescents is currently not subsidised on the PBS.

Financial considerations

It is unlikely people living with HIV will require admission to hospital for treatment of HIV-related morbidities. Most require only regular check-ups and monitoring, either in specialised general practices or in hospital outpatient departments, every 3–6 months. Table 5 provides a summary of the cost of therapies for HIV. Table 6 provides a summary of costings for a broader range of medications commonly used in the management of patients with HIV. Table 7 provides a summary of costings on medical benefits provided to people with HIV.

Table 5: *Pharmaceutical costs of preferred antiretroviral regimens as of April 2020*

Drug	PBS item no.	Usual dose/ frequency	Unit cost	Estimated annual cost
Co-formulated preparations				
Abacavir 300 mg + lamivudine 150 mg + zidovudine 300 mg tablet, 60 (Trizivir)	10305J	1 tablet twice daily	$339.40	$4,129
Abacavir 600 mg + lamivudine 300 mg tablet, 30 (Kivexa)	10357D	Once daily	$262.69	$3,196
Tenofovir disoproxil fumarate 300 mg + emtricitabine 200 mg + efavirenz 600 mg tablet, 30 (Atripla)	10297Y	Once daily	$325.12	$3,956
Tenofovir disoproxil fumarate 300 mg + emtricitabine 200 mg tablet, 30	10347N	Once daily	$99.89	$1,215
Lopinavir 200 mg + ritonavir 50 mg tablet, 120 (Kaletra)	10272P	2 tablets twice daily	$693.31	$8,435
Lamivudine 150 mg + zidovudine 300 mg tablet, 60 (Combivir)	10284G	1 tablet twice daily	$108.75	$1,323
Dolutegravir 50 mg + abacavir 600 mg + lamivudine 300 mg tablet, 30 (Triumeq)	10345L	Once daily	$853.73	$10,387
Emtricitabine 200 mg + tenofovir alafenamide 25 mg tablet, 30 (Descovy)	11113X	Once daily	$723.76	$8,806
Tenofovir alafenamide 10 mg + emtricitabine 200 mg + elvitegravir 150 mg + cobicistat 150 mg tablet, 30 (Genvoya)	11114Y	Once daily	$981.76	$11,945
Emtricitabine 200 mg + rilpivirine 25 mg + tenofovir alafenamide 25 mg tablet, 30 (Odefsey)	11104K	Once daily	$981.76	$11,945
Bictegravir 50 mg + emtricitabine 200 mg + tenofovir alafenamide 25 mg tablet, 30 (Biktarvy)	11649D	Once daily	$924.04	$11,242

Drug	PBS item no.	Usual dose/ frequency	Unit cost	Estimated annual cost
Dolutegravir 50 mg + rilpivirine 25 mg tablet, 30 (Juluca)	11540J	Once daily	$866.13	$10,538
Dolutegravir 50 mg + lamivudine 300 mg tablet, 30 (Dovato)	11843H	Once daily	$721.48	$8,778
Raltegravir 600 mg tablet, 60	11248B	Once daily	$592.74	$3,606
Source of unit cost data: Schedule of Pharmaceutical Benefits, Effective 1–30 April 2020.[13] Available from: www.pbs.gov.au/info/publication/schedule/archive Unit cost of drug = Dispensed Price for Maximum Quantity (DPMQ/Max qty packs. Unit values are presented up to 2 decimal places. Total costs have been computed on these unit values, and rounded to the nearest whole number.				

Table 6: *Pharmaceutical costs of commonly prescribed prophylactic medications as of April 2020*

Drug	PBS item no.	Usual dose/ frequency	Unit cost	Estimated annual cost	Usual indications
Aciclovir 200 mg tablet, 25	1003T	200 mg three times daily	$12.57	$550	Herpes simplex virus
Famciclovir 500 mg tablet, 56	8896F	500 mg twice daily	$72.34	$943	Herpes simplex virus
Valaciclovir 500 mg tablet, 42	8064K	Once daily	$31.44	$273	Herpes simplex virus
Ganciclovir 500 mg injection, 5 vials	5749N	Once daily	$158.37	$11,561	Cytomegalovirus
Valganciclovir 450 mg tablet, 60	9569P	2 tablets daily (maintenance)	$713.52	$8,681	Cytomegalovirus
Trimethoprim 160 mg + sulfamethoxazole 800 mg tablet, 10	2951H	Once daily	$13.37	$488	*Pneumocystis carinii* (jiroveci) pneumonia/toxoplasmosis
Dapsone 100 mg tablet, 100	1272Y	Once daily	$302.92	$1,106	*Pneumocystis carinii* (jiroveci) pneumonia
Trimethoprim 300 mg tablet, 7	2922T	Once daily	$13.18	$687	*Pneumocystis carinii* (jiroveci) pneumonia
Itraconazole 100 mg capsule, 60	8196J	Once daily	$129.05	$785	Oral candidiasis; other fungal infections
Fluconazole 200 mg capsule, 28	1475P	200 mg daily	$51.85	$676	Oral candidiasis; Cryptococcus
Clindamycin 150 mg capsule, 24	3138E	1 capsule daily	$12.62	$192	Toxoplasmosis
Clarithromycin 250 mg tablet, 14	8318T	500 mg twice daily	$14.44	$1,506	*Mycobacterium avium* complex
Azithromycin 600 mg tablet, 8	5616N	600 mg x 2 once a week	$55.38	$720	*Mycobacterium avium* complex
Rifabutin 150 mg capsule, 30	9541E	Twice daily (prophylaxis)	$131.46	$3,199	*Mycobacterium avium* complex

Source of unit cost data: Schedule of Pharmaceutical Benefits, Effective 1–30 April 2020.[13] Available from: www.pbs.gov.au/info/publication/schedule/archive

Unit cost of drug = Dispensed Price for Maximum Quantity (DPMQ)/Max qty packs.

Drug	PBS item no.	Usual dose/ frequency	Unit cost	Estimated annual cost	Usual indications
Unit values are presented up to 2 decimal places. Total costs have been computed on these unit values, and rounded to the nearest whole number.					

Table 7: *Medicare Benefits Schedule and other medical service costs as of April 2020*

Service	MBS item no.	Frequency	Unit cost	Estimated annual cost
Medical				
General practitioner consultations	23	3–6-monthly	$38.20	$153
Specialist consultations – initial treatment and management plan	132	Once only	$272.15	$272
Specialist consultations – review of plan	133	Annual	$136.25	$136
Specialist consultations – subsequent	116	6-monthly	$77.90	$156
Nurse support	10956	Monthly	$63.25	$759
Chronic disease management plan	721	Annual	$146.55	$147
Diagnostics				
Renal function test	12524	3–6-monthly	$160.90	$644
FBE, including: Erythrocyte count, haematocrit, haemoglobin, calculation or measurement of red cell index or indices, platelet count, leucocyte count and manual or instrument generated differential count	65070	3-monthly	$16.95	$68
Liver Function Tests, fasting lipids	66512	3–6-monthly	$17.70	$71
HIV viral load	69378/ 69381	3–6-monthly	$180.25	$721
Genotypic testing for HIV antiretroviral resistance (in a patient with confirmed HIV infection if the patient's viral load is greater than 1,000 copies/mL)	69380	Maximum 2 tests in a 12-month period	$770.30	$1,541
CD4 T-cell lymphocyte count	71139	3–6-monthly	$104.05	$416
Quantitation of 1 antibody to microbial antigens (including CMV)	69384	As required	$15.65	$16

Service	MBS item no.	Frequency	Unit cost	Estimated annual cost
Fasting glucose	66551	Annual	$16.80	$17
Ambulatory ECG (optional)	11710	Annual	$52.75	$53
Chest x-ray (requested)	58503	Once	$47.15	$47
Mantoux test	73811	Once	$11.20	$11
HIV genotyping	71151	Once	$118.85	$119

Source of unit cost data: Medicare Benefits Schedule operating from 01 March 2020.[12] Available from: www.mbsonline.gov.au/internet/mbsonline/publishing.nsf/Content/Home

Unit values are presented up to 2 decimal places. Total costs have been computed on these unit values, and rounded to the nearest whole number.

Prejudice to access and scarcity of resources

With reference to 'Sch4/4005-4007 – The health requirement' on the health-related criteria at the time of this publication, none of the services considered short in supply are applicable.

Effect on applicant's ability to work

In most people with a CD4 count greater than 200 cells/mm^3 (that is, greater than the range for diagnosis of AIDS), HIV infection will not affect an individual's ability to work. If opportunistic infections or cancers occur (in particular, rare AIDS illnesses, such as HIV dementia or wasting), then there may be an impact on an individual's capacity to work. HIV does not impact an individual's ability to work.

Many individuals who have been unwell have subsequently returned to work once they have responded to ART. Factors that may play a role in returning to work, including sex, age, race/ethnicity, health status and the belief that health will improve if employed, independently were associated with contemplating a return to work.

Very few insurance companies now accept the diagnosis of HIV alone as indicative of total and permanent disability, because of the likelihood of a future return to work. Most breaks from work as a result of ill health now are considered temporary. It would seem reasonable to correlate the probability of disability, and time to disability, with progression to AIDS. There should be awareness that many of those who respond to therapy will return to work once their HIV infection is under control.

Appendices

Appendix A: HIV testing on Australian visa applicants

Venepuncture should be performed onsite at the panel clinic once the applicant's identity has been confirmed.

The visa case officer will generate testing requirements for HIV, based on the type of visa and intended occupation in Australia. A summary is provided below in Table 8.

Table 8: *HIV testing requirements*

Type of applicant	Test for HIV?
Permanent visa applicants, 15 years of age or older	Yes
Non-migrating relatives of Permanent visa applicants, aged 15 years or older, if requested by the visa case officer to undertake medicals	Yes
Children who have been, or are to be, adopted by Australian residents	Yes
Unaccompanied minor refugee children	Yes
Children aged 14 years of age or younger with clinical suspicion for HIV infection, a history of blood transfusions or haemophilia, or if the mother is HIV seropositive	Yes
Temporary entry applicants with clinical signs of AIDS	Yes
All applicants who intend to work as, or study to be a physician, nurse, paramedic or dentist*	Yes
Persons known or found to be infected with hepatitis C	Yes
Persons where there is evidence of previous or current intravenous drug use	Yes
Persons where active TB is diagnosed	Yes

Source: Australian Panel Member Instructions: Immigration Medical Exams.[14]

* Other allied health professionals, including physiotherapists, occupational and speech therapists, laboratory technicians and veterinarians, do not routinely need testing for HIV, hepatitis B or C.

Acceptable screening tests for HIV

There are four categories of HIV tests: simple/rapid anti-HIV tests, EIAs, immunoblot tests and NATs. First line HIV screening should ideally be performed with a fourth-generation EIA-based kit. Third-generation kits are acceptable if fourth-generation kits cannot be accessed. Machine-based ELISA assays are acceptable as a first-line screen.

Note: For any reactive initial screening test, this should be re-checked on the same blood sample with an alternate HIV test, and if still reactive or indeterminate, there is the need for formal confirmatory testing.

Confirmatory and supplementary tests results are as listed below.

- Screening test negative – no further action is needed.
- Screening test indeterminate – proceed to confirmatory testing with immunoblot. If this is not available, re-testing with a different EIA method to the original test is advised.
- Screening test reactive – a second supplemental test to clarify the status of the sample should be performed with a confirmatory immunoblot assay. If these are not available, re-testing with two alternative kits is advised.

Appendix B: Algorithm for early infant diagnosis

Source: WHO consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection.[40] Available from: www.who.int/hiv/pub/arv/arv-2016/en/

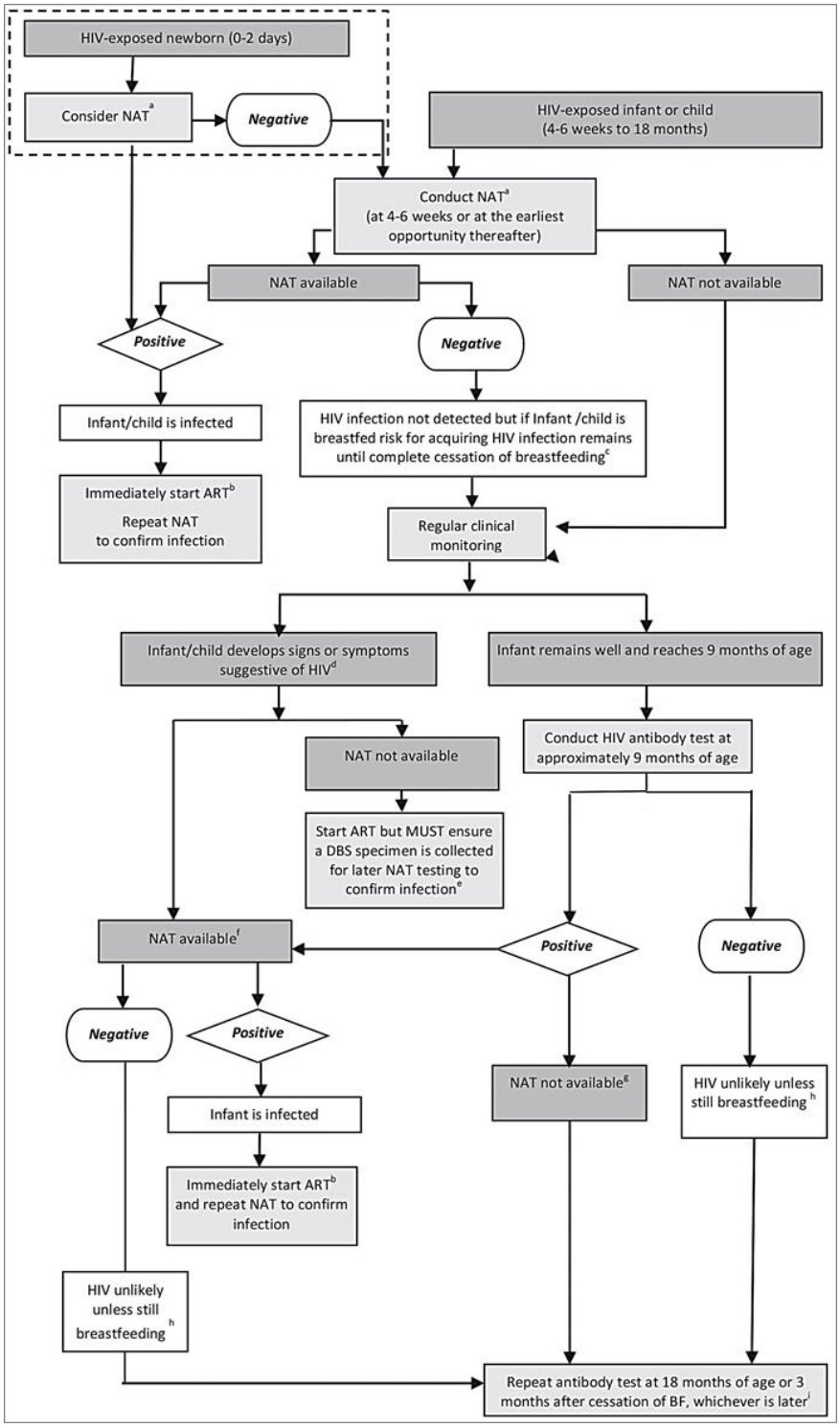

Figure 1: *Algorithm for Early Infant Diagnosis of HIV Infection*

Notes on Figure 1

[a] Based on these revised Guidelines addition of NAT at birth to the existing testing algorithm can be considered. POC NAT can be used to diagnose HIV infection at birth, but positive results should be confirmed using laboratory-based NAT assays, because of limited experience with POC assays close to birth.

[b] Start ART, without delay. At the same time, retest to confirm infection. As maternal treatment is scaled up and MTCT transmission rates decrease, false-positive results are expected to increase and re-testing after a first positive NAT is important to avoid unnecessarily treatment, particularly in settings with lower transmission rates. If the second test is negative, a third NAT should be done before interrupting ART.

[c] For children who were never breastfed additional testing following a negative NAT at 4-6 weeks is included in this algorithm to account for potential false-negative NAT results.

[d] Signs and symptoms suggestive of HIV (oral thrush, recurrent or severe bacterial infections such as pneumonia or sepsis, FTT/wasting or AIDS indicator condition).

[e] If infant presents with signs and symptoms of HIV disease (see footnote d above) but NAT is unavailable, consider starting ART, especially if an antibody test is conducted and result positive at 9 months or later. A DBS specimen must be collected prior to starting treatment for later NAT testing to confirm HIV diagnosis, because subsequent diagnostic testing while already on ART might be difficult to interpret.

[f] If infant presents with signs and symptoms of HIV disease (see footnote d above) consider starting ART while waiting for NAT result. However, another DBS specimen should be collected prior to starting treatment for later NAT testing to confirm HIV diagnosis.

[g] Regular and periodic monitoring should be ensured while waiting for NAT to be available or for antibody testing to be conducted at 18 months. If infant presents with signs and symptoms of HIV disease should be managed as described previously (see footnote e).

[h] The risk of HIV transmission remains as long as breastfeeding continues. If the 9 months antibody testing is conducted earlier than 3 months after cessation of breastfeeding, infections acquired in the last days of breastfeeding may be missed so retesting at 18 months should be ensured for final assessment of HIV status.

[i] If breastfeeding beyond 18 months, final diagnosis of HIV status can only be assessed at the end of breastfeeding. If breastfeeding ends before 18 months, final diagnosis of HIV status with antibody testing can only be assessed at 18 months. Antibody testing should be undertaken at least 3 months after cessation of breastfeeding (to allow for development of HIV antibodies). For infants < 18 months of age positive antibody testing requires NAT to confirm infection. If infant is > 18 months, negative antibody testing confirms infant is uninfected; positive antibody testing confirms infant is infected

Appendix C: Antiretroviral fixed-dose combination tablets

Table 9: *Minimum body weights and considerations for fixed-dose combination tablets in children and adolescents as of April 2020*

FDC by brand name	Generic products	FDC components	PBS number	Minimum body weight (kg) or age	Food requirements
NRTI					
Combivir	Lamivudine 150 mg + zidovudine 300 mg tablet, 60	3TC 150 mg/ZDV 300 mg	10284G	30 kg	Take with or without food
Descovy	Emtricitabine 200 mg + tenofovir alafenamide 25 mg tablet, 30	FTC 200 mg/TAF 25 mg	11113X	25 kg with INSTI or NNRTI, 35 kg with boosted PI	Take with or without food
Trizivir	Abacavir 300 mg + lamivudine 150 mg + zidovudine 300 mg tablet, 60	ABC/3TC/ZDV	10305J	40 kg	Take with or without food
Truvada	Tenofovir disoproxil fumarate 300 mg + emtricitabine 200 mg tablet, 30	FTC/TDF	10347N	35 kg	Take with or without food
NRTI/NNRTI					
Atripla	Tenofovir disoproxil fumarate 300 mg + emtricitabine 200 mg + efavirenz 600 mg tablet, 30	EFV/FTC/TDF	10297Y	40 kg	Take on an empty stomach
Odefsey	Emtricitabine 200 mg + rilpivirine 25 mg + tenofovir alafenamide 25 mg tablet, 30	FTC/RPV/TAF	11104K	35 kg and ≥12 years	Take with a meal

FDC by brand name	Generic products	FDC components	PBS number	Minimum body weight (kg) or age	Food requirements
NRTI/INSTI					
Biktarvy	Bictegravir 50 mg + emtricitabine 200 mg + tenofovir alafenamide 25 mg tablet, 30	BIC/FTC/TAF	11649D	≥25 kg	Take with or without food
Dovato	Dolutegravir 50 mg + lamivudine 300 mg tablet, 30	DTG/3TC	11843H	Adults	Take with or without food
Triumeq	Dolutegravir 50 mg + abacavir 600 mg + lamivudine 300 mg tablet, 30	ABC/DTG/3TC	10345L	40 kg and a minimum 12 years of age	Take with or without food
NNRTI/INSTI					
Juluca	Dolutegravir 50 mg + rilpivirine 25 mg tablet, 30	DTG/RPV	11540J	Adults	Take with a meal
NRTI/INSTI/COBI					
Genvoya	Tenofovir alafenamide 10 mg + emtricitabine 200 mg + elvitegravir 150 mg + cobicistat 150 mg tablet, 30	EVG/COBI/FTC/TAF	11114Y	25 kg	Take with food
PI/COBI					
Evotaz	Atazanavir 300 mg + cobicistat 150 mg tablet, 30	ATV/COBI	10692R	35 kg	Take with food

FDC by brand name	Generic products	FDC components	PBS number	Minimum body weight (kg) or age	Food requirements
Prezcobix	Darunavir 800 mg + cobicistat 150 mg tablet, 30	DRV/COBI	10903W	40 kg	Take with food
PI/RTV					
Kaletra	Lopinavir 400 mg/5 mL + ritonavir 100 mg/5 mL oral liquid, 60 mL	LPV/RTV	10327M	Postmenstrual age of 42 weeks and a postnatal age >14 days (no minimum weight)	Take with or without food
	Lopinavir 200 mg + ritonavir 50 mg tablet, 120		10272P		
	Lopinavir 100 mg + ritonavir 25 mg tablet, 60		10285H		
Adapted from: US DHHS. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV infection.[33] Schedule of Pharmaceutical Benefits, Effective 1–30 April 2020.[13] Available from: www.pbs.gov.au/info/publication/schedule/archive					

Appendix D: Scenarios

Scenario 1 – HIV-1 infection

A 22-year-old Thai man who currently holds a student visa for a 4-year stay has been in Australia for 3 years and has applied for a permanent visa. The applicant was diagnosed as being HIV antibody-seropositive 1 year after arriving in Australia and is asymptomatic. He denies intravenous drug use and has no coinfection with HBV or HCV.

His CD4+ T-cell count and HIV viral load were measured in the previous 12 months; the results were 600 cells/mm^3 and fewer than 10,000 copies/mL, respectively.

Clinical opinion

Since the presentation of the START and TEMPRANO trials in mid-2015, the consensus on treatment is everyone should be initiated with ART as soon as possible after receiving an HIV diagnosis, regardless of their CD4+ T-cell count. The START trial demonstrated that patients who defer ART fare worse than those who started ART immediately, resulting in more HIV-related and non-HIV-related adverse events.

Regarding the success of treatment, the most recent trials of first-line ART using INSTI plus 2 NRTIs demonstrate approximately 90% of patients have an undetectable viral load (<50 copies/mL) at 48 weeks.[18] Guideline advice regarding preferred initiation ART options is constantly evolving.

Based on current recommendations, initiation of ART would involve 1 of the 5 regimens listed below.

- Triumeq (dolutegravir + abacavir + lamivudine)/DTG+ABC+3TC
- Tivicay (dolutegravir) and Descovy (emtricitabine + tenofovir alafenamide)/DTG+TAF/FTC or TDF/FTC
- Biktarvy (bictegravir/tenofovir alafenamide/emtricitabine)/BIC+TAF+FTC
- Dovato (dolutegravir/lamivudine)/DTG+3TC
- Raltegravir+TAF+FTC or TDF+FTC

Table 10: *Scenario 1: Prospective regimen/service profile and costs involved as of April 2020*

Description	Item reference	Code	Unit cost	Year 1		Years 2–10	
				Frequency	Annual cost	Frequency	Annual cost
MEDICAL							
General practitioner consultations	MBS	23	$38.20	3-monthly	$153	3-monthly	$153
Specialist consultations – initial treatment and management plan	MBS	132	$272.15	Once only	$272	-	-
Specialist consultations – review of plan	MBS	133	$136.25	Once	$136	-	-
Specialist review consultations	MBS	116	$77.90	6-monthly	$156	Yearly	$78

Description	Item reference	Code	Unit cost	Year 1		Years 2–10	
				Frequency	Annual cost	Frequency	Annual cost
Subtotal					$717		$231
DIAGNOSTICS							
FBE: Liver enzymes/renal Glucose/lipids	MBS	65070	$16.95	3-monthly	$68	Once yearly	$17
CD4 T-cell lymphocyte count	MBS	71139	$104.05	3-monthly	$416	Once yearly	$104
HIV viral load	MBS	69378	$180.25	3-monthly	$721	Once yearly	$180
Toxoplasma antibody	MBS	71121	$20.80	Once	$21	-	-
CMV antibody							
Mantoux test	MBS	73811	$11.20	Once	$11	-	-
Chest x-ray	MBS	58503	$47.15	Once	$47	-	-
Subtotal					$1,284		$301
PHARMACEUTICAL AGENTS							
Bictegravir 50 mg + emtricitabine 200 mg + tenofovir alafenamide 25 mg tablet, 30 (Biktarvy)	PBS	11649D	$924.04	Once daily	$11,242	Once daily	$11,242
Totals				**$13,243**		**$11,774**	
TOTAL COST OVER 10 YEARS				**$119,209**			
Unit values are presented up to 2 decimal places. Total costs have been computed on these unit values, and rounded to the nearest whole number.							

Scenario 2 – HIV-2 infection in woman of reproductive age

A 28-year-old female refugee from Sudan who is applying for a Subclass 200 refugee visa was found to be HIV seropositive (HIV-2). She is married without children. HIV-2 circulates in Africa (mainly Western Africa). HIV-2 does not respond to NNRTI class ARVs. She currently is asymptomatic and has a CD4+ T-cell count of 270 cells/mm^3 and a viral load of 50,000 copies/mL.

Clinical opinion

As the patient is sexually active and of child-bearing age, a dolutegravir regimen would not be recommended for use due to possible conception. Based on current recommendations, initiation of a first-line ART regimen based on raltegravir would be used: Raltegravir plus (emtricitabine or lamivudine) plus tenofovir alafenamide or tenofovir disoproxil fumerate,

This regimen would be continued indefinitely unless intolerability or adverse effects lead to a switch to an alternative first-line regimen, or virological failure leads to a change to a guideline-recommended second-line ART regimen. A pregnancy test should be performed prior to initiation of ART or contraceptive counselling provided.

If the patient continues to be adherent to ART, the viral load will remain suppressed. The increase in her CD4+ T-cell count is expected to be in the order of 50–100 cells/mm^3 after 6 months, and thereafter should return to a level within the normal range. She would have an 85–90% likelihood of having a viral load <50 copies/mL after 6 months of ART, assuming adequate adherence to ART. Once the viraemia is suppressed, it should remain that way for the foreseeable future, again assuming adequate ART adherence.

Table 11: *Scenario 2: Prospective regimen/service profile and costs involved as of April 2020*

Description	Item reference	Code	Unit cost	Year 1		Years 2–10	
				Frequency	Annual cost	Frequency	Annual cost
MEDICAL							
General practitioner consultations	MBS	23	$38.20	3-monthly	$153	3-monthly	$153
Specialist review consultations	MBS	116	$77.90	6-monthly	$156	6-monthly	$156
Subtotal					$309		$309
DIAGNOSTICS							
FBE: Liver enzymes/renal Glucose/lipids	MBS	65070	$16.95	3-monthly	$68	Once yearly	$17
CD4 T-cell lymphocyte count	MBS	71139	$104.05	3-monthly	$416	Once yearly	$104
HIV viral load	MBS	69378	$180.25	3-monthly	$721	Once yearly	$180
Toxoplasma antibody	MBS	71121	$20.80	Once	$21	-	-

Description	Item reference	Code	Unit cost	Year 1		Years 2–10	
				Frequency	Annual cost	Frequency	Annual cost
CMV antibody							
Mantoux test	MBS	73811	$11.20	Once	$11	-	-
Chest x-ray	MBS	58503	$47.15	Once	$47	-	-
Pregnancy test	MBS	73806	$10.15	Once	$10		
Subtotal					$1,294		$301
PHARMACEUTICAL AGENTS							
Raltegravir 600 mg tablet, 60	PBS	11248B	$592.74	Once daily	$3,606	Once daily	$3,606
Tenofovir disoproxil fumarate 300 mg + emtricitabine 200 mg tablet, 30	PBS	10347N	$99.89	Once daily	$1,215	Once daily	$1,215
Subtotal					$4,821		$4,821
Totals				**$6,424**		**$5,431**	
TOTAL COST OVER 10 YEARS*				**$55,303**			
Unit values are presented up to 2 decimal places. Total costs have been computed on these unit values and rounded to the nearest whole number.							

Scenario 3 – HIV infection with first-line drug resistance

A 45-year-old US citizen, who is the long-term partner of an Australian citizen resident in the United States, wishes to visit for business reasons. He currently is receiving treatment comprising tenofovir, emtricitabine and raltegravir. He has a CD4+ T-cell count of 100 cells/mm^3 and a viral load of greater than 100,000 copies/mL. He has experienced recent hospitalisation for *Pneumocystis jirovecii* pneumonia but is now symptom-free. He tolerates Bactrim for prophylaxis of *Pneumocystis jirovecii* infection (this medication would cease after virological control is achieved and maintained at CD4 count >200 cells/mm^3 for 3 months).

Clinical opinion

The plasma viral load in this patient suggests either very poor adherence to ART and/or high-level resistance to the agents the patient has been prescribed. Strong consideration should be given to having an honest discussion about the medication adherence. He has had a previous AIDS-defining illness. His current CD4+ T-cell count is 100 cells/mm^3 and the HIV viral load is high. Consideration should also be given to changing the ART to a combination with the potential to fully suppress the patient's plasma viral load, and thereby raise the CD4+ T-cell count.

In order to optimise the ART regimen choice a genotypic antiretroviral resistance test should be requested while the patient is taking the failing ARV regimen (or within 4 weeks of discontinuing treatment), in addition to a genotypic test to assess the patient's viral coreceptor tropism (this latter test will provide information regarding the potential use of maraviroc, a CCR5 attachment inhibitor). Once these results are available, the physician can construct a new ART regimen which should contain at least 2, but preferably 3 fully active agents. Attention would need to be paid to the patient's past exposure to ARVs, a record (or recollection) of any intolerance, or virological failure for any of these and previous drug resistance test results. Once this has been established to the best of the patient's and physician's ability, the patient should commence the new optimised regimen.

A combination of boosted PI, such as ritonavir-boosted darunavir 600/100 mg every 24 hours plus a second-generation integrase inhibitor, such as dolutegravir, can offer ART activity from the resistance test. A balance must be found between an effective, yet tolerable regimen in order to optimise patient adherence. In the setting of adequate adherence, the patient would have an 80–90% chance of achieving full virological suppression within 20 weeks of initiation, together with a concomitant CD4+ T-cell count rise.

The patient would require prophylaxis with cotrimoxazole (Bactrim) 800/160 mg every 24 hours for *Pneumocystis jirovecii* pneumonia. He would not require prophylaxis against infections with *Mycobacterium avium* complex (azithromycin) or CMV (ganciclovir).

The patient's CD4+ T-cell count may rise in response to the drop in viral load to a level where his risk of progression to AIDS would decrease, although the degree of CD4+ cell count rise may be compromised by this low nadir and his relatively older age (both these variables are associated with a poorer CD4+ T-cell recovery). It is plausible that this response would be sustained in the presence of adequate adherence to ART.

Table 12: *Scenario 3: Prospective regimen/service profile and costs involved as of April 2020*

Description	Item reference	Code	Unit cost	Year 1		Years 2–10	
				Frequency	Annual cost	Frequency	Annual cost
MEDICAL							
General practitioner consultations	MBS	23	$38.20	3-monthly	$153	3-monthly	$153
Specialist review consultations	MBS	116	$77.90	6-monthly	$156	6-monthly	$156
Subtotal					$309		$309
DIAGNOSTICS							
FBE: Liver enzymes/renal Glucose/lipids	MBS	65070	$16.95	3-monthly	$68	Once yearly	$17
CD4 T-cell lymphocyte count	MBS	71139	$104.05	3-monthly	$416	Once yearly	$104
HIV viral load	MBS	69378	$180.25	3-monthly	$721	Once yearly	$180
Genotypic testing for HIV antiretroviral resistance (in a patient with confirmed HIV infection if the patient's viral load is greater than 1,000 copies/mL)	MBS	69380	$770.30	Maximum 2 tests within 12 months	$1,541	-	-
Subtotal					$2,746		$301
PHARMACEUTICAL AGENTS							
Darunavir 600 mg tablet, 60	PBS	10329P	$920.34	2 tablets twice daily	$22,395	2 tablets twice daily	$22,395
Ritonavir 100 mg tablet, 30	PBS	10273Q	$34.90	1 tablet twice daily	$849	-	-

Description	Item reference	Code	Unit cost	Year 1		Years 2–10	
				Frequency	Annual cost	Frequency	Annual cost
Dolutegravir 50 mg tablet, 30	PBS	10283F	$655.97	-	-	Once daily	$7,981
Trimethoprim 160 mg + sulfamethoxazole 800 mg tablet, 10 (Cotrimoxazole) (Prophylaxis for *Pneumocystis* pneumonia)	PBS	2951H	$13.37	-	-	1 tablet once daily	$488
Subtotal					$23,244		$30,864
Totals				**$26,299**		**$31,474**	
TOTAL COST OVER 10 YEARS*				**$309,565**			
Unit values are presented up to 2 decimal places. Total costs have been computed on these unit values, and rounded to the nearest whole number.							

Scenario 4 – Paediatric HIV infection

A 9-month-old boy from South East Asia, currently living in an orphanage, is being adopted by an Australian couple. Screening for blood–borne viruses revealed a positive HIV antibody test. No family or medical history is available. The infant weighs 8 kg.

Clinical opinion

It is recommended that HIV virological testing (such as HIV RNA and HIV DNA NATs) be used to diagnose HIV infection in infants and children younger than 18 months of age with perinatal and postnatal HIV exposure. A positive NAT combined with the positive antibody result confirms this child to be HIV infected.

In all children younger than 12 years old who are not exposed to ARVs, or whose exposure to ARVs is unknown, ART should be initiated regardless of CD4 count or WHO clinical stage from the following regimens recommended for initial therapy of ARV naive children (see also Table 3).

For children 9 months old who weigh over 2 kg:

- 2 NRTIs plus LPV/r; or
- 2 NRTIs plus RAL.

For children 3 years of age to12 years of age who weigh less than 25 kg:

- 2 NRTIs plus ATV/r; or
- 2 NRTIs plus DRV/r; or
- 2 NRTIs plus RAL.

For children 3 years of age–12 years of age who weigh more than 25 kg:

- 2 NRTIs plus DTG; or
- 2 NRTIs plus EVG/COBI.

See Table 14 for the 10-year costs involved for this patient.

Table 13: *Scenario 4: Prospective regimen/service profile and costs involved as of April 2020*

Description	Item reference	Code	Unit cost	Years 1–2		Years 3–10*	
				Frequency	Annual costs	Frequency	Annual costs
MEDICAL							
General practitioner consultations	MBS	23	$38.20	3-monthly	$153	3-monthly	$153
Paediatric specialist consultations – initial treatment and management plan	MBS	132	$272.15	Once only	$272	-	-
Paediatric specialist consultations – review of plan	MBS	133	$136.25	Once	$136	-	-
Paediatric specialist review consultations	MBS	116	$77.90	6-monthly	$156	Annually	$78
Subtotal					$717		$231
DIAGNOSTICS							
HIV viral load	MBS	69378	$180.25	3-monthly	$721	3-monthly	$721
PHARMACEUTICAL AGENTS							
Abacavir 20 mg/mL oral liquid, 240 mL	PBS	10356C	$70.31	6 mL twice daily	$1,283	15 mL (300 mg) twice daily	$3,208
Lamivudine 10 mg/mL oral liquid, 240 mL	PBS	10320E	$59.14	6 mL twice daily	$1,079	6 mL twice daily	$1,079
Lopinavir 400 mg/5 mL + ritonavir 100 mg/5 mL oral liquid, 60 mL (Kaletra)	PBS	10327M	$130.89	1.9 mL twice daily	$3,026	n/a	n/a

Raltegravir 25 mg chewable tablet, 60	PBS	10299C	$76.26	n/a	n/a	100–150 mg twice daily	$5,567
Subtotal					$5,388		$9,854
Totals				**$6,826**		**$10,806**	
TOTAL COST OVER 10 YEARS				**$100,100**			

Unit values are presented up to 2 decimal places. Total costs have been computed on these unit values, and rounded to the nearest whole number.

*Assumes weight of <25 kg for the remaining 9 years

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