2018 MEETING REPORT

The 2018 art of ART Meeting, held in Sydney, Australia, was a series of plenary sessions and interactive workshops for S100 prescribers, nurses and pharmacists with a focus on the nuances of antiretroviral therapy (ART) prescribing and contemporary HIV management in Australasia. This report provides a summary of key learnings. The meeting is a complimentary event provided by ASHM through an unconditional educational grant provided by ViiV Healthcare.

Videos and slides of the presentations and workshops are now available on the art of ART 2018 program page.

Update on ART – Simplification of salvage, switching treatment, resistance

Take Home Messages

1. Viral control has become increasingly achievable with more potent, better tolerated and co-formulated ART regimens. 48-week virological suppression rates now exceed 90%.
2. The current DHHS and IAS-USA guidelines now recommend that all preferred first line regimens contain an integrase inhibitor. This is based on both high efficacy and improved toxicity profiles.
3. Despite this, many people living with HIV remain on older regimens which were considered first line when they were initiated.
4. There is a growing body of evidence to support consideration of switching patient regimens to address resistance, improve tolerability, decrease toxicity and reduce drug-drug interactions.

Why switch?

In the setting of virological control: What could make life better for the patient?	**In the setting of virological failure and resistance: When switching becomes a medical imperative.**
• To simplify regimen	• To re-suppress virus to undetectable levels
• To improve tolerability & decrease long-term toxicity	• To improve tolerability & decrease long-term toxicity
• To reduce chance of drug-drug interactions	• To reduce chance of drug-drug interactions
• If pregnant	

Note: We advise right clicking on links and selecting 'open link in new tab' to facilitate easy reading of the report.

Which drugs to switch from

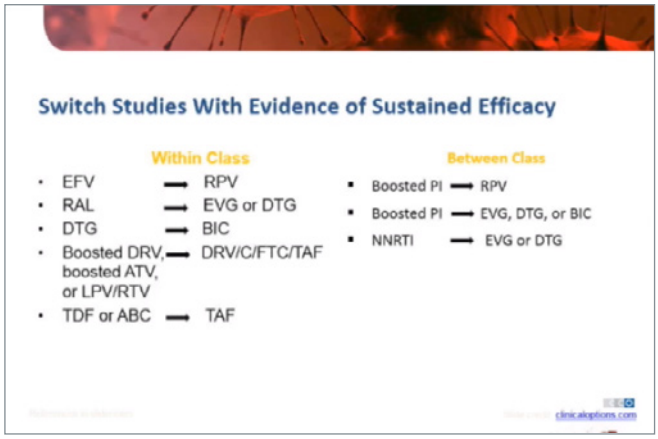
DRUG	WHY SWITCH?	DISCUSSION
Tenofovir Disoproxil Fumarate (TDF)	Reduce renal, bone toxicity	Avoid renal/bone toxicity associated with TDF by switching to tenofovir alafenamide (TAF) except where drug-drug interactions mean switch is not possible. A number of older NRTIs are no longer prescribed due to their toxicity. For example, most people previously taking TDF are now on TAF.
Abacavir (ABC)	Reduce potential cardiovascular risk	An association has been made between ABC myocardial infarction risk. Note: event numbers were small in some studies (8 events in the STEAL Study) whereas other studies had greater numbers (580 events in the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D Study). The latter showed an increased risk associated with current rather than cumulative ABC use.
Protease Inhibitors (PIs)	Avoid gastro-intestinal intolerance/ myocardial infarction (MI) risk	The D:A:D Study has shown an association between MI risk with cumulative use of ritonavir boosted indinavir (IDV), lopinavir(LPV) and darunavir (DRV). The NEAT 022 Study is assessing the risks and benefits of switching patients (aged over 50 with Framingham risk > 10% at 10 years) stable on PI based regimens, off their PI to dolutegravir (DTG). Treatment efficacy was non-inferior but lipid profiles and carotid intima media thickness (C-IMT) improved in the switch arm. Clinical event/MI data is yet to be presented.
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	Avoid lower potency, CNS intolerance	These have low genetic barriers to resistance and must be used with high barrier partners. Other weaknesses include: • Efavirenz (EFV): sleep disturbance, CNS issues, suicide risk, 'brain fog'. • Nevirapine (NVP): Hepatoxicity rash at initiation, chronic GGT elevation and hepatic impairment – the view used to be that a switch was probably not necessary but that view is changing. • Rilpivirine (RPV): PPI interactions, food requirements, less efficacious with high viral loads.

What is the evidence base for changing therapy?

- There is an evidence base to say you can switch treatment in people who are virologically suppressed.
- Some switches are clearly established, others still lack compelling evidence.

Switching and Resistance

- Earlier HIV regimens may have contained only one or two antiretroviral agents and may have consisted of drugs with low genetic barriers to resistance.
- There are numerous clinical trials examining third drug switches both within class and to other classes, which have shown non-inferiority.
- Switching suppressed patients on triple therapy to dual therapy regimens is also being explored to minimise potential drug toxicity.
- It is possible to successfully switch patients with archived resistance. The new regimen should include:
  - » At least 1 new antiretroviral with a high genetic barrier (DTG, BIC, DRV/r, LPV/r)
  - » 1 active NRTI (if possible).
- Refer to SWITCHMRK Study and DAWNING Study.



Other issues to consider

While switching ART may improve certain co-morbidities and toxicities, traditional screening for and management of co-morbidities such as hypertension, cigarette smoking, dyslipidaemia, metabolic complications, mental health and substance use remains a crucial component of good HIV care.

- View the plenary presentation video.
- View the workshop video with its discussion of case studies.
- View the conference program page for all video and slide links.

HIV in Minority Populations
Aboriginal and Torres Strait Islander Health

Take Home Messages

1. **HIV is steadily increasing** in the Aboriginal and Torres Strait Islander population - rates have increased by 33% since 2012. There are concerns over the potential of HIV to rapidly escalate.
2. **Diverging epidemic:** New HIV diagnoses in the Aboriginal and Torres Strait Islander population are now at more than double the rate of Australia's non Indigenous population. There is higher incidence of HIV due to injecting drug use and heterosexual sex.
3. **Poor engagement in prevention and care:** Despite advances in medicine and technology Aboriginal and Torres Strait Islander people are not well engaged in TasP or PrEP. Of the 17,000 people on PrEP in Australia only around 200 have identified as Indigenous.
4. **Targeted action is required** in policy, clinical services and advocacy to address the rising rates of HIV.

HIV Data - What does it tell us?

Characteristics of HIV 1996-2015

Sex	Indigenous	Non-Indigenous
Males	355 (77)	10395 (94)
Females	105 (23)	609 (6)
Missing	1 (0.2)	27 (0·2)
Route of exposure		
MSM	210 (46)	8205 (74)
IDU	75 (16)	322 (3)
MSM & IDU dual risk	38 (8)	564 (5)
Heterosexual sex	114 (25)	1295 (12)
Other/unknown	24 (5)	645 (6)

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Characteristics of HIV 1996-2015

Area of residence	Indigenous	Non-Indigenous
Major cities	263 (57)	9154 (83)
Regional (inner/outer)	128 (27·8)	1342 (12·2)
Remote and very remote	51 (11·1)	58 (·5)
Missing	19 (4·1)	477 (4·3)
Clinical information	**Indigenous**	**Non Indigenous**
Late diagnoses (exc. advanced)	57 (12·4)	1452 (13·2)
Advanced diagnoses	96 (20·8)	1662 (15·1)
Not late	218 (47·3)	5814 (52·7)
Missing	90 (19·5)	2103 (19·1)

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- There is little reported information about treatment access, linkage and timeliness of care, treatment adherence and prevalence of drug resistance in the Aboriginal population.
- Notable differences between HIV in Aboriginal and Torres Strait Islander people compared to non Indigenous Australians include younger age, gender, regions, rates, exposure, late diagnosis, higher undiagnosed.
  - » Fewer diagnoses are in major cities.
  - » Higher proportion of females are acquiring HIV through injecting drug use.
  - » Men who have sex with men continue to make up the majority of cases.
- WA Stands out as having 10% of the Indigenous population but 20% of the diagnoses.
- Small HIV outbreaks are occurring around Australia with most new infections in NSW + QLD.

Areas of concern

- Syphilis outbreak:
  - » Young, heterosexual Indigenous people in northern Australia mostly affected.
  - » Concern that HIV may occur in conjunction with syphilis outbreak as coinfection common.
- Injecting drug use:
  - » Lack of access to Needle Syringe Programs especially in remote areas.
  - » Increasing use of the methamphetamines in communities with significant proportion injecting. Key danger area for HIV infections unless PreP and TasP employed.

Key elements of primary medical care

- Larger numbers remain undiagnosed: initial modelling suggests 18% compared to 8%.
- Follow up and HIV testing after a positive STI diagnosis is poor in remote communities with only around 1/3 followed up with an HIV test.
- Less access to and engagement in HIV care.
- Fewer Aboriginal and Torres Strait Islander people have a suppressed viral load compared to non-Indigenous people: approximately 80% compared to 93%.
- Should eligibility criteria for PrEP be different for Aboriginal and Torres Strait Islander people?

Social context and challenges

- Small HIV numbers and geographical diversity makes PrEP and TasP roll out difficult.
- Remoteness, interruption of treatment, and racism may all be contributing to lower levels of viral suppression for those on treatment.
- Greater IDU sharing amongst larger sharing groups increases HIV transmission risk.
- Awareness raising without stigmatising populations is challenging.

Awareness of targeted prevention strategies

- Several HIV and PrEP resources have recently been developed:
  - » www.atsihiv.org.au
  - » www.youngdeadlyfree.org.au

View the plenary presentation video.
View the workshop slides with their discussion of cases studies.
Read SAMHSA's Concept of Trauma and Guidance for a Trauma-Informed Approach
View the conference program page for all video and slide links.

HIV in Minority Populations
Gender Diverse Populations

Take Home Messages

1. HIV in Australian transgender population low compared to global prevalence: ≈5% vs 19%
2. PrEP and TasP can minimise transmission.
3. PrEP is safe and effective for transgender people, but they might not ask for it.
4. ART and hormone therapy may interact but there are a number of treatment options.
5. We need work harder to engage transgender people in care.
6. We need to get better at identifying transgender people in data collection.

Transgender Data in Australia

- The 2016 Australian Census was the first where an individual could identify as other than male or female, however individuals had to request an additional form to complete this information so data is inaccurate.
- Of the transgender HIV+ population in Australia the majority are transgender women with extremely limited data collected on transgender men.

Social context and challenges

- TGW have a high lifetime rate of suicide attempts, commonly experience rejection from family and friends, encounter discrimination, are likely to experience physical and sexual violence, and are less likely to negotiate safe sex and access health services and have lower levels of knowledge regarding HIV prevention and sexual health.
- Many TG Australians are born overseas, are Medicare ineligible and seeking asylum in Australia due to serious harm they have experienced in their home country.
- Most TGW have not had gender affirmation surgery and may be taking hormone replacement therapy which can result in erectile disfunction. Receptive anal sex with partners is most common.
- Transactional sex with limited STI + BBV screening common. Hep B co-infection common.
- Some TGW have transitioned from MSM.

Key elements of Primary Medical Care

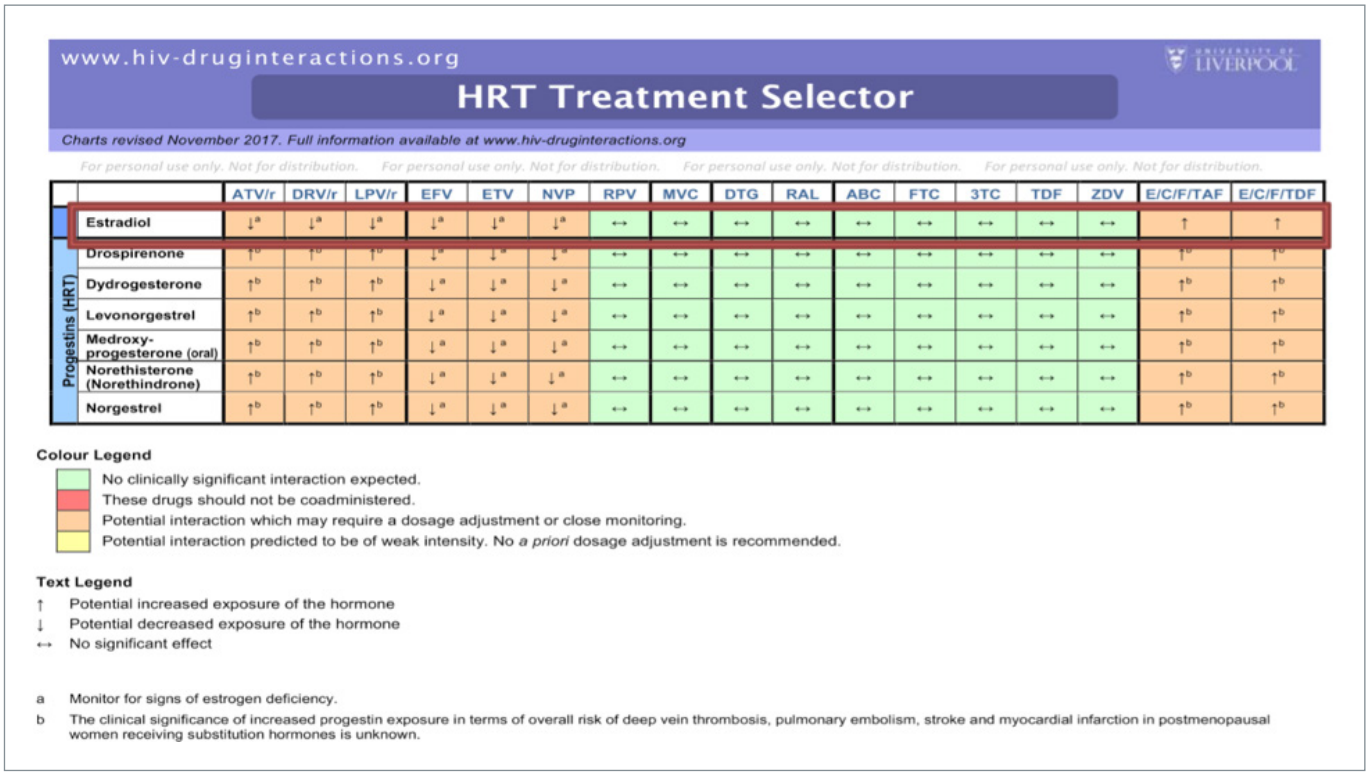
Barriers to HIV testing

- Lower levels of knowledge of sexual health and HIV prevention.
- Variable perception of risk (both Dr and patient).
- Lack of resources specifically targeting TG people.
- TG historically included in MSM funding but TG may not identify with “gay” clinics.
- TGM considered to be a low risk group for HIV, however some TGM are MSM and are unlikely to be offered HIV and STI testing.

HIV management

Issues include stigma, access to ARVs, transitioning, lower retention in care, co-existing mental illness, and drug-drug interactions if on hormone therapy.

- PrEP is safe and effective. Eligibility dependant on sexual history.
- Hormone therapy is likely to be lifelong so ARVs that have no or minimal drug interactions should be used. Many patients fear decreased effectiveness of hormones.
  - » pay attention to hormone levels after starting ART
  - » avoid ethinyl oestradiol which cannot be measured
- Pregnancy/contraception and STI screening including Trichomonas and cervical screening should be offered to TGM.



www.hiv-druginteractions.org

UNIVERSITY OF LIVERPOOL

HRT Treatment Selector

Charts revised November 2017. Full information available at www.hiv-druginteractions.org

		ATV/r	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	RAL	ABC	FTC	3TC	TDF	ZDV	E/C/F/TAF	E/C/F/TDF
	Estradiol	↓[a]	↓[a]	↓[a]	↓[a]	↓[a]	↓[a]	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↑
Progestins (HRT)	Drospirenone	↑[b]	↑[b]	↑[b]	↓[a]	↓[a]	↓[a]	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑[b]	↑[b]
	Dydrogesterone	↑[b]	↑[b]	↑[b]	↓[a]	↓[a]	↓[a]	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑[b]	↑[b]
	Levonorgestrel	↑[b]	↑[b]	↑[b]	↓[a]	↓[a]	↓[a]	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑[b]	↑[b]
	Medroxy-progesterone (oral)	↑[b]	↑[b]	↑[b]	↓[a]	↓[a]	↓[a]	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑[b]	↑[b]
	Norethisterone (Norethindrone)	↑[b]	↑[b]	↑[b]	↓[a]	↓[a]	↓[a]	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑[b]	↑[b]
	Norgestrel	↑[b]	↑[b]	↑[b]	↓[a]	↓[a]	↓[a]	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑[b]	↑[b]

Colour Legend

- No clinically significant interaction expected.
- These drugs should not be coadministered.
- Potential interaction which may require a dosage adjustment or close monitoring.
- Potential interaction predicted to be of weak intensity. No *a priori* dosage adjustment is recommended.

Text Legend

↑ Potential increased exposure of the hormone
↓ Potential decreased exposure of the hormone
↔ No significant effect

a Monitor for signs of estrogen deficiency.
b The clinical significance of increased progestin exposure in terms of overall risk of deep vein thrombosis, pulmonary embolism, stroke and myocardial infarction in postmenopausal women receiving substitution hormones is unknown.

DRUG	INTERACTION
Cobicistat	May increase E,P, EE and cyproterone by inhibiting CYP3A4
Efavirenz	May decrease E,P and cyproterone by inducing CYP3A4
PIs and ritonavir	May decrease E by inducing CYP1A2 (definite decrease in EE in OCP)
Darunavir	May increase cyproterone by inhibiting CYP3A4
Bictegravir/FTC/TAF	No interactions
ABC/3TC/DTG	No interactions

Incorporating culturally appropriate management and prevention strategies into practice

- Make your clinic trans-friendly and encourage retention in care.
- Include gender-inclusive registration, gender-neutral toilets, preferred names, the use of pronouns, inclusive posters, and display the transgender flag.
- By far the most important action is to ask patients about pronouns and preferred name, record it somewhere and make sure everyone uses it.

View the plenary presentation video.
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HIV and the LAW

Take Home Messages

1. Each state and territory in Australia has differing laws concerning HIV transmission.
2. In all states and territories criminal law can be used in cases of reckless HIV transmission.
3. Disclosing your HIV status is now not legally required in any part of Australia, provided you take "reasonable precautions" to prevent the transmission of HIV.
4. Condoms as a 'reasonable precaution' in HIV criminal cases has precedent in Australia.
5. Treatment as Prevention (TaSP)/undetectable viral load (U=U) - not yet tested legally.
6. Sex with someone on PrEP does not currently qualify as a 'reasonable precaution' as the legal liability lies with the HIV positive partner.
7. We continue to operate in an area of considerable legal uncertainty.

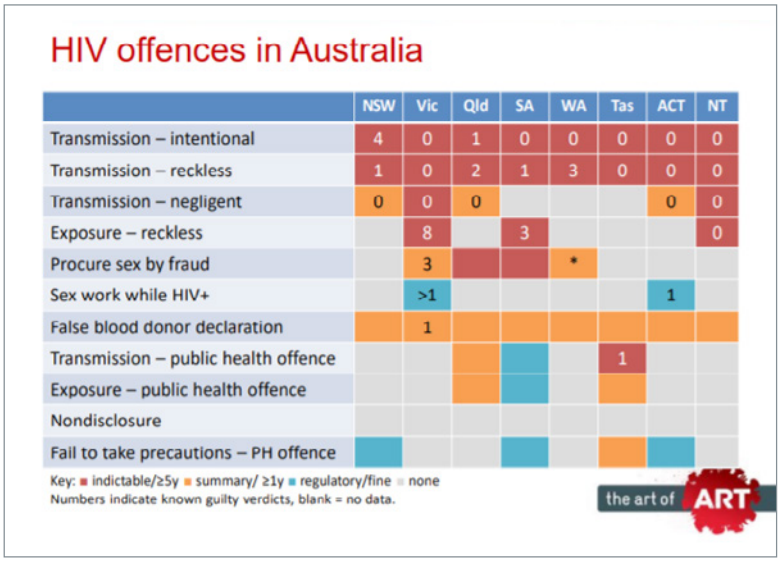
HIV: The biomedical evidence

- Three studies have provided data evidencing TaSP, *HPTN 052*, *Opposites Attract* and *Partners Study*.
- PrEP is proven to be 99% effective in prevention of HIV transmission when taken daily.

What are the laws today?

In every state and territory intentional or reckless transmission of HIV is a crime.

- **Intentional** transmission means where the accused person has the infection of the other party as their desired and intended outcome, and transmission actually occurs;
- **Reckless** transmission is where the accused knew the transmission of HIV was a possible or probable consequence of their actions, and they failed to take adequate precautions to prevent it occurring.
- In Victoria, SA and the NT, prosecutions are also possible for endangerment/'reckless exposure' — merely for placing another person in danger of contracting HIV.



- Procure sex by fraud: specifically applies to a situation where someone lies about their HIV status. There doesn't need to have been any risk, just need to show complainant was deceived and that they wouldn't have given consent if they had known of HIV status.
- About 40 prosecutions and 20 convictions in Australia.
- In HIV, it is consent, not disclosure, that makes the sex lawful. Disclosure of HIV status is generally considered the most reliable way to ensure consent.
- Disclosure is not required if reasonable precautions to prevent HIV transmission are taken.
- No court in Australia has ruled that undetectable viral load alone (U=U) is enough to satisfy the "reasonable precautions" test. This may change in the future, but in the meantime there's a risk someone living with HIV might fall foul of the law if they don't disclose and don't use condoms.
- It is not clear at present what the courts will say about PrEP.

HIV transmission as a crime - concerns

- HIV is the only sexually transmitted virus that is criminalised.
- Criminal laws place all of the burden for HIV transmission on the HIV positive person. This makes it particularly difficult in relation to PrEP, which relies on the HIV negative partner.
- Prosecutions are harmful for the HIV+ person and can counteract public health messaging.
- Consent to sex and disclosure are different.
- To the law, consent means free and voluntary agreement, given without co ercion, and in knowledge of all the relevant facts. The reality is that sexual consent is incredibly complex and shared trust is central.
- The criminalisation of HIV in the law is based on the assumption that people with HIV want to use their HIV as a weapon.
- Courts assume that nobody wants to be exposed to the slightest risk of harm: that HIV infection is such a profound risk that it is assumed no one would willingly put themselves in such harm's way.
- There is no such thing as 100% risk-free sex but this is the standard that the courts apply.
- The criminalisation of HIV has made no difference to epidemic of HIV in Australia.

Health education and awareness

- HIV is a health problem and should require a health response, however, the law is what it is.
- Refer people to community standards through your local AIDS Council. Be aware disclosure is always hard and can be difficult for individuals.
- Be clear when giving advice on U=U and seek data: When talking about U=U, clinicians should talk about the risk being NEGLIGIBLE - so low that there is virtually no chance of transmission - NOT low risk. Language is important as the law deals in certainty.
  - » Links:
    - Read the Australian Medical Consensus Statement on HIV and the Law
    - U=U – prevention access campaign
    - Australian contact tracing guidelines

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Medicinal Cannabis for people living with HIV

Take Home Messages

1. Medical cannabis products represent a new approach to help patients living with chronic pain and other distressing symptoms.
2. There is good data that medical cannabis can be effective in managing neuropathic pain in people living with HIV.
3. Although the application process is complex these products are of great potential benefit for patients living with HIV.

Pharmacology

- The main active cannabinoids are the psychoactive, euphoric tetrahydrocannabinol (THC) and the psychoactive non-euphoric cannabidiol (CBD).
- THC is responsable for the euphoric effects as well as many of the medical effects including analgesic, antiemetic, appetite stimulant and anti-spasticity properties.
- CBD opposes the euphoric effect of THC but also has anticonvulsant, analgesic and antiemetic effects.

Clinical applications

- There are comprehensive guidelines for the use of cannabis products published in Australia and around the world. For Australia refer to the TGA Guidance Overview.
- Chronic pain is likely to be the main indication. Neuropathic pain is common in PLWHIV. See TGA Guidance for non-cancer pain.
- Other indications include spasticity, nausea, epilepsy and terminal care.
- Note: medicinal cannabis is not considered a first-line therapy for any indication.
- In many cases there is very limited data from which to draw specific recommendations.

Routes of administration

- All products available in Australia are oro-mucosal drops that contain varying ratios of **Tetrahydrocannabinol (THC) and Cannabidiol (CBD)** - mostly used twice daily.

Administration considerations

	SMOKING OR VAPORISATION	ORAL	OROMUCOSAL
ONSET (MINUTES)	5–10	60–180	15–45
DURATION (HOURS)	2–4	6–8	6–8
PRO	Rapid action, good for acute or episodic symptoms such as pain or nausea	Convenient, discrete, advantage for chronic symptoms and disease	Only products currently available in Australia, well documented efficacy and safety
CON	No legal product in Australia, vaporisers are expensive	No legal product in Australia, can be hard to titrate due to delayed onset	Expensive

Prescribing medical cannabis in Australia

- For a good reference to prescribing refer to Caroline A. MacCallum, Ethan B. Russ p 12–19.
- Begin with comprehensive clinicial assessment and discussion of products and costs.
- Most patients will have chronic pain and the standard therapy is a THC 1:1 CBD ratio.
- Prescribers need to be aware of dosing (start slow go slow), possible adverse events (usually mild) potential drug interactions (few) and monitoring requirements.
- All products have recommended dosing schedules.
- Most products require a detailed Special Access Scheme (SAS) application via the TGA along with an application to the State Health Department. After authorisation the prescriber writes an S8 script with dispensing from a community pharmacy.
- One product - *Sativex* - is TGA registered for patients with moderate to severe spasticity due to multiple sclerosis (MS) but can be prescribed 'off-label' for pain. This requires an application to your state health department but does not need an SAS application. It is quite expensive, about $750 for a box of 3.
- Other products include *Tilray*, *Canntrust* and *Cannimed*. They are cheaper but will require an SAS application. This will usually be a Category B form. Category A is for terminal illness. You will need to complete the patient details on the application and may need to include a cover letter. In NSW the Cannabis Medicines Advisory Service can assist with this form and a cover letter (ph 1800 217 257). You will also need to include the complete product details on the application.
- Refer to Access to Medicinal Cannabis Products.

Sides effects

- Side effects are usually mild (reference as above) and can be reduced by a 'start low go slow' approach to dosing.
- Patients are advised not to drive or operate machinery while under treatment.

VERY COMMON	COMMON	RARE
• Dizziness • Drowsiness • Fatigue • Dry mouth • Cough, phlegm, bronchitis (smoked cannabis) • Anxiety • Nausea • Cognitive effects	• Euphoria • Blurred vision • Headache	• Orthostatic hypotension • Psychosis/paranoia • Depression • Ataxia/dyscoordination • Tachycardia (after titration) • Cannabis hyperemesis • Diarrhoea

Contraindications

- In pregnancy and lactation, psychosis or in the presence of hypersensitivity to cannabinoids.
- Cautions include unstable cardiac conditions, such as angina, (due to tachycardia and possible hypotension due to THC) in children and teens (remains the subject of debate) and smoked products should be avoided in COPD and asthma.

Drug interactions

- Limited interaction data available. Of note CYP3A4 inducers, such as rifampicin, have been shown to reduce THC levels and this will probably apply to other inducers. See SATIVEX Product information.
- Care should be taken with hypnotics, sedatives and drugs with potential sedating effects as there may be an additive effect on sedation and muscle relaxing effects. THC may interact with alcohol, affecting co-ordination, concentration and ability to respond quickly.

Monitoring and follow-up:

- Each patient will need a specified monitoring plan. Ideally you will have a preferred, standardised pain monitoring form or patient diary that you can use to monitor patient response to medication.
- It is suggested that an initial treatment plan indicate that the medicinal cannabis product be used for a one-month trial to determine the effectiveness of the medication for the patient's symptoms.
- The application will need to renewed every year.

View the plenary presentation video.
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With Thanks

The art of ART is funded by an unrestricted educational grant from ViiV Healthcare. The content of the program is at the sole discretion of the Independent Faculty and is not influenced by the Secretariat or ViiV Healthcare