

Lancashire Formulary for Anti Retroviral Therapy (ART)

Antiretroviral therapy is a complex issue and is rapidly changing as new guidelines are published based on good clinical trial data. It is essential to have access to all antiretroviral therapy, but the majority of patients can be managed with very few drug combinations.

When to start ART

The decision to start therapy is based principally on the CD4 count. All patients should have had ART discussed in detail by the time the CD4 count falls to the level of 350 cells/mm³, and ideally should be starting therapy. The 350 level may change in the near future as more evidence accrues for starting therapy at higher CD4 counts.

Other factors that may need to be taken into account include:

- Viral load
- Age
- Co morbidities e.g. CVS, CNS, renal, hepatic and bone disease need to be considered
- Hepatitis B/C co infection
- Symptomatic HIV infection
- Primary HIV infection
- AIDS defining conditions including non-Hodgkin's lymphoma and Kaposi's sarcoma
- Pregnancy
- HIV negative sexual partner
- Commercial sex workers
- Patients requesting treatment outside of the CD4 count range
- Cost of particular therapies

This list is not exhaustive, but gives an idea of the complexity of starting ART.

Initial therapy

Where possible especially in patients starting ART electively, viral resistance should be available to guide therapy.

HLAB5701 status needs to be available prior to using Abacavir and viral loads should generally not be greater than 100,000 copies when using Abacavir.

Routine blood tests, urinalysis and cardiovascular risk assessment should be available.

First line:

TRUVADA backbone plus EFAVIRENZ (prescribed separately or as ATRIPLA)

(Consider viral resistance, psychiatric/psychological status, occupation, pregnancy status and risk of pregnancy)

KIVEXA backbone plus EFAVIRENZ

EVIPLERA (this should be prescribed on a limited basis)
For Eviplera in Naïve patients

Consider when VL is less than 100,000 copies/ml
Patient able to take medication with a meal consistently
Not on acid lowering drugs
No background relevant viral resistance
For switch patients
No background nucleoside resistance
Consider getting VL undetectable consistently for 6/12 before switching

First-line alternative:

TRUVADA or KIVEXA backbone plus:

NEVIRAPINE or RALTEGRAVIR

Second-line:

TRUVADA or KIVEXA backbone plus:

DARUNAVIR or ATAZANAVIR (with RITONAVIR)

The majority of patients can be managed with the above agents and if intolerance develops then it is possible to switch between the agents.

In planned pregnancy or a pregnant woman starting treatment for the first time then the backbone should ideally be Combivir or Truvada combined with Kaletra or Nevirapine or Atazanavir. This is a relatively small cohort of patients and so is better individualised.

Raltegravir, a new integrase inhibitor is finding its way into guidelines and it is relatively inexpensive in the NW of England, is very well tolerated and is useful where a rapid drop in viral load is needed. It is also relatively lipid neutral. It may be considered where there is no viral resistance or no virological failure and then in combination with Truvada.

If a NNRTI is considered necessary before a PI and Efavirenz and Nevirapine are not appropriate then Etravirine may be considered with a Truvada or KIVEXA backbone. It does not have an ART naïve licence.

There will be an exceedingly small number of patients (usually guided by resistance testing) where the above agents will not be suitable.

Therapy after first virological failure

This must be guided by viral resistance testing and will usually involve a protease inhibitor (Darunavir or Atazanavir with Ritonavir). A further 2 active agents will be necessary and may include Raltegravir, Etravirine and Maraviroc (with co receptor typing) or other NRTI's as dictated by the resistance testing.

Maraviroc should only be used as a special indication on a case by case basis.

Therapy after second virological failure

This again needs to be guided by resistance testing and past ART therapy and is where the full range of ART needs to be available.

With better adherence support, easier tablet regimes including reduced pill burdens, virological failure should reduce although we are at a crossroad with treatment and support, length of time between appointments, primary care support and length of time many of our patients have been infected. This is clearly an evolving process and we should have the necessary resources and flexibility to respond.

Traffic Light status for HIV drugs

RED Traffic Light – RED medicines should be initiated by specialists only and prescribing retained within secondary care; primary care prescriber initiation or continuation of treatment is **not** recommended. These treatments often require specialist knowledge, monitoring, dose adjustment or further evaluation in use.

East Lancs website - <http://www.elmmb.nhs.uk/search/?q=hiv>

HIV formulary drugs list with cost comparison

	Comments	Usual daily dose	Cost comparison*
First-line			
Truvada + efavirenz (tenofovir 300mg + emtricitabine 200mg + efavirenz 600mg) <i>or prescribed as combination</i>	<i>Atripla is more expensive than prescribing separately as Truvada + efavirenz</i>	1 x daily Truvada + 1 x daily efavirenz 600mg	££££
Atripla (tenofovir 300mg + emtricitabine 200mg + efavirenz 600mg)		1 x daily	££££
Kivexa + efavirenz (abacavir 600mg + lamuvidine 300mg + efavirenz 600mg)		1 x daily Kivexa 1 x daily efavirenz 600mg	£££
First-line alternative			
Truvada or Kivexa + nevirapine		2 x daily nevirapine 200mg	£
Truvada or Kivexa + raltegravir	<i>Where tolerance is a problem or rapid drop in viral load is needed</i>	1 x raltegravir 400mg twice daily	££
	<i>Add backbone price</i>	<i>Kivexa backbone</i> <i>Truvada backbone</i>	££ £££
Second-line			
Truvada or Kivexa + darunavir ritonavir	<i>Treatment naïve dose</i>	2 x darunavir 400mg + ritonavir 100mg daily	££
Truvada or Kivexa + atazanavir ritonavir		1 x atazanavir 300mg + 1 x ritonavir 100mg daily	££
	<i>Add backbone price</i>	<i>Kivexa backbone</i> <i>Truvada backbone</i>	££ £££
The majority of patients can be managed with the above agents and if intolerance develops then it is possible to switch between the agents.			
Third-line			
	If a NNRTI is considered necessary before a PI and Efavirenz and Nevirapine are not appropriate then Etravirine may be considered with a Truvada or Kivexa backbone. <i>It does not have an ART naïve licence.</i>		
Truvada or Kivexa + etravirine	<i>Does not have ART naïve licence</i>	2 x etravirine 100mg twice daily	££
	<i>Add backbone price</i>	<i>Kivexa backbone</i> <i>Truvada backbone</i>	££ £££

Pregnancy	In planned pregnancy or a pregnant woman starting treatment for the first time then the backbone should ideally be Truvada or Kivexa with a NNRTI such as Nevirapine, Efavirenz or a boosted PI such as boosted Atazanavir or boosted Darunavir or Kaletra. The choice of ART should be individualised.		
Truvada OR Kivexa		1 tablet a day 1 tablet a day	££ ££
In the absence of contraindications, the third agent should be one of the following:			
Nevirapine (if CD4 count <250 cells/mm ³) OR Efavirenz OR Boosted Atazanavir OR Boosted Darunavir OR Kaletra		200mg twice a day 600mg once a day 300mg + 100mg Ritonavir once a day 600mg + 100mg Ritonavir twice a day 2 tablets twice a day	££ ££ ££ ££ ££
The dosing of Darunavir should be twice a day during pregnancy.			
Therapeutic drug levels (TDM) are advisable in the third trimester particularly if combining Tenofovir and Atazanavir			

Therapy after first virological failure.	This must be guided by viral resistance testing and will usually involve a protease inhibitor (Darunavir or Atazanavir with Ritonavir). A further 2 active agents will be necessary and may include Raltegravir, Etravirine and Mavaviroc (with co receptor typing) or other NRTI's as dictated by the resistance testing.		
Maraviroc <i>Only to be used as a special indication on a case by case basis.</i>	<i>Comparative price – used in combination with other agents</i>	150mg or 300mg or 600mg twice daily depending on ARV combination Need to add in cost of tropism test (£300)	££££
Therapy after second virological failure	This again needs to be guided by resistance testing and past ART therapy and is where the full range of ART needs to be available. With better adherence support, easier tablet regimes including lower pill burdens, virological failure should reduce although we are at a crossroad with treatment and support, length of time between appointments, primary care support and length of time many of our patients have been infected. This is clearly an evolving process and we should have the necessary resources and flexibility to respond.		

**Based on the range of actual costs paid by Lancashire PCTs in the period August 2011- February 2012. Prices include VAT if this is paid under current supply arrangements*

HIV assisted drugs list

This is a limited list of HIV assisted drugs which are approved for use.

- Aciclovir 400mg tablets
- Azithromycin 250mg
- Co-trimoxazole 480mg and 960mg tablets
- Dapsone 100mg tablets
- Pentamidine 300mg nebuliser solution
- Valganciclovir 450mg tablets
- Loperamide 2mg capsules
- Domperidone 10mg tablets

Appendix

PEPSE

For post exposure follow national guidelines

Dose optimisation

In some cases with some drugs twice daily dosing may be preferable when initiating therapy or to minimise side effects. However if this is not the case it is usually less expensive to prescribe 1 x higher strength than 2 x lower

For example:

Lamuvudine 2 x 150mg – change to Lamuvudine 1 x 300mg

Maraviroc 4 x 150mg – change to Maraviroc 2 x 300mg

Additional points to consider

- Nevirapine is due off patent in December 2012 and costs may subsequently fall. The company plans to launch a modified release product, but this will be a patented drug and likely to be more expensive.
- Efavirenz is due off patent in November 2013. When the patent expires the price differential between Atripla compared to prescribing Truvada + efavirenz is likely to increase.
- <http://www.bashh.org/documents/4076.pdf>