

HIV antiretroviral medicines: Utilisation analysis using MedicineInsight data

Drug utilisation sub-committee (DUSC)

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Abstract

Purpose

PBAC requested a review of the utilisation of medicines used for the treatment of Human Immunodeficiency Virus (HIV) and for pre-exposure prophylaxis of HIV at its June 2021 meeting. The analyses in this report are for the HIV antiretroviral medicines and are based on general practice data from MedicineInsight.

Data Source / methodology

This study is a descriptive analysis of MedicineInsight data exploring the prescribing of HIV antiretroviral medicines to patients attending general practice. It uses de-identified patient data from the clinical information systems (CIS) of 145 individual practices for the study period 1 (1 January 2018 to 31 December 2019) and 117 individual practices for study period 2 (calendar year 2020).

Key Findings

- This study includes 5.0–5.5% of the approximately 27,500 Australians living with HIV in Australia.
- Patients with diagnosed HIV using antiretroviral medicines were overwhelmingly male (~95%), from higher socioeconomic backgrounds (~62%) and living in major cities (~87%). On average they were aged 50 years.
- Mental illnesses were the most commonly reported co-morbidity. Approximately 40% of patients had a prior or current record of depression and approximately 30% had a prior or current record of anxiety.
- A quarter of patients had been diagnosed with hypertension and 30% had a record of dyslipidaemia.
- Approximately 14% of patients had been diagnosed with both HIV and chronic hepatitis C.
- Even though the majority of patients were males aged in their 50s, 8.7–8.9% of patients had been diagnosed with osteoporosis.
- Fixed dose combination (FDC) antiretroviral medicines were the most commonly prescribed. The FDC bictegravir + tenofovir alafenamide + emtricitabine (Biktarvy)

was prescribed for 31.0% of patients and was the most commonly prescribed individual medicine.

- The HIV Protease Inhibitors (HIV-PIs) are associated with increased cardiovascular risk. Among all patients who were prescribed an antiretroviral medicine, the number of patients with recorded cardiovascular disease, at risk of cardiovascular disease or with recorded dyslipidaemia who were prescribed an HIV-PI was 32 (2.1%), 97 (6.4%) and 66 (4.4%), respectively.
- Regimens including rilpivirine or efavirenz should be used in caution in patients with mental illness due to a higher risk of central nervous system side effects. Among all patients who were prescribed an antiretroviral medicine, the number of patients with a prior or current record of mental illness who were prescribed rilpivirine or efavirenz was 116 (7.6%) and 34 (2.2%), respectively.

Purpose of analysis

At its June 2021 meeting, DUSC requested a review of antiretroviral medicines for the treatment or prevention of HIV. DUSC noted that the previous review of these medicines had been conducted in 2013. Since this time there have been a number of changes including:

- PBS restrictions limiting the use of antiretroviral medicines to patients with CD4+ counts^a of less than 500 cells/mm³ or symptomatic HIV disease were removed in late 2013;¹
- the addition of new antiretroviral medicines and new combination regimens to treat HIV to the PBS. DUSC noted substantial growth in the utilisation of some of the newer antiretroviral combination regimens in recent years;²
- the addition of PrEP which prevents infection in HIV negative people to the PBS in 2018.

DUSC sought to understand the impacts of these changes on the utilisation of HIV medicines. DUSC requested that the utilisation of antiretroviral medicines for the treatment and prevention of HIV be reviewed using both PBS dispensing data and MedicineInsight data.

This paper reports on the MedicineInsight analysis.

Background

Clinical situation

The HIV virus attacks the body's immune system. Left untreated it will cause severe damage to the immune system within 10 years and the development of acquired immunodeficiency syndrome (AIDS). HIV is transmitted through unprotected sex, by blood-to-blood contact including through injecting drug use, and from mother to child. Currently HIV cannot be cured but can be controlled with effective treatments that enable people living with HIV (PLWHIV) to live long healthy lives and to protect their partners from infection.³

It has been estimated that 0.14% of the Australian population, or approximately 27,500 Australians, are living with HIV.⁴ Since 2012, there has been a general trend towards fewer new HIV diagnoses being made each year. This is thought to be due to more people living with HIV being aware of their HIV status, earlier treatment of the disease and the strong uptake of PrEP among gay and bisexual men. However, in 2019, the number of Australian diagnosed with HIV increased from 839 in 2018 to 901 in 2019.⁵

^a The number of CD4+ white blood cells per cubic millimetre of blood. CD4 cells alert other immune cells to the presence of viral or bacterial threats. A low CD4+ count is an indicator of a weakened immune system.

Most new infections are in males. The number of cases that have been transmitted through male to male sex has fallen substantially in the last 5 years while transmission via heterosexual sex or due to overseas infections have remained steady. While numbers are small, the rate at which Aboriginal and Torres Strait Islander people are diagnosed with HIV is higher than for other Australians. In 2017, the notification rate among Aboriginal and Torres Strait Islander people was 1.6 times higher than in other Australians.^{4,5}

In 2018, PrEP was added to the PBS. PrEP involves HIV negative people taking antiretroviral drugs to protect them and prevent HIV infection.

Treatment

HIV is not curable. However, antiretroviral medicines significantly reduce HIV-related morbidity, mortality and transmission of the virus to others. As a result, HIV infection is now seen as a manageable chronic condition.

Since 2015, Australian guidelines have recommended antiretroviral medicines as soon as possible for all patients diagnosed with HIV infection irrespective of clinical stage, HIV viral load^b and CD4+ count.⁶

There are six classes of antiretroviral medicines available in Australia. Each target HIV at different stages of the life cycle and different medicines from different classes are used in combination to suppress the virus. At least three antiretroviral drugs are needed for initial therapy although some patients can change to a two-drug regimen once viral suppression is achieved.⁷

The different classes of medicines include the⁸⁻¹⁰:

- nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs); abacavir, didanosine, emtricitabine, lamivudine, stavudine, tenofovir and zidovudine
- non-nucleoside reverse transcriptase inhibitors (NNRTIs); efavirenz, etravirine, nevirapine and rilpivirine
- HIV protease inhibitors (HIV-PIs); atazanavir, darunavir, fosamprenavir, lopinavir, ritonavir, saquinavir and tipranavir
- integrase strand transfer inhibitors (INSTIs); bictegravir, dolutegravir, elvitegravir and raltegravir
- entry inhibitors
 - fusion inhibitors; enfuvirtide
 - CCR5 inhibitors; maraviroc.

Guidelines recommend taking into account both patient and regimen-specific factors, such as efficacy, potential adverse effects, potential drug-drug interactions, comorbidities and coinfections, pregnancy status, ease of use and preferences when choosing initial

^b Viral load refers to the number of HIV particles per unit of blood. A high viral load is an indication of untreated or poorly controlled HIV infection

treatment regimens. However, the following initial treatment regimens are recommended for most PLWHIV:⁸

- bictegravir plus tenofovir alafenamide plus emtricitabine
- dolutegravir plus abacavir plus lamivudine^c
- dolutegravir plus (emtricitabine or lamivudine) plus (tenofovir alafenamide or tenofovir disoproxil fumarate)
- dolutegravir plus lamivudine^d
- raltegravir plus (emtricitabine or lamivudine) plus (tenofovir alafenamide or tenofovir disoproxil).

Table 1 shows the various combinations of medicines that can be used for each of the above regimens.

Table 1: Options for recommended initial antiretroviral regimens

Regimen	Combinations of medicines
bictegravir plus tenofovir alafenamide plus emtricitabine	bictegravir + tenofovir alafenamide + emtricitabine (Biktarvy)
dolutegravir plus abacavir plus lamivudine	abacavir + dolutegravir + lamivudine (Triumeq) OR abacavir + lamivudine (Kivexa) plus dolutegravir (Tivicay) OR dolutegravir + lamivudine (Dovato) plus abacavir (Ziagen) OR dolutegravir (Tivicay) plus abacavir (Ziagen) plus lamivudine (various brands)
dolutegravir plus (emtricitabine or lamivudine) plus (tenofovir alafenamide or tenofovir disoproxil fumarate)	dolutegravir + lamivudine (Dovato) plus tenofovir disoproxil (various brands) OR dolutegravir (Tivicay) plus emtricitabine + tenofovir alafenamide (Descovy) OR dolutegravir (Tivicay) plus emtricitabine + tenofovir disoproxil (Truvada and generics)
dolutegravir plus lamivudine	dolutegravir + lamivudine (Dovato) OR dolutegravir (Tivicay) plus lamivudine (various brands)
raltegravir plus (emtricitabine or lamivudine) plus (tenofovir alafenamide or tenofovir disoproxil)	raltegravir (Isentress) plus emtricitabine + tenofovir alafenamide (Descovy) OR raltegravir (Isentress) plus emtricitabine + tenofovir disoproxil (Truvada and generics)

^c Only for individuals who are HLA-B*5701 negative and without chronic hepatitis B virus (HBV) coinfection

^d Not recommended for individuals with HIV RNA >500,000 copies/mL, HBV co-infection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

Regimen	Combinations of medicines
	OR raltegravir (Isentress) plus lamuvidine (various brands) plus tenofovir disproxil (various brands)

The other antiretrovirals are largely reserved for treatment of drug-resistant strains of HIV.⁶

Prescribing ART in patients with comorbidities

Given antiretroviral medicines are used indefinitely, and patients with HIV now live for many years with the condition, there is a need to consider the adverse effects of these medicines on comorbidities or the risk of developing conditions such as cardiovascular or kidney disease. A number of antiretroviral medicines have adverse effect profiles that mean they should be avoided or used cautiously in patients with certain comorbidities or risk factors, including:^{8,10}

- cardiovascular disease (CVD) or high risk of CVD (diabetes, hypertension, hyperlipidaemia);
- mental health conditions (e.g., depression);
- chronic kidney disease (CKD) or risk of CKD (diabetes, hypertension); and
- osteoporosis.

Pharmacology

The different classes of antiretroviral medicines target HIV at different stages of the life cycle:⁹

- the NRTIs inhibit viral reverse transcriptase and viral DNA synthesis, preventing HIV replication;
- the NNRTIs reversibly inhibit HIV-1 reverse transcriptase, reducing viral DNA synthesis;
- the HIV-PIs inhibit HIV-1 and HIV-2 proteases, preventing viral maturation and replication;
- the INSTIs inhibit HIV integrase, which prevents viral replication by stopping insertion of viral DNA into the host DNA;
- enfuvirtide binds to viral glycoprotein subunit gp41 and, by inhibiting its function, blocks viral fusion with the CD4 receptor of the host cell and thus viral entry to the cell;
- maraviroc prevents the entry of CCR5-tropic (R5) strains of HIV by selectively binding to the CCR5 receptor.

Therapeutic Goods Administration (TGA) approved indications

A summary of the TGA approved indication for each of the antiretroviral HIV medicines can be found in Appendix A.

Most are registered for the treatment (alone or in combination) for the treatment of HIV-1 infection in adults and children. Maraviroc is only indicated for adult patients infected with CCR5-tropic HIV-1.

Emtricitabine + tenofovir alafenamide (Descovy) and tenofovir disoproxil + emtricitabine (Truvada) are also indicated for PrEP.

Lamivudine as a single active ingredient is also indicated for chronic hepatitis B with evidence of hepatitis B virus (HBV) replication.

Dosage and administration

The dose and frequency of administration of antiviral HIV medicines listed on the PBS is summarised in Appendix B.⁹

The current Product Informations (PI) and Consumer Medicine Informations (CMI) are available through [the TGA website product information access page](#) and [the TGA website consumer medicines information access page](#).

PBS listing details (as at July 2021)

Table 2 lists the antiretroviral medicines for the treatment of HIV by medicine class. It also includes a summary of the listing dates and relevant changes to the listings of HIV medicines from 2013 onwards.

Current PBS listing details are available from www.pbs.gov.au

Table 2: Antiretroviral medicines listed for the treatment of HIV, by drug class, as at July 2021

Drug class	Medicine name (Brand name – doesn't include generics)	ATC code	PBS item
Nucleoside analogue reverse transcriptase inhibitors	abacavir (Ziagen)	J05AF06	10294T (listed July 2015) 10356C (listed July 2015)
	lamivudine + zidovudine (Combivir)	J05AR01	10284G (listed July 2015)
	didanosine (Videx EC)	J05AF02	10313T (listed July 2015; deleted May 2018) 10364L (listed July 2015; deleted May 2018)
	emtricitabine (Emtriva)	J05AF09	10274R (listed July 2015, deleted Sep 2018)
	abacavir + lamivudine (Kivexa)	J05AR02	10357D (listed July 2015) 11246X (listed Feb 2018)
	lamivudine (Zeffix and various generics)	J05AF05	10311Q (listed July 2015) 10320E (listed July 2015) 10348P (listed July 2015)
	stavudine (Zerit)	J05AF04	10271N (listed July 2015; deleted May 2018) 10312R (listed July 2015; deleted May 2018)
	abacavir + lamivudine + zidovudine (Trizivir)	J05AR04	10305J (listed July 2015)
	emtricitabine + tenofovir disoproxil (Truvada, Apotex, Cipla)	J05AR03	10347N (listed July 2015; deleted July 2017) 10946D (listed Dec 2016; deleted Apr 2017) 10966E (listed Dec 2016; deleted Apr 2017) 11146P (listed June 2021) 11149T (listed June 2021) 12506F (listed June 2021)
	emtricitabine + tenofovir alafenamide (Descovy)	J05AR17	11099E (listed May 2017) 11113X (listed May 2017)

Drug class	Medicine name (Brand name – doesn't include generics)	ATC code	PBS item
	tenofovir disoproxil (Viread)	J05AF07	10310P (listed July 2015; deleted July 2017) 11142K (listed Aug 2017) 11155D (listed Aug 2017)
	zidovudine (Retrovir)	J05AF01	10266H (listed July 2015) 10360G (listed July 2015) 10361H (listed July 2015)
Non-nucleoside analogue reverse transcriptase inhibitors	efavirenz (Stocrin)	J05AG03	10275T (listed July 2015) 10336B (listed July 2015) 10366N (listed July 2015)
	etravirine (Intelence)	J05AG04	10301E (listed July 2015)
	nevirapine (Viramune)	J05AG01	10303G (listed July 2015) 10304H (listed July 2015) 10319D (listed July 2015)
	rilpivirine (Edurant)	J05AG05	10298B (listed July 2015)
Protease inhibitors	atazanavir (Reyataz)	J05AE08	10276W (listed July 2015; deleted Mar 2020) 10321F (listed July 2015) 10349Q (listed July 2015) 11657M (listed April 2019)
	darunavir (Prezista)	J05AE10	10367P (listed July 2015)
	darunavir + cobicistat (Prezcobix)	J05AR14	10903W (listed Oct 2016)
	fosamprenavir (Telzir)	J05AE07	10337C (listed July 2015)
	indinavir (Crixivan)	J05AE02	10363K (listed July 2015; deleted Sep 2018)
	lopinavir+ ritonavir (Kaletra)	J05AR10	10272P (listed July 2015) 10285H (listed July 2015) 10327M (listed July 2015)

Drug class	Medicine name (Brand name – doesn't include generics)	ATC code	PBS item
	ritonavir (Norvir)	J05AE03	10273Q (listed July 2015) 10300D (listed July 2015; deleted June 2019))
	saquinavir (Invirase)	J05AE01	10335Y (listed July 2015)
	tipranavir (Aptivus)	J05AE09	10344K (listed July 2015)
	atazanavir + cobicistat (Evotaz)	J05AR15	10692R (listed Apr 2016)
Entry inhibitors	enfuvirtide (Fuzeon)	J05AX07	10365M (listed July 2015)
	maraviroc (Celsentri)	J05AX09	10318C (listed July 2015) 10355B (listed July 2015)
Integrase inhibitors	dolutegravir (Tivicay)	J05AX12 J05AJ03	10283F (listed July 2015)
	raltegravir (Isentress)	J05AX08 J05AJ01	10286J (listed July 2015) 10299C (listed July 2015) 10326L (listed July 2015) 11248B (listed Feb 2018)
Combination class agents	efavirenz + emtricitabine + tenofovir disoproxil (Atripla)	J05AR06	10297Y (listed July 2015) 11732L (listed Aug 2019)
	rilpivirine + emtricitabine + tenofovir disoproxil (Eviplera)	J05AR08	10314W (listed July 2015; deleted Feb 2020)
	elvitegravir + cobicistat + tenofovir disoproxil + emtricitabine (Stribild)	J05AR09	10307L (listed July 2015; deleted Feb 2020)
	abacavir + dolutegravir + lamivudine (Triumeq)	J05AR13	10345L (listed July 2015)
	emtricitabine + rilpivirine + tenofovir alafenamide (Odefsey)	J05AR19	11104K (listed May 2017)
	elvitegravir + cobicistat + emtricitabine + tenofovir alafenamide (Genvoya)	J05AR18	11114Y (listed May 2017)
	bictegravir + tenofovir alafenamide + emtricitabine (Biktarvy)	J05AR20	11649D (listed Mar 2019)

Drug class	Medicine name (Brand name – doesn't include generics)	ATC code	PBS item
	dolutegravir + rilpivirine (Juluca)	J05AR21	11540J (listed Dec 2018)
	darunavir + cobicistat + emtricitabine + tenofovir alafenamide (Symtuza)	J05AR22	11955F (listed Oct 2016)
	dolutegravir + lamivudine (Dovato)	J05AR25	11843H (listed Dec 2019; deleted Nov 2020)

Relevant aspects of consideration by the Pharmaceutical Benefits Advisory Committee (PBAC)

At its November 2013 meeting, the PBAC recommended the removal of the CD4+ requirement from the PBS restrictions for initiation of first-line antiretroviral therapy. The change to the listings was recommended on the basis of acceptable cost-effectiveness over no treatment (deferred therapy).¹

Since this date the PBAC has recommended the listing of the following medicines for the treatment of HIV:

- dolutegravir + abacavir + lamivudine (Triumeq) in November 2014;
- atazanavir + cobicistat (Evotaz) in November 2015;
- tenofovir alafenamide + emtricitabine + elvitegravir + cobicistat (Genvoya) in November 2015;
- darunavir + cobicistat (Prezcobix) in March 2016;
- tenofovir alafenamide + emtricitabine + rilpivirine (Odefsey) in November 2016
- tenofovir alafenamide + emtricitabine (Descovy) in November 2016
- a new 600mg formulation of raltegravir (Isentress) in November 2017
- dolutegravir + rilpivirine (Juluca) in July 2018
- tenofovir alafenamide + emtricitabine + bicittegravir (Biktarvy) in July 2018
- dolutegravir + lamivudine (Dovato) in August 2019. In July 2020, this listing was extended to include the treatment of HIV infection in antiretroviral therapy experienced patients
- darunavir + cobicistat + emtricitabine + tenofovir alafenamide (Symtuza) in November 2019.

In December 2017, the PBAC recommended the listing of tenofovir disoproxil + emtricitabine (Truvada and generics) for HIV pre-exposure prophylaxis (PrEP) for adults at medium to high risk of HIV infections. In September 2020, the PBAC recommended amending this listing to allow use in a broader population of at-risk individuals, following the 2019 update to the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) Guidelines.

In November 2019, the PBAC endorsed authorised nurse practitioner prescribing for HIV medicines under the Highly Specialised Drugs program.

Previous reviews by the DUSC

In 2013, DUSC reviewed the utilisation of antiretroviral medicines for the treatment of HIV.² At this meeting, it noted:

- increasing utilisation of medicines for the treatment of HIV infection was aligned with the increasing population of people living with HIV, increased awareness and diagnosis, lifelong therapy, and government endorsed treatment targets
- prescribing was in accordance with clinical guidelines

- consistent with best practice recommendations patients were being started earlier on treatment.

At the time, DUSC noted that the PBS restrictions for most antiretrovirals limited use to patients with a CD4+ count less than 500 cells/mm³ or symptomatic HIV.

For details of the DUSC consideration of HIV medicines, refer to the [Public Release Document](#) from the 2013 DUSC meeting.

Methods

MedicineInsight

MedicineInsight is a large-scale primary care data set of longitudinal de-identified electronic health records (EHR) in Australia. MedicineInsight was initially established by NPS MedicineWise in 2011, with core funding from the Australian Government Department of Health, to collect general practice data to support quality improvement in Australian primary care and post-market surveillance of medicines. The monthly collation of collected data can be analysed for the purposes of improving patient care, quality improvement and evaluation, performing population health analysis, research and developing health policy.

MedicineInsight uses third-party data extraction tools which extract, de-identify, encrypt and securely transmit whole-of-practice data from the clinical information systems (CIS) of over 700 general practices. Patient level data are de-identified 'at source' meaning patients' personal identifiers such as name, date of birth and address are not extracted by the tool, although year of birth and postcode are extracted, enabling the calculation of age and Socio-Economic Indexes for Areas [SEIFA]. Each patient is assigned a unique number within the dataset which allows all the records (clinical, prescription, referral etc) held in the database to be linked to the associated patient identifying number. Further information is available online: <https://www.nps.org.au/medicine-insight>

This is a descriptive analysis of 3 years of data extracted from practices that participate in the national MedicineInsight program and meet data quality criteria. The study period is from 1 January 2018 to 31 December 2020. Historical records outside of this study period were consulted when exploring patient demographics and diagnoses.

Study ethics and approval

This project was given approval in July 2021 by the Royal Australian College of General Practitioners (RACGP) National Research and Evaluation Ethics Committee (NREEC 21-086).

The use of MedicineInsight data for the purposes of this report was approved by the independent Data Governance Committee (2021–012) in July 2021.

Practices and patients that had withdrawn their consent to participate in MedicineInsight were not included in the study.

Eligible practices

Two separate studies with different study periods were conducted on antiretroviral medicine use in patients diagnosed with HIV.

Analyses were conducted using de-identified patient data from:

- 145 individual general practices which met the standard data quality criteria in between 1 January 2018 and 31 December 2019 (study 1) and had at least one patient with diagnosed HIV; and
- 117 individual general practices which met the standard data quality criteria in calendar year 2020 (study 2) and had at least one patient with diagnosed HIV ^e

Eligible patients

Records outside the two study periods were consulted when exploring patient demographics and diagnoses.

Fewer than 5 patients were identified as being of indeterminate gender in the study cohort. To preserve privacy, these patients were excluded from the study.

Study 1

Study 1 describes patients prescribed at least one antiretroviral HIV medicine from 1 January 2018 to 31 December 2019. Records outside the study period were consulted when exploring patient demographics and diagnoses.

Patients were eligible for inclusion in the study 1 population if they:

- had valid information for age and sex (male or female only)
- were aged 18–74 years in 2019;
- had at least two clinical encounters^f during the 2-year study period (1 January 2018 to 31 December 2019);
- had a record of being diagnosed with HIV at any period up until the end of the study period; and
- were prescribed at least one antiretroviral HIV medicine in the study period.

Study 2

Study 2 describes patients prescribed at least one antiretroviral HIV medicine during calendar year 2020. Records outside the study period were consulted when exploring patient demographics and diagnoses.

^e Eligible criteria were that the site had been established for at least 2 years as of May 2021; and had no significant interruptions (of longer than 2 months in the 2 years prior) to their practice data and met the minimum threshold of clinical activity (i.e., at least 50 patients in the last 2 years).

^f A clinical encounter, or any professional exchange between a patient and a healthcare professional (GP or nurse), was defined as all those encounters at the practice site that were: a) not identified as administrator entries nor encounters that have been transferred/imported from another practice and b) were not identified by pre-defined 'administration-type' terms found in the 'reason for encounter' field such as "administrative reasons", "forms", and "recall".

Patients were eligible for inclusion in the study 2 population if they:

- had valid information for age and sex (male or female only);
- were aged 18–74 years in 2020;
- had at least two clinical encounters between 1 January 2019 to 31 December 2020;
- had a record of being diagnosed with HIV at any period up until the end of the study period; and
- were prescribed at least one antiretroviral HIV medicine in calendar year 2020.

Antiretroviral HIV medicines

Patients were defined as having had a prescription for an antiretroviral HIV medicine if they had at least one record of a medicine in Table 1. Information about antiretroviral HIV medicines was taken from four fields in the clinical information software:

- the 'script item' table using ATC codes
- the 'medicine active ingredient' or 'medicine name' fields (provided the script date is between 1 January 2018 and 31 December 2020)
- the 'prescription' table (provided the 'last date' is between 1 January 2018 and 31 December 2020).

Definitions

Socio-demographics in the analysis included age, sex, SEIFA, remoteness and Aboriginal and Torres Strait Islander status (as reported in the CIS).

Patients were defined as having a condition if they had a relevant coded (Docle, Pyefinch) or free text entry in one of the three diagnosis fields – diagnosis, reason for encounter or reason for prescription - recorded at any time from the patient's earliest record up to the end of the study period. The conditions of interest were:

- HIV
- chronic hepatitis C
- hepatitis B
- cardiovascular disease (CVD)
- at risk of CVD (defined as patients with type 2 diabetes, hypertension or dyslipidaemia)
- chronic kidney disease (CKD)
- at risk of CKD (defined as patients with type 2 diabetes or hypertension)
- mental illness (depression, anxiety, bipolar disorder or schizophrenia)
- osteoporosis.

A list of the terms used to identify patients with each of the above conditions can be found in Appendix C.

Medicines that should be avoided or used with caution in patients with certain co-morbidities were identified from Australian and US guidelines (Table 2).^{8,10}

Table 2: Considerations for initial antiretroviral medicine choice based upon patient comorbidities^{8,10}

Condition/group	Medicines to use with caution
At risk of CKD	Avoid: tenofovir disoproxil ⁸
CKD	Avoid: tenofovir disoproxil ⁸ Moderate CKD (<50ml/min): not recommended FDC Atripla, Combivir, Triumeq, or Trizivir ⁸ Severe CKD (<30) not recommended: Biktarvy, Descovy, Genvoya, Odefsey, Symtuza, and Truvada ⁸
Psychiatric illnesses	Avoid: rilpivirine and efavirenz ^{8,10}
At risk of CVD	Avoid: abacavir ⁸ Association with increased risk: HIV-PIs (with the possible exception of atazanavir) ⁸
Cardiovascular disease	Association with increased risk: HIV-PIs (with the possible exception of atazanavir) ⁸
Osteoporosis	Avoid: tenofovir disoproxil ⁸
Diabetes	Associated with hyperglycaemia: HIV-PIs ⁸
Dyslipidaemia	Associated with dyslipidaemia: <ul style="list-style-type: none"> cobicistat or ritonavir-boosted HIV-PIs⁸ efavirenz⁸ regimens containing elvitegravir + cobicistat⁸

Statistical analysis

Analyses were conducted on the October 2020 download of MedicineInsight data using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA), including the use of the SURVEYFREQ procedure. Measures included descriptive statistics, frequencies, proportions and odds ratios as appropriate. To indicate the reliability of the estimates of prevalence and proportions, 95% confidence intervals (adjusted for clustering by practice site) and p-values are reported as needed.

If a particular result was only reported in 1–4 patients, this result has been reported as < 5 (with the exception of missing variables).

Guide to interpreting MedicineInsight data

When interpreting the information presented in this report, readers should note some of the limitations or caveats related to the MedicineInsight data:

- To be included in the study patients had to have both a record as having been diagnosed with HIV and at least one antiretroviral medicine prescribed. This is likely to have underestimated the number of patients seen in general practice with HIV because:

- some patients and GPs may choose not to record HIV status in the CIS to preserve patient confidentiality;
- HIV status may not be recorded in a field accessible to MedicineInsight;
- patients are likely to be managed by specialists and information about antiretroviral use may not be recorded in the CIS or may be recorded in a field that is not accessible to MedicineInsight.
- Information in CIS is collected to provide clinical care to a patient, not for research purposes. All analyses are therefore dependent upon on the accuracy and completeness of data recorded in, and available for extraction from, the general practice CISs.
- Medicines use information from MedicineInsight relates to records of GP prescribing, and therefore differs in several important ways from national PBS dispensing data as not all prescriptions and repeats will be dispensed. Specialist and hospital prescriptions are not included. There may be a delay of up to 12 months between prescribing and dispensing.
- Practices were recruited to MedicineInsight using non-random sampling, and systematic sampling differences between regions cannot be ruled out.
- Due to confidentiality issues we do not have access to progress notes or access to correspondence, which may contain further information on reasons for prescriptions, reasons for encounters and diagnoses.
- Patients are free to visit multiple other practices. We do not have data on patients from non-MedicineInsight clinics. Currently we cannot identify patients who have attended multiple MedicineInsight practices.

Results

This study identified 1,518 patients with HIV using antiretroviral therapy during 2018 and 2019 in study period 1 and 1,391 patients in 2020. This is 5.0–5.5% of the approximately 27,500 Australians living with HIV in Australia.

Sociodemographic characteristics of patients

The sociodemographics of patients in both study periods were similar. Table 3 shows the sociodemographic characteristics of MedicineInsight patients recorded as having a diagnosis of HIV and at least one antiretroviral medicine prescribed during the study periods.

Consistent with other Australia data sources, the majority of patients were male, from higher socioeconomic backgrounds and living in major cities. The life expectancy of PLWHIV has been steadily increasing and almost half are now aged 50 year or older.^{4,11} The mean age of MedicineInsight patients was 49.1 years (95% CI 42.3 to 51.9) in study period 1 and 51.1 years (95% CI 48.4 to 53.9) in study period 2. Among patients who had their Indigenous status recorded in the CIS, 2.8% identified as an Aboriginal or Torres Strait Islander.

Most patients received care from practices with more than 100 patients diagnosed with HIV (high caseload practices).

Table 3: Sociodemographic characteristics of patients with diagnosed HIV prescribed at least 1 HIV medicine between 1 January 2018 and 31 December 2019 and in 2020

	2018 and 2019 population		2020 population	
	Number	% (95% CI)	Number	% (95% CI)
Total	1518	100	1391	100
Sex				
Male	1448	95.4 (91.7, 99.1)	1342	96.5 (94.3, 98.7)
Female	70	4.6 (0.9, 8.3)	49	3.5 (1.3, 5.7)
Age group				
18–29	74	4.9 (2.2, 7.5)	45	3.2 (1.2, 5.3)
30–39	250	16.5 (11.0, 21.9)	193	13.9 (7.7, 20.0)
40–49	416	27.4 (24.1, 30.7)	324	23.3 (19.7, 26.9)
50+	778	51.3 (40.3, 62.2)	829	59.6 (48.1, 71.1)
Sex-age group				
Male 18–29	67	15.3 (10.7, 20.0)	43	59.6 (48.1, 71.1)
Male 30–39	233	25.8 (22.6, 28.9)	185	0.1 (0.0, 0.4)
Male 40–49	391	49.9 (38.5, 61.2)	305	0.6 (0.0, 1.3)
Male 50+	757	50.0 (0.0, 100.0)	809	1.4 (0.6, 2.2)
Female 18–29	7	0.5 (0.0, 1.1)	<5	-
Female 30–39	17	1.1 (0.0, 2.4)	<10	-
Female 40–49	25	1.6 (0.5, 2.8)	19	13.3 (7.6, 19.0)
Female 50+	21	1.4 (0.4, 2.4)	20	21.9 (18.8, 25.0)
State				
ACT	0	-	<5	-
NSW	759	50.0 (0.0, 100.0)	738	53.1 (0.0, 100.0)
NT	<5	-	<5	-
QLD	61	4.0 (0.0, 8.8)	38	2.7 (0.0, 6.1)
SA	<10	-	<5	-
TAS	19	1.3 (0.0, 2.8)	10	0.7 (0.0, 1.6)
VIC	657	43.3 (0.0, 98.5)	589	42.3 (0.0, 99.4)
WA	14	0.9 (0.0, 2.2)	11	0.8 (0.0, 1.9)
Rurality				
Major city	1316	86.7 (79.5, 93.9)	1230	88.4 (82.2, 94.7)
Inner regional	160	10.5 (5.3, 15.8)	132	9.5 (4.6, 14.4)

	2018 and 2019 population		2020 population	
	Number	% (95% CI)	Number	% (95% CI)
Outer regional/remote	42	2.8 (0.4, 5.1)	29	2.0 (0.3, 3.9)
Socioeconomic status				
1 (most disadvantaged)	121	8.0 (3.1, 12.8)	99	7.1 (3.2, 11.1)
2	91	6.0 (3.3, 8.7)	78	5.6 (3.2, 8.0)
3	118	7.8 (2.4, 13.2)	100	7.2 (2.8, 11.5)
4	258	17.0 (10.5, 23.5)	232	16.7 (9.6, 23.7)
5 (most advantaged)	930	61.3 (43.1, 79.4)	882	63.4 (46.5, 80.3)
Aboriginal and Torres Strait Islander status				
Aboriginal and Torres Strait Islander	31	2.0 (0.9, 3.2) 2.8% of reported status	26	1.9 (1.0, 2.8) 2.6% of reported status
Not Aboriginal and Torres Strait Islander	1071	70.6 (46.8, 94.3)	981	70.5 (44.4, 96.7)
Not reported	416	27.4 (3.9, 50.9)	384	27.6 (2.1, 53.1)
HIV caseload of the practice				
High caseload†	1278	84.2 (65.0, 100.0)	1198	86.1 (68.2, 100.0)
Low-medium caseload	240	15.8 (0.0, 35.0)	193	13.9 (0.0, 31.8)

*Defined as a practice with more than 100 patients diagnosed with HIV.

Clinical characteristics of patients

The clinical characteristics of patients in both study periods were similar (Table 4).

The most commonly reported co-morbidity among MedicineInsight patients with diagnosed HIV using antiretroviral medicines was mental illness. Just over half of patients in both study periods had a record of at least one mental illness (Table 4). Four out of every 10 patients had a record of depression and three out of every 10 patients had a record of anxiety. This is consistent with other Australian research – in a 2019 survey of people living with HIV, 55.2% and 43.0% of respondents reported a history of depression and anxiety, respectively.¹²

A quarter of patients had been diagnosed with hypertension and 30% had a record of dyslipidaemia. Almost half were classified as being at risk of developing cardiovascular disease because they had diagnoses of one or more of diabetes, hypertension or dyslipidaemia.

Injecting drug use is a risk factor for both the transmission of HIV and hepatitis C.^{4,6} In the MedicineInsight cohort, approximately 14% of patients had been diagnosed with both HIV and chronic hepatitis C. This is consistent with other Australian research.¹²

Despite the majority of patients being males with an average age of 50 year, 8.7–8.9% of patients had been diagnosed with osteoporosis. Both antiretroviral medicines and the virus itself are thought to play a role in increasing the risk of osteoporosis in people with HIV.⁶

Table 4: Clinical characteristics of patients with diagnosed HIV prescribed at least 1 HIV medicine between 1 January 2018 and 31 December 2019 and in 2020

	2018 and 2019 population		2020 population	
	Number	% (95% CI)	Number	% (95% CI)
Total	1518	100	1391	100
Co-morbidities				
Chronic HCV	203	13.4 (11.1, 15.7)	195	14.0 (11.4, 16.6)
Hepatitis B	89	5.9 (1.7, 10.0)	91	6.5 (2.5, 10.6)
CVD	128	8.4 (6.5, 10.4)	135	9.7 (7.4, 12.0)
CKD	54	3.6 (1.4, 5.7)	48	3.5 (1.8, 5.1)
Osteoporosis	132	8.7 (7.3, 10.1)	124	8.9 (7.7, 10.1)
Mental health (any)	811	53.4 (49.6, 57.2)	760	54.6 (50.9, 58.3)
Depression	627	41.3 (37.5, 45.1)	586	42.1 (38.1, 46.1)
Anxiety	450	29.6 (25.8, 33.5)	443	31.8 (27.8, 35.9)
Bipolar disorder	69	4.5 (4.0, 5.1)	66	4.7 (4.1, 5.4)
Schizophrenia	33	2.2 (0.9, 3.4)	29	2.1 (1.2, 2.9)
Alcohol or opioid problem	124	8.2 (3.5, 12.9)	113	8.1 (3.7, 12.5)
Risk of developing CVD or CKD*				
Total risk of CVD	667	43.9 (37.4, 50.4)	670	48.2 (44.2, 52.2)
Total risk of CKD	418	27.5 (23.0, 32.1)	412	29.6 (27.2, 32.0)
Diabetes (type 1, type 2 or unspecified)	104	6.9 (5.2, 8.5)	104	7.5 (5.9, 9.0)
Hypertension	361	23.8 (19.7, 27.9)	357	25.7 (23.4, 27.9)
Dyslipidaemia	443	29.2 (25.1, 33.2)	466	33.5 (30.3, 36.7)

*CKD: chronic kidney disease; CVD: cardiovascular disease; HCV: hepatitis C

*Patients were classified as being at risk of CVD if they had a record of one or more of diabetes, hypertension or dyslipidaemia. They were classified as being at risk of CKD if they had a record of diabetes or hypertension.

Patients prescribed HIV meds

The combination antiretroviral medicines were the most commonly prescribed to MedicineInsight patients in 2018 and 2019 (Figure 1 and Table 5).

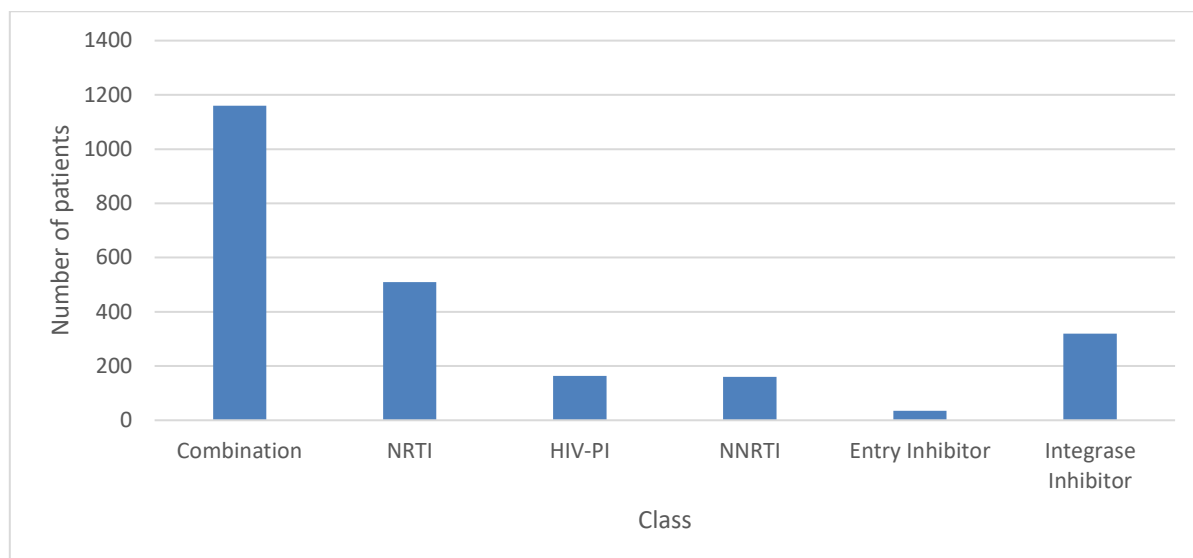


Figure 1: Number of patients treated with different classes of antiretroviral medicines in 2018 or 2019

NRTI: Nucleoside and nucleotide reverse transcriptase inhibitor. HIV-PI: HIV protease inhibitors; NNRTI: Non-nucleoside analogue reverse transcriptase inhibitors.

The most commonly prescribed of all the medicines was bictegravir + tenofovir alafenamide + emtricitabine (Biktarvy) which is one of the regimens recommended for initial treatment in Australian guidelines (Figure 2 and Table 5).

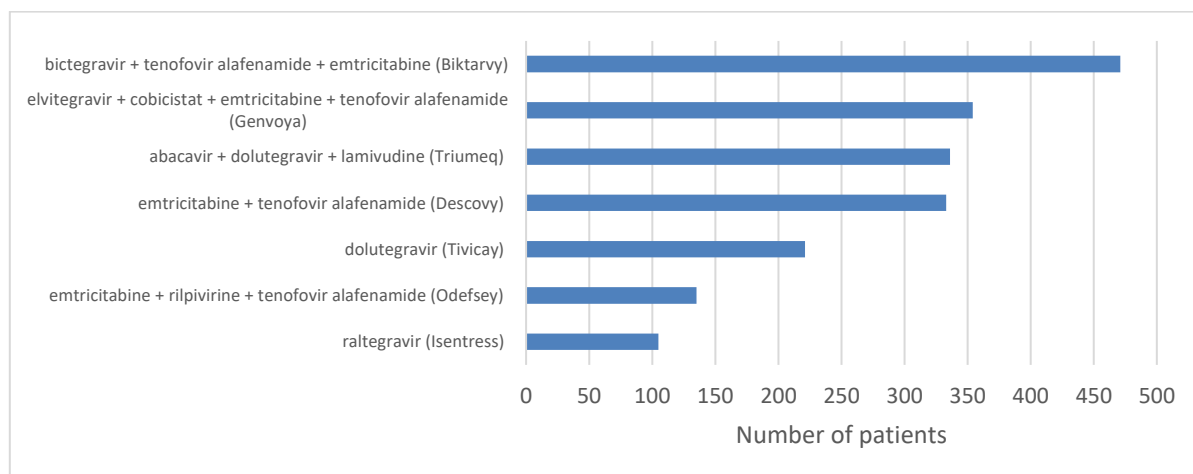


Figure 2: Number of patients treated with different individual medicines (excluding medicines where fewer than 100 patients were prescribed the medicine) in 2018 or 2019

Most of the other commonly used medicines are also medicines that are recommended as part of initiating treatment for HIV. However, the FDCs of elvitegravir + cobicistat + emtricitabine + tenofovir alafenamide (Genvoya) and emtricitabine + rilpivirine + tenofovir alafenamide (Odefsey) are not included in this group of medicines.

Two of the NRTIs, didanosine and stavudine, were removed from the PBS in mid-2018 and were rarely prescribed to MedicineInsight patients during the study period.

Table 5: Number of patients* prescribed HIV antiretroviral medicines, by active ingredient and class

Active ingredient	2018 and 2019 ART population* No. (%)
Nucleoside and nucleotide reverse transcriptase inhibitor (NRTI)	
abacavir (Ziagen)	24 (1.6)
lamivudine + zidovudine (Combivir)	6 (0.4)
didanosine (Videx EC)	<5
emtricitabine (Emtriva)	<5
abacavir + lamivudine (Kivexa)	65 (4.3)
lamivudine (Zeffix)	37 (2.4)
stavudine (Zerit)	0 (0.0)
tenofovir disoproxil (Viread)	11 (0.7)
abacavir + lamivudine + zidovudine (Trizivir)	0 (0.0)
emtricitabine + tenofovir disoproxil (Truvada, Apotex, Cipla)	76 (5.0)
emtricitabine + tenofovir alafenamide (Descovy)	333 (21.9)
zidovudine (Retrovir)	<5
NRTI total	510 (33.6)
Non-nucleoside analogue reverse transcriptase inhibitors (NNRTIs)	
efavirenz (Stocrin)	26 (1.7)
etravirine (Intelence)	24 (1.6)
nevirapine (Viramune)	82 (5.4)
rilpivirine (Edurant)	29 (1.9)
NNRTI total	160 (10.5)
HIV protease inhibitors (HIV-PIs)	
atazanavir (Reyataz)	31 (2.0)
darunavir (Prezista)	65 (4.3)
darunavir + cobicistat (Prezcobix)	53 (3.5)
fosamprenavir (Telzir)	<5
indinavir (Crixivan)	0 (0.0)
lopinavir + ritonavir (Kaletra)	9 (0.6)
ritonavir (Norvir)	66 (4.3)
saquinavir (Invirase)	0 (0.0)
tipranavir (Aptivus)	0 (0.0)

Active ingredient	2018 and 2019 ART population* No. (%)
atazanavir + cobicistat (Evotaz)	13 (0.9)
HIV-PI total	164 (10.8)
Entry inhibitors (Fusion inhibitors and CCR5 inhibitors)	
enfuvirtide (Fuzeon)	0 (0.0)
maraviroc (Celsentri)	35 (2.3)
Entry inhibitor total	35 (2.3)
Integrase inhibitors	
dolutegravir (Tivicay)	221 (14.6)
raltegravir (Isentress)	105 (6.9)
Integrase Inhibitor total	319 (21.0)
Combination class ART	
efavirenz + emtricitabine + tenofovir disoproxil (Atripla)	67 (4.4)
rilpivirine + emtricitabine + tenofovir (Eviplera)	41 (2.7)
elvitegravir + cobicistat + tenofovir disoproxil + emtricitabine (Stribild)	18 (1.2)
abacavir + dolutegravir + lamivudine (Triumeq)	336 (22.1)
emtricitabine + rilpivirine + tenofovir alafenamide (Odefsey)	135 (8.9)
elvitegravir + cobicistat + emtricitabine + tenofovir alafenamide (Genvoya)	354 (23.3)
bictegravir + tenofovir alafenamide + emtricitabine (Biktarvy)	471 (31.0)
dolutegravir + rilpivirine (Juluca)	40 (2.6)
darunavir + cobicistat + emtricitabine + tenofovir alafenamide (Symtuza)	0 (0.0)
dolutegravir + lamivudine (Dovato)	<5
Combination product total	1160 (76.4)

*Note that patients could be prescribed more than one medicine. Therefore totals within each class and overall will be greater than 100.0%.

Medicines to avoid or use cautiously in patients with co-morbidities

There are a number of antiretroviral medicines that should be used with caution or avoided in patients with HIV and particular co-morbidities.^{8,10}

Table 6 explores the extent to which these medicines are being used in patients with HIV and co-morbidities. However, it should be borne in mind that patients may have been prescribed these medicines at any point during 2018 or 2019 or been diagnosed with these conditions at any point up until 31 December 2019. It is possible that this analysis may have overestimated the extent to which these medicines are being used as we did not attempt to confirm whether the diagnosis had been made at the time that the prescription was

issued. It is also possible that clinicians may have changed regimens in response to newly diagnosed co-morbidities which would not have been captured in this analysis.

The HIV-PIs are associated with increased cardiovascular risk with the possible exception of atazanavir.⁸ A quarter of patients (n=32) with a history of cardiovascular disease were prescribed an HIV-PI in 2018–19. Among patients identified as being at risk of CVD 14.5% (n=97) were prescribed an HIV-PI. As a percentage of all patients who were prescribed an antiretroviral medicine, the number of patients with recorded cardiovascular disease, at risk of cardiovascular disease or with recorded dyslipidaemia who were prescribed an HIV-PI was 2.1%, 6.4% and 4.4%, respectively.

It is recommended that regimens including rilpivirine or efavirenz be avoided in patient with mental illness due to a higher risk of central nervous system side effects. However, rilpivirine is preferred over efavirenz. Among patients with a prior or current record of mental illness, 116 patients (14.3%) were prescribed rilpivirine and 34 (3.8%) were prescribed efavirenz.

The proportion of patients with a record of dyslipidaemia who were prescribed medicines associated with an increase in lipid levels ranged from 7.0% to 25.5%. Most commonly this was due to the use of FDCs that include both elvitegravir and cobicistat (Genvoya or Stribild).

Patients with both HIV and a record of CKD were highly unlikely to be treated with medicines that are not recommended for use. Only 7 of the 132 patients (5.3%) with recorded osteoporosis were prescribed tenofovir disoproxil.

Table 6: Proportion of patients prescribed at least 1 HIV medicine between 1 January 2018 and 31 December 2019, with potentially inappropriate prescribing of ART by co-morbidities

Potentially inappropriate regimen % (95% CI)	Number	% (95% CI) of patients with HIV and the condition of interest	% (95% CI) of all patients prescribed an antiretroviral medicine
At risk of CKD			
tenofovir disoproxil – avoid	48	11.5 (8.3, 14.7)	3.2 (1.9, 4.4)
CKD			
tenofovir disoproxil – avoid	<5	-	-
Not recommended in: Moderate or severe CKD: Atripla OR Combivir OR Trumeq OR Trizivir Not recommended in severe CKD: Biktarvy OR Descovy OR Genvoya OR Odefsey OR Symtuza OR Truvada in	<5	-	-
Mental health disorder			
rilpivirine – avoid	116	14.3 (12.7, 16.0)	7.6 (6.4, 8.9)

Potentially inappropriate regimen % (95% CI)	Number	% (95% CI) of patients with HIV and the condition of interest	% (95% CI) of all patients prescribed an antiretroviral medicine
rilpivirine – avoid (depression patients only)	89	14.2 (11.8, 16.6)	5.9 (4.5, 7.3)
efavirenz – avoid	34	4.2 (1.8, 6.6)	2.2 (0.9, 3.6)
efavirenz – avoid (depression patients only)	24	3.8 (1.8, 5.9)	1.6 (0.7, 2.5)
CVD			
HIV-PIs*	32	25.0 (17.3, 32.7)	2.1 (1.0, 3.2)
At risk of CVD			
HIV-PIs*	97	14.5 (12.8, 16.3)	6.4 (5.1, 7.7)
abacavir	184	27.6 (19.8, 35.3)	12.1 (7.0, 17.2)
Diabetes (Type 1, 2 or unspecified)			
HIV-PIs	19	18.3 (13.1, 23.5)	1.3 (1.0, 1.5)
Dyslipidaemia			
HIV-PIs*	66	14.9 (13.1, 16.7)	4.4 (3.6, 5.1)
efavirenz	31	7.0 (2.5, 11.5)	2.0 (0.5, 3.6)
elvitegravir + cobicistat	113	25.5 (22.0, 29.0)	7.4 (5.7, 9.2)
cobicistat or ritonavir-boosted HIV-PIs	31	7.0 (5.9, 8.1)	2.0 (1.6, 2.4)
Osteoporosis			
tenofovir disoproxil - avoid	7	5.3 (2.0, 8.6)	0.5 (0.2, 0.7)

*The HIV-PIs are associated with increased cardiovascular risk with the possible exception of atazanavir⁸

Discussion

This study includes 5.0–5.5% of the approximately 27,500 Australians living with HIV in Australia. Consistent with other Australian studies, MedicineInsight patients with diagnosed HIV using antiretroviral medicines were overwhelmingly male (~95%), from higher socioeconomic backgrounds (~62%) and living in major cities (~87%).

Mental illnesses were the most commonly reported co-morbidity. Approximately 40% of patients had a record of depression and approximately 30% had a record of anxiety. However, patients also commonly had been diagnosed with cardiovascular risk factors such as hypertension and dyslipidaemia.

Fixed dose combination (FDC) antiretroviral medicines were the most commonly prescribed to patients with HIV. The FDC bictegravir + tenofovir alafenamide + emtricitabine (Biktarvy) was prescribed for 31.0% of patients and was the most commonly prescribed individual medicine.

Most patients received care from practices with more than 100 patients diagnosed with HIV (high caseload practices).

Actions undertaken by the DUSC Secretariat

DUSC requested that the report be provided to the PBAC for consideration.

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Appendix A: Summary of TGA approved indications

	Active ingredient(s)	Brand name	TGA registration
NRTIs	abacavir	Ziagen	Antiretroviral combination therapy for the treatment of Human Immunodeficiency Virus (HIV) infection in adults and children.
	abacavir + lamivudine	Kivexa	Antiretroviral combination therapy for the treatment of Human Immunodeficiency Virus (HIV) infection in adults and adolescents from 12 years of age.
	abacavir + lamivudine + zidovudine	Trizivir	Antiretroviral therapy for the treatment of Human Immunodeficiency Virus (HIV) infected adults and adolescents over the age of 12 years. Trizivir should not be administered to adults and adolescents who weigh less than 40kg because it is a fixed dose tablet, and the dose cannot be adjusted for this patient population.
	emtricitabine	Emtriva	Treatment of HIV in combination with other antiretroviral agents in adults and paediatric patients 12 years of age and older, weighing more than 33 kg.
	emtricitabine + rilpivirine + tenofovir alafenamide	Odefsey	Treatment of HIV-1 infection in adults and adolescents (12 years and older with body weight at least 35 kg) with plasma HIV-1 RNA \leq 100,000 copies/mL at the start of therapy. The patients must not have a history of treatment failure or known mutations associated with resistance to the individual components of ODEFSEY.
	emtricitabine + tenofovir alafenamide	Descovy	<p>Treatment of HIV-1 Infection: In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and paediatric patients weighing at least 25kg. The patients must not have a history of treatment failure or known mutations associated with resistance to the individual components of DESCOVY</p> <p>HIV-1 Pre-Exposure Prophylaxis: pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in at-risk adults and adolescents weighing at least 35 kg, excluding individuals at risk from receptive vaginal sex.</p>

	lamivudine	Zeffix, Zetlam	Zeffix (lamivudine) is indicated for the treatment of children (2 years and above), adolescent and adult patients with chronic hepatitis B and evidence of hepatitis B virus (HBV) replication. Children and adolescent also require evidence of active hepatic inflammation. The safety and efficacy of Zeffix (lamivudine) have not been established in patients with decompensated liver disease in placebo controlled studies. However, Zeffix (lamivudine) has been shown to reduce HBV DNA levels prior to and post liver transplantation
	lamivudine + zidovudine	Combivir	For use alone or in combination with other antiretroviral therapies in the treatment of HIV infection.
	tenofovir disoproxil	Viread, Tenofovir Disoproxil Mylan, Tenofovir GH	Treatment in combination with other antiretroviral agents of HIV-infected adults and paediatric patients 12 years of age and older. Treatment of chronic hepatitis B in adults and treatment of chronic hepatitis B in paediatric patients 12 years of age and older with compensated liver disease and with evidence of immune active disease, i.e. active viral replication, persistently elevated serum ALT levels or evidence of active inflammation.
	tenofovir alafenamide + emtricitabine + elvitegravir + cobicistat	Genvoya	Single tablet regimen for the treatment of HIV-1 infection in adults and paediatric patients weighing at least 25 kg who are either treatment-naïve; or virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen at start of therapy in order to replace their current antiretroviral treatment regimen. Patients must not have a history of treatment failure or known mutations associated with resistance to the antiretroviral components of GENVOYA.
	tenofovir disoproxil with emtricitabine	Tenofovir/Emtricitabine, Truvada	<p>Treatment of HIV-1 infection for infected adults over the age of 18 years, in combination with other antiretroviral agents.</p> <p>Pre-Exposure Prophylaxis TRUVADA is indicated in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk. This indication is based on clinical trials in men who have sex with men (MSM) at high risk for HIV-1 infection and in heterosexual serodiscordant couples.</p>

	tenofovir disoproxil + emtricitabine + efavirenz	Atripla	Treatment of HIV infected adults over the age of 18 years.
	zidovudine	Retrovir	Treatment of adult patients with severe symptomatic human immunodeficiency virus infection (AIDS or advanced AIDS related complex). Treatment of other HIV-positive adult patients with less than 500 CD4 cells/mm ³ . Combination therapy in advanced HIV infection: The addition of HIVID (zalcitabine) may be considered for the management of adult patients with advanced HIV infection and CD4 + cell counts less than or equal to 200/mm ³ , who have received Retrovir monotherapy for less than 12 months. Retrovir (zidovudine) is indicated for the treatment of HIV infection, alone and in combination with other antiretroviral therapies.
NNRTIs	efavirenz	Stocrin	For use in combination with other antiviral agents for the treatment of HIV-1 infection in adults and children.
	etravirine	Intelence	Treatment in combination with other antiretroviral agents of HIV-1 infection in antiretroviral treatment-experienced adults who have evidence of viral replication and resistance to Non-nucleoside Transcriptase Inhibitors and other antiretroviral agents. Treatment history of patients and genotypic testing should be performed to guide the use of etravirine.
	nevirapine	Nevirapine, Viramune, Viramune XR	Immediate-release tablets and oral suspension in combination with antiretroviral agents is indicated for the treatment of HIV-1 infection in adults and children over the age of 2 months. Extended-release tablets in combination with antiretroviral agents is indicated for the treatment of HIV-1 infection in adults and children over the age of three years. Extended-release tablets are not suitable for the 14 day lead-in period for patients starting nevirapine. Other nevirapine formulations, such as immediate-release tablets or oral suspension should be used. Resistant virus emerges rapidly when administered as monotherapy or in dual combination therapy with an antiretroviral agent. Therefore, it should always be administered in combination with at least two additional antiretroviral agent

	rilpivirine	Edurant	Treatment in combination with other antiretroviral medicinal products of human immunodeficiency virus type 1 (HIV-1) infection in antiretroviral treatment-naïve adult patients with viral load less than or equal to 100,000 copies/mL at baseline.
HIV-PIs	atazanavir	Reyataz	Treatment of HIV 1 infection, in combination with other antiretroviral agents
	atazanavir + cobicistat	Evotaz	Use in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults
	darunavir	Prezista	Treatment (with low dose ritonavir as a pharmacokinetic enhancer) in combination with other antiretroviral agents of human immunodeficiency virus-1 (HIV-1) infection in adult patients. Treatment (with low dose ritonavir as a pharmacokinetic enhancer) in combination with other antiretroviral agents of human immunodeficiency virus (HIV) infection in treatment-experienced paediatric patients aged 6 years and older, weighing at least 20 kg.
	darunavir + cobicistat	Prezcobix	Treatment in combination with other antiretroviral agents of adult patients with human immunodeficiency virus-1 (HIV-1) infection in: antiretroviral treatment-naïve patients, antiretroviral treatment-experienced patients with no darunavir resistance associated mutations and who have plasma HIV-1 RNA <100,000 copies/mL, or antiretroviral treatment-experienced but HIV protease inhibitor-naïve patients for whom HIV-1 genotype testing is unavailable
	darunavir + cobicistat + emtricitabine + tenofovir alafenamide	Symtuza	Treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults and adolescents (aged 12 years and older with body weight at least 40 kg). Genotypic testing should guide the use of SYMTUZA
	fosamprenavir	Telzir	Treatment, in combination with low dose ritonavir, of Human Immunodeficiency Virus Type 1 (HIV-1) infected adults, adolescents and children of 6 years and above in combination with other antiretroviral medicinal products.
	lopinavir + ritonavir	Kaletra	Treatment of HIV-1 infection, in combination with other antiretroviral agents in adults and children aged 2 years and older.
	ritonavir	Norvir	Use in combination with appropriate antiretroviral agents or as monotherapy if combination therapy is inappropriate, for the treatment of HIV-1 infection in adults and children aged 12 years and older.

	saquinavir	Invirase	Treatment of HIV/AIDS in adults and children 12 years of age or older. Clinical studies indicate that saquinavir should only be used in combination with ritonavir and other anti-retroviral therapies
	tipranavir	Aptivus	For combination treatment, co-administered with low dose ritonavir, of HIV infection in antiretroviral treatment experienced adults and adolescents aged 12 years and older, with evidence of viral replication, who have HIV-1 strains resistant to more than one protease inhibitor. In deciding to initiate therapy with APTIVUS/ritonavir, careful consideration should be given to treatment history of the individual patient and the patterns of mutations associated with different agents. Genotypic testing should be performed to guide the use of APTIVUS.
INSTIs	bictegravir + emtricitabine + tenofovir alafenamide	Biktarvy	BIKTARVY is indicated for the treatment of HIV-1 infection in adults and paediatric patients weighing at least 25 kg who are antiretroviral therapy (ART)-naïve or to replace the current antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen at the start of therapy with no history of treatment failure, and no known substitutions associated with resistance to the individual components of BIKTARVY
	dolutegravir	Tivicay	Treatment of human immunodeficiency virus (HIV) infection in combination with other antiretroviral agents in adults and children over 6 years of age
	dolutegravir + abacavir + lamivudine	Triumeq	Treatment of Human Immunodeficiency Virus (HIV) infection in adults and adolescents from 12 years of age who are antiretroviral treatment-naïve or are infected with HIV without documented or clinically suspected resistance to any of the three antiretroviral agents (dolutegravir, abacavir or lamivudine) in TRIUMEQ
	dolutegravir + lamivudine	Dovato	Treatment of Human Immunodeficiency Virus-1 (HIV-1) infection in adults and adolescents (from 12 years of age weighing at least 40kg): in antiretroviral treatment-naïve patients with no antiretroviral treatment history who have no known or suspected resistance to either antiretroviral component; or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable

			antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to the integrase inhibitor class or lamivudine
	dolutegravir with rilpivirine	Juluca	Treatment of human immunodeficiency virus-1 (HIV-1) infection in adults who are virologically-suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 6 months with no history of virological failure and no known or suspected resistance to any non-nucleoside reverse transcriptase inhibitor or integrase inhibitor
	raltegravir	Isentress	Treatment in combination with other antiretroviral agents of human immunodeficiency virus (HIV-1) infection in adults, adolescents and children from the age of 2 years.
	enfuvirtide	Fuzeon	Treatment in combination with other antiretroviral agents for the treatment of HIV-1 infection in antiretroviral experienced patients with treatment failure due to intolerance to previous antiretroviral agents or with evidence of HIV-1 replication despite ongoing therapy.
	maraviroc	Celsentri	Treatment in combination with other antiretroviral medicinal products of adult patients infected with only CCR5-tropic HIV-1. The use of other active agents with CELSENTRI is associated with a greater likelihood of treatment response

Appendix B: Dosage and frequency of administration for antiretroviral HIV medicines⁹

	Active ingredient(s)	Brand name	Adult dose for patients without comorbidities
NRTIs	abacavir	Ziagen	Oral, 300 mg twice daily or 600 mg once daily
	abacavir + lamivudine	Kivexa	1 tablet (abacavir 600 mg, lamivudine 300 mg) daily
	abacavir + lamivudine + zidovudine	Trizivir	1 tablet (abacavir 300 mg, lamivudine 150 mg, zidovudine 300 mg) daily
	emtricitabine	Emtriva	200 mg once daily
	emtricitabine + rilpivirine + tenofovir alafenamide	Odefsey	1 tablet once (emtricitabine 200 mg, rilpivirine 25 mg, tenofovir alafenamide 25 mg) daily with food
	emtricitabine + tenofovir alafenamide	Descovy	1 tablet once (emtricitabine 200 mg, tenofovir alafenamide 25 mg) daily with food OR with combinations of atazanavir or darunavir (boosted with either ritonavir or cobicistat) or lopinavir/ritonavir, 1 tablet (emtricitabine 200 mg, tenofovir alafenamide 10 mg) once daily
	lamivudine	Zeffix, Zetlam	Oral, 100 mg once daily
	lamivudine + zidovudine	Combivir	1 tablet (lamivudine 150 mg, zidovudine 300 mg) twice daily
	tenofovir disoproxil	Viread, Tenofovir Disoproxil Mylan, Tenofovir GH	1 tablet once daily with food
	tenofovir alafenamide + emtricitabine + elvitegravir + cobicistat	Genvoya	1 tablet (tenofovir alafenamide fumarate 10 mg, emtricitabine 200 mg, elvitegravir 150 mg, cobicistat 150 mg) once daily with food
	tenofovir disoproxil with emtricitabine	Tenofovir/Emtricitabine, Truvada	1 tablet (tenofovir disoproxil 300 mg, emtricitabine 200 mg) once daily with food
	tenofovir disoproxil + emtricitabine + efavirenz	Atripla	1 tablet (tenofovir disoproxil 300 mg, emtricitabine 200 mg, efavirenz 600 mg) once daily
	zidovudine	Retrovir	Oral, 250–300 mg twice daily
NNRTIs	efavirenz	Stocrin	Oral, 600 mg once daily. With voriconazole, 300 mg once daily
	etravirine	Intelence	Oral, 200 mg twice daily after food
	nevirapine	Nevirapine, Viramune, Viramune XR	Initial dose: Conventional tablet, oral liquid, 200 mg once daily for 14 days. Maintenance dose: Conventional tablet, oral liquid, 200 mg twice daily. Controlled release tablet, 400 mg once daily.
	rilpivirine	Edurant	Oral, 25 mg once daily. With rifabutin, oral 50 mg once daily
	atazanavir	Reyataz	Treatment-naïve: Oral, 300 mg atazanavir (with 100 mg ritonavir) once daily or 400 mg atazanavir once daily. With efavirenz, 400 mg atazanavir (with 100 mg ritonavir) once daily. With tenofovir disoproxil, 300 mg atazanavir (with 100 mg ritonavir) once daily.

		Treatment-experienced: 300 mg atazanavir (with 100 mg ritonavir) once daily
atazanavir + cobicistat	Evotaz	1 tablet (atazanavir 300 mg, cobicistat 150 mg) once daily
darunavir	Prezista	No darunavir resistance substitutions and viral load <100 000 copies/mL; or HIV-PI naive when genotype testing is not available, oral 800 mg (with 100 mg ritonavir) once daily. Darunavir resistance substitutions or viral load >100 000 copies/mL; or HIV-PI experienced when genotype testing is not available, oral 600 mg (with 100 mg ritonavir) twice daily
darunavir + cobicistat	Prezcobix	1 tablet (darunavir 800 mg, cobicistat 150 mg) once daily with food
darunavir + cobicistat + emtricitabine + tenofovir alafenamide	Symtuza	1 tablet (darunavir 800 mg, cobicistat 150 mg, emtricitabine 200 mg, tenofovir alafenamide 10 mg) once daily with food
fosamprenavir	Telzir	No previous antiretroviral treatment, oral 1400 mg (with 200 mg ritonavir) once daily or 700 mg (with 100 mg ritonavir) twice daily. Previous HIV-PI treatment, oral 700 mg (with 100 mg ritonavir) twice daily.
lopinavir + ritonavir	Kaletra	Treatment-naïve: Oral, 400/100 mg twice daily or 800/200 mg once daily (lopinavir 100 mg, ritonavir 25/50 mg) . With efavirenz, nevirapine, carbamazepine, phenytoin or phenobarbital, oral 400/100 mg twice daily. Treatment-experienced: Oral, 400/100 mg twice daily. With efavirenz, nevirapine, oral 500/125 mg twice daily if decreased susceptibility to lopinavir is suspected.
ritonavir	Norvir	Low-dose ritonavir regimens: With atazanavir, darunavir (treatment-naïve), oral 100 mg once daily. With darunavir (treatment-experienced) or saquinavir, oral 100 mg twice daily. With fosamprenavir twice daily regimen, oral 100 mg twice daily. With fosamprenavir once daily regimen, oral 200 mg once daily. With tipranavir, oral 200 mg twice daily
saquinavir	Invirase	Treatment-naïve: Oral, 500 mg (with 100 mg ritonavir) twice a day for 7 days, then increase to 1000 mg (with 100 mg ritonavir) twice a day. Treatment-experienced: Use for patients switching from another HIV-PI with ritonavir or from a NNRTI (except rilpivirine). Oral, 1000 mg (with 100 mg ritonavir) twice a day

	tipranavir	Aptivus	Oral, 500 mg (with 200 mg ritonavir) twice daily
INSTIs	bictegravir + emtricitabine + tenofovir alafenamide	Biktarvy	1 tablet (bictegravir 50 mg, emtricitabine 200 mg, tenofovir alafenamide fumarate 25 mg) once daily
	dolutegravir	Tivicay	Oral, 50 mg once daily
	dolutegravir + abacavir + lamivudine	Triumeq	1 tablet (dolutegravir 50 mg, abacavir 600 mg, lamivudine 300 mg) once daily
	dolutegravir + lamivudine	Dovato	1 tablet (dolutegravir 50 mg, lamivudine 300 mg) once daily
	dolutegravir with rilpivirine	Juluca	1 tablet (dolutegravir 50 mg, rilpivirine 25 mg) once daily with a meal
	raltegravir	Isentress	400 mg tablet: oral 400 mg twice daily. 600 mg tablet: Do not use for treatment-experienced patients unless virologically suppressed on initial regimen of raltegravir 400 mg twice daily. Oral, 1200 mg once daily.
	enfuvirtide	Fuzeon	subcutaneous, 90 mg twice daily
	maraviroc	Celsentri	Oral, 300 mg twice daily. With nevirapine or tipranavir/ritonavir, oral 300 mg twice daily. With strong CYP3A4 inhibitors (with or without a CYP3A4 inducer), eg clarithromycin, HIV-PIs (except tipranavir/ritonavir), elvitegravir with cobicistat, itraconazole, oral 150 mg twice daily. With CYP3A4 inducers (without a strong CYP3A4 inhibitor), eg efavirenz, etravirine, rifampicin, carbamazepine, phenytoin, oral 600 mg twice daily

Appendix C: Terms used to identify HIV infection or conditions to consider when prescribing antiretroviral medicines

Condition	Included terms
HIV infection	HIV, HIV carrier, AIDS, but excludes HIV embryopathy
Alcohol use disorder	(abuse or dependence or addiction) of alcohol, alcohol addiction, alcohol dependence, alcohol related brain injury, alcohol use disorder, alcoholic, alcohol withdrawal, alcoholism, antabuse type reaction, delirium tremens, Korsakoff's dementia
Anxiety	anxiety, generalised anxiety disorder, mixed anxiety/depression, obsessive compulsive disorder (OCD), post-traumatic stress disorder (PTSD)
Bipolar disorder	bipolar affective disorder, bipolar 1 disorder, bipolar 2 disorder, bipolar spectrum disorder, manic depressive illness, manic depressive psychosis
Cardiovascular disease (CVD)	atherosclerosis, coronary heart disease (including myocardial infarction and angina), peripheral vascular disease, stroke and transient ischaemic attack.
Chronic Kidney Disease (CKD)	anaemia - chronic renal failure, capd, catheterisation of peritoneum, chronic kidney disease or CKD (all stages), chronic renal disease (all stages), chronic renal failure, chronic renal failure – hyperparathyroidism, chronic renal insufficiency, continuous ambulatory peritoneal dialysis, CRF, dialysis, haemodialysis, hemodialysis, peritoneal catheterisation for dialysis, peritoneal dialysis renal dialysis or surgery - abdomen - dialysis - catheterisation
Depression	depression, post-natal depression, adjustment disorder with depression, mixed anxiety/depression
Diabetes (Type I, II and unspecified)	diabetes mellitus (idm or type I or type 1), idm, insulin dependent diabetes mellitus, juvenile onset diabetes, diabetes, diabetes (controlled or cortisone induced or unstable), diabetes mellitus, diabetes mellitus (niddm, or type ii or type 2 or type 3c), latent autoimmune diabetes of adults, niddm, non insulin dependent diabetes mellitus, pancreatogenic diabetes, t2dm, t11, tii
Dyslipidaemia	dyslipidaemia, dyslip, familial (hypercholesterolaemia or hypercholesterolemia), hdl, high cholesterol, high cholest, high lipids, hypercholesterolaemia, hyperlipidaemia, hyperlipoproteinaemia (type 2 or type iv or type iia), hypertriglyceridaemia, hypercho, hyperlip, hypertr
Hypertension	antihypertensive agent prescription, (blood pressure or bp) and (labile or review or unstable), hbp, high blood pressure, ht, hypertension, hypertension (controlled or diastolic or essential or isolated systolic or labile or life style management or malignant or pregnancy or primary or renal or renovascular or review or unstable), pih, pregnancy induced hypertension or severe refractory hypertension
Opioid use disorder	(abuse or dependence or addiction) of an opiate, drug addict, IDU, injecting drug user, intravenous drug use, IV drug use, long term opiate use
Osteoporosis	osteoporosis, osteoporosis (corticosteroid induced or no fracture or with fracture or disuse or steroid induced), pathological fracture due to osteoporosis, post menopausal osteoporosis, steroid osteopathy
Schizophrenia or schizoaffective disorder	borderline or brief or brief reactive or catatonic or chronic or disorganised or hebephrenic or para or paranoid) schizophrenia, personality disorder (schizoid or

Condition	Included terms
	schizotypal), residual schizophrenia, schizoaffective disorder, schizophrenia, schizophreniform disorder, undifferentiated schizophrenia