National antiretroviral treatment prescribing toolkit

HIV CRG Drugs Subgroup

February 2022

NHS England and NHS Improvement

Content

Introduction

- This toolkit has been developed collaboratively by the HIV Clinical Reference Drugs Sub-group & will be reviewed regularly through their quarterly meetings.
- This toolkit has been developed to:
  - Support the new national ARV procurement contracts that start in February 2022
  - Support cost-effective, clinically appropriate ARV prescribing, through the prescribing aid & based on relevant BHIVA guidance, NICE TAs & NHSEI Best Practice in HIV Prescribing and Multidisciplinary Teams guidance
- Where several regimens are considered clinically appropriate, the use of those regimens in the lowest cost bands are preferred.
- At the time of writing, existing NHSEI separate commissioning policies still apply. The list of regimens requiring MDT approval may change when NHSEI review existing policies with respect to to this new guidance.

Patient Choice

- People living with HIV should be involved in decisions about their treatment. This should be supported by latest information. Ideally, peer support should also be available.
- Choice of treatment should be a joint decision between the patient and prescriber. This needs to be based upon clinical suitability, consideration of cost and informed choice. As several similar options will usually be available, HIV positive people should be included in this choice. The clinical team remain responsible for making sure that the choice is clinically suitable and in line with the national prescribing algorithm and national prescribing guidelines.

Generics

- Switching to generic drugs from the branded equivalent, whether components or full regimens, should start from 01/02/22 which is when the new contract prices commence.
- Switch to generics should be discussed with patients at their next routine clinic visit, including information about the formulation, pill count, dosing, name and safety.
- Switching treatment should avoid drug wastage i.e. as the brand prescription ends with existing supplies finished first.
- An updated PIL about generics will be available.

TAF use: where a tenofovir-containing regimen is necessary with absolute or relative contra-indications to TDF

- Patients who need a tenofovir-containing regimen, with absolute contra-indications to TDF
  - Confirmed osteoporosis or high fracture risk (FRAX)
  - CKD stage G3 or G1/2 + A3 proteinuria
  - TDF-related renal toxicity
  - Intolerance to TDF or other contra-indication
- Patients who need a tenofovir-containing regimen, with relative contra-indications to TDF
  - Approaching the bone and renal thresholds outlined above
- Patients who need an unboosted integrase-based regimen but have contra-indications to raltegravir or dolutegravir can be considered for Biktarvy regardless of TAF eligibility

Based on NHSE commissioning policies ref 16043/P 2016 & ref 170131P 2019

Regimens which must be discussed at MDT

- TAF-based therapy in the absence of absolute TDF & ABC contra-indications
- All two-drug regimens
- Doravirine-based regimens
- Eviplera®, Evotaz®, Rezolsta®, Symtuza®, & all cobicistat-based ART
- Injectable cabotegravir/rilpivirine
- All high cost regimens within bands 3 or 4 on the national prescribing guide
- **All complex ART:**
  - HIV resistance, complex co-morbidities,
  - complex polypharmacy, pregnancy or
  - other complexities impacting choice

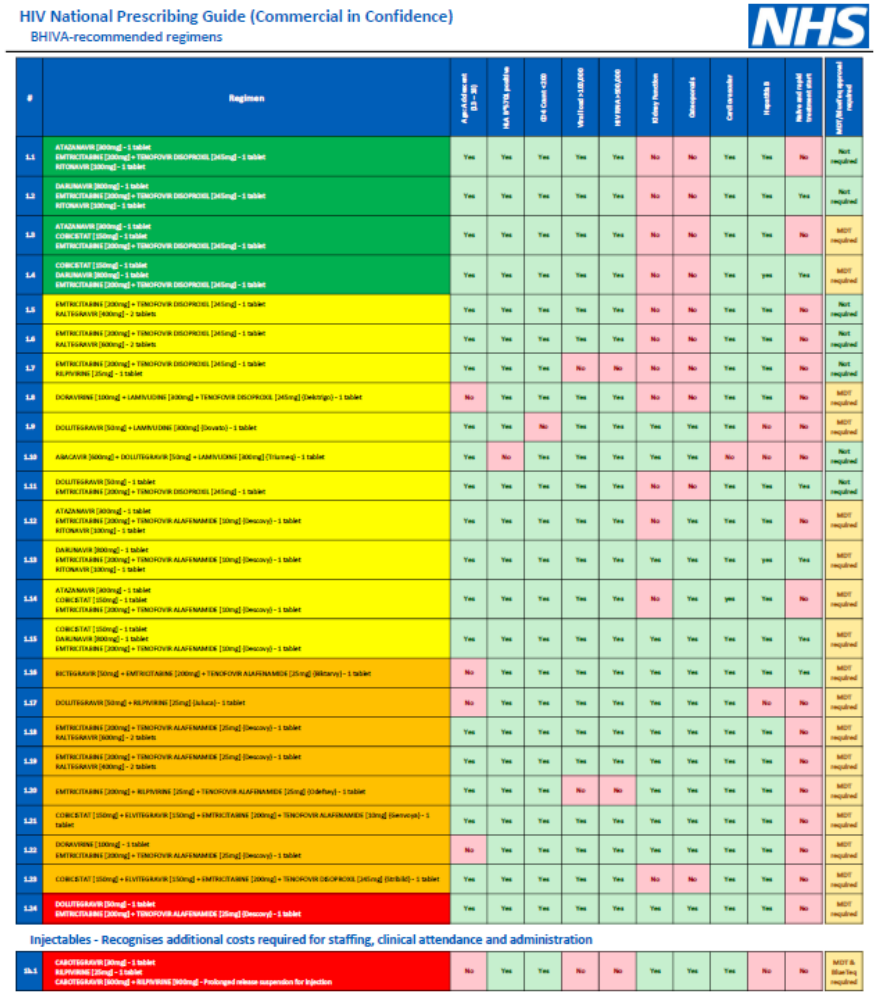
Regimens already approved at MDT do not need re-discussion unless they also need Blueteq approval, in which case new MDT discussion is required.

Regimens which also require Blueteq

- Blueteq is a prior approval system that NHSEI has used for high cost drugs since 2016
- Blueteq will already be in use in many Trusts
- Regimens that require a Blueteq are:
  - Eviplera®, Evotaz®, Rezolsta®, Symtuza®
  - Injectable cabotegravir/rilpivirine
- All regimens requiring Blueteq will need a documented new MDT discussion, even if agreed at MDT in the past
- Blueteq approval will be required ONCE during this tender period, not at every prescription
- If Blueteq is not available at first prescription of a relevant medication after 01/02/2022 it should be completed at next prescription

Using the HIV National Prescribing Guide and the NHS National ARV Algorithm

When prescribing first-line ART or switching between ART regimens; clinicians should refer to the HIV National Prescribing Guide and the NHS National ARV Algorithm.



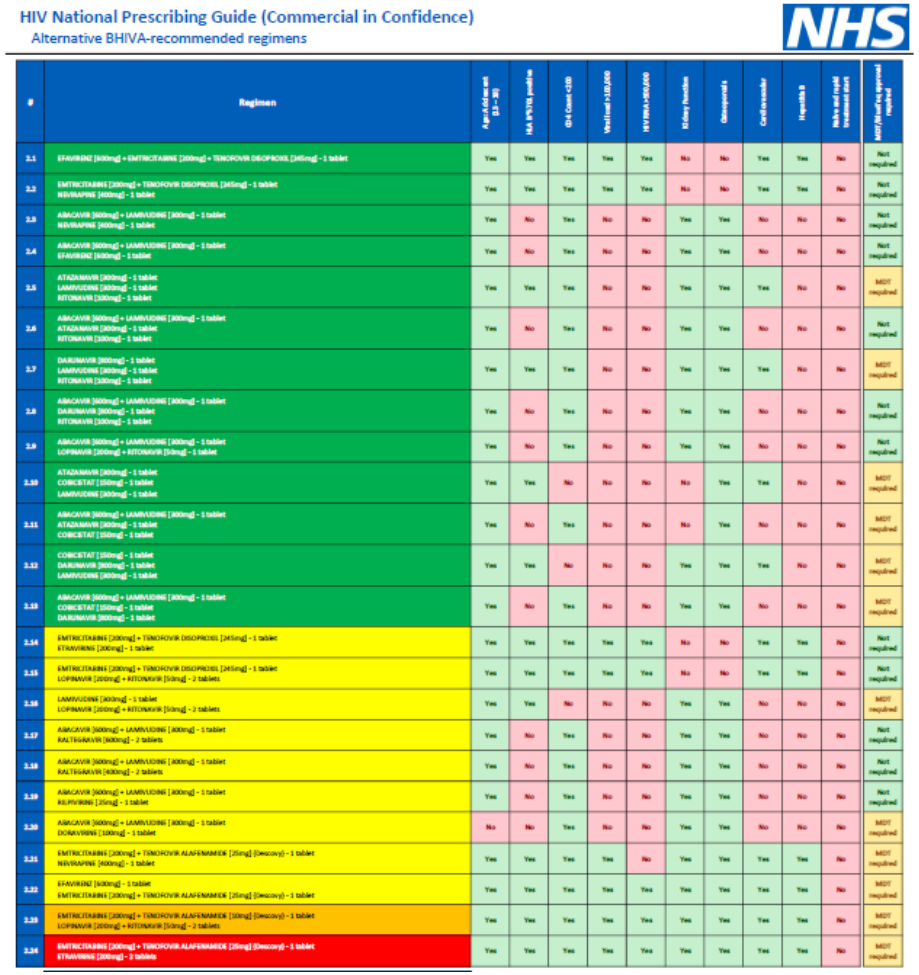
HIV National Prescribing Guide (Commercial in Confidence)

BHIVA-recommended regimens

#	Regimen	Age Adjustment (13 – 25)	HLA B*5701 positive	CD4 Count <200	Viral load >100,000	HIV RNA >500,000	Kidney function	Osteoporosis	Cardiovascular	Hepatitis B	Naïve and rapid treatment start	MDT/Allied Rx approval required
1.1	ATAZANAVIR [300mg] - 1 tablet EMTRICITABINE [200mg] + TENOFOVIR DISOPROXIL [245mg] - 1 tablet RITONAVIR [100mg] - 1 tablet	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Not required
1.2	DARUNAVIR [800mg] - 1 tablet EMTRICITABINE [200mg] + TENOFOVIR DISOPROXIL [245mg] - 1 tablet RITONAVIR [100mg] - 1 tablet	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Not required
1.3	ATAZANAVIR [300mg] - 1 tablet COBICISTAT [150mg] - 1 tablet EMTRICITABINE [200mg] + TENOFOVIR DISOPROXIL [245mg] - 1 tablet	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	MDT required
1.4	COBICISTAT [150mg] - 1 tablet DARUNAVIR [800mg] - 1 tablet EMTRICITABINE [200mg] + TENOFOVIR DISOPROXIL [245mg] - 1 tablet	Yes	Yes	Yes	Yes	Yes	No	No	Yes	yes	Yes	MDT required
1.5	EMTRICITABINE [200mg] + TENOFOVIR DISOPROXIL [245mg] - 1 tablet RALTEGRAVIR [400mg] - 2 tablets	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Not required
1.6	EMTRICITABINE [200mg] + TENOFOVIR DISOPROXIL [245mg] - 1 tablet RALTEGRAVIR [600mg] - 2 tablets	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Not required
1.7	EMTRICITABINE [200mg] + TENOFOVIR DISOPROXIL [245mg] - 1 tablet RILPIVIRINE [25mg] - 1 tablet	Yes	Yes	Yes	No	No	No	No	Yes	Yes	No	Not required
1.8	DORAVIRINE [100mg] + LAMIVUDINE [300mg] + TENOFOVIR DISOPROXIL [245mg] (Delstrigo) - 1 tablet	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	MDT required
1.9	DOLUTEGRAVIR [50mg] + LAMIVUDINE [300mg] (Dovato) - 1 tablet	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	MDT required
1.10	ABACAVIR [600mg] + DOLUTEGRAVIR [50mg] + LAMIVUDINE [300mg] (Triumeq) - 1 tablet	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	No	Not required
1.11	DOLUTEGRAVIR [50mg] - 1 tablet EMTRICITABINE [200mg] + TENOFOVIR DISOPROXIL [245mg] - 1 tablet	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Not required
1.12	ATAZANAVIR [300mg] - 1 tablet EMTRICITABINE [200mg] + TENOFOVIR ALAFENAMIDE [10mg] (Descovy) - 1 tablet RITONAVIR [100mg] - 1 tablet	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	MDT required
1.13	DARUNAVIR [800mg] - 1 tablet EMTRICITABINE [200mg] + TENOFOVIR ALAFENAMIDE [10mg] (Descovy) - 1 tablet RITONAVIR [100mg] - 1 tablet	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	yes	Yes	MDT required
1.14	ATAZANAVIR [300mg] - 1 tablet COBICISTAT [150mg] - 1 tablet EMTRICITABINE [200mg] + TENOFOVIR ALAFENAMIDE [10mg] (Descovy) - 1 tablet	Yes	Yes	Yes	Yes	Yes	No	Yes	yes	Yes	No	MDT required
1.15	COBICISTAT [150mg] - 1 tablet DARUNAVIR [800mg] - 1 tablet EMTRICITABINE [200mg] + TENOFOVIR ALAFENAMIDE [10mg] (Descovy) - 1 tablet	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	MDT required
1.16	BICTEGRAVIR [50mg] + EMTRICITABINE [200mg] + TENOFOVIR ALAFENAMIDE [25mg] (Biktarvy) - 1 tablet	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	MDT required
1.17	DOLUTEGRAVIR [50mg] + RILPIVIRINE [25mg] (Juluca) - 1 tablet	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	MDT required
1.18	EMTRICITABINE [200mg] + TENOFOVIR ALAFENAMIDE [25mg] (Descovy) - 1 tablet RALTEGRAVIR [600mg] - 2 tablets	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	MDT required
1.19	EMTRICITABINE [200mg] + TENOFOVIR ALAFENAMIDE [25mg] (Descovy) - 1 tablet RALTEGRAVIR [400mg] - 2 tablets	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	MDT required
1.20	EMTRICITABINE [200mg] + RILPIVIRINE [25mg] + TENOFOVIR ALAFENAMIDE [25mg] (Odefsey) - 1 tablet	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	MDT required
1.21	COBICISTAT [150mg] + ELVITEGRAVIR [150mg] + EMTRICITABINE [200mg] + TENOFOVIR ALAFENAMIDE [10mg] (Genvoya) - 1 tablet	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	MDT required
1.22	DORAVIRINE [100mg] - 1 tablet EMTRICITABINE [200mg] + TENOFOVIR ALAFENAMIDE [25mg] (Descovy) - 1 tablet	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	MDT required
1.23	COBICISTAT [150mg] + ELVITEGRAVIR [150mg] + EMTRICITABINE [200mg] + TENOFOVIR DISOPROXIL [245mg] (Stribild) - 1 tablet	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	MDT required
1.24	DOLUTEGRAVIR [50mg] - 1 tablet EMTRICITABINE [200mg] + TENOFOVIR ALAFENAMIDE [25mg] (Descovy) - 1 tablet	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	MDT required

Injectables - Recognises additional costs required for staffing, clinical attendance and administration

1b.1	CABOTEGRAVIR [200mg] - 1 tablet RILPIVIRINE [25mg] – 1 tablet CABOTEGRAVIR [600mg] + RILPIVIRINE [900mg] - Prolonged release suspension for injection	No	Yes	Yes	No	No	Yes	Yes	Yes	No	No	MDT & Shan'ara required



HIV National Prescribing Guide (Commercial in Confidence)

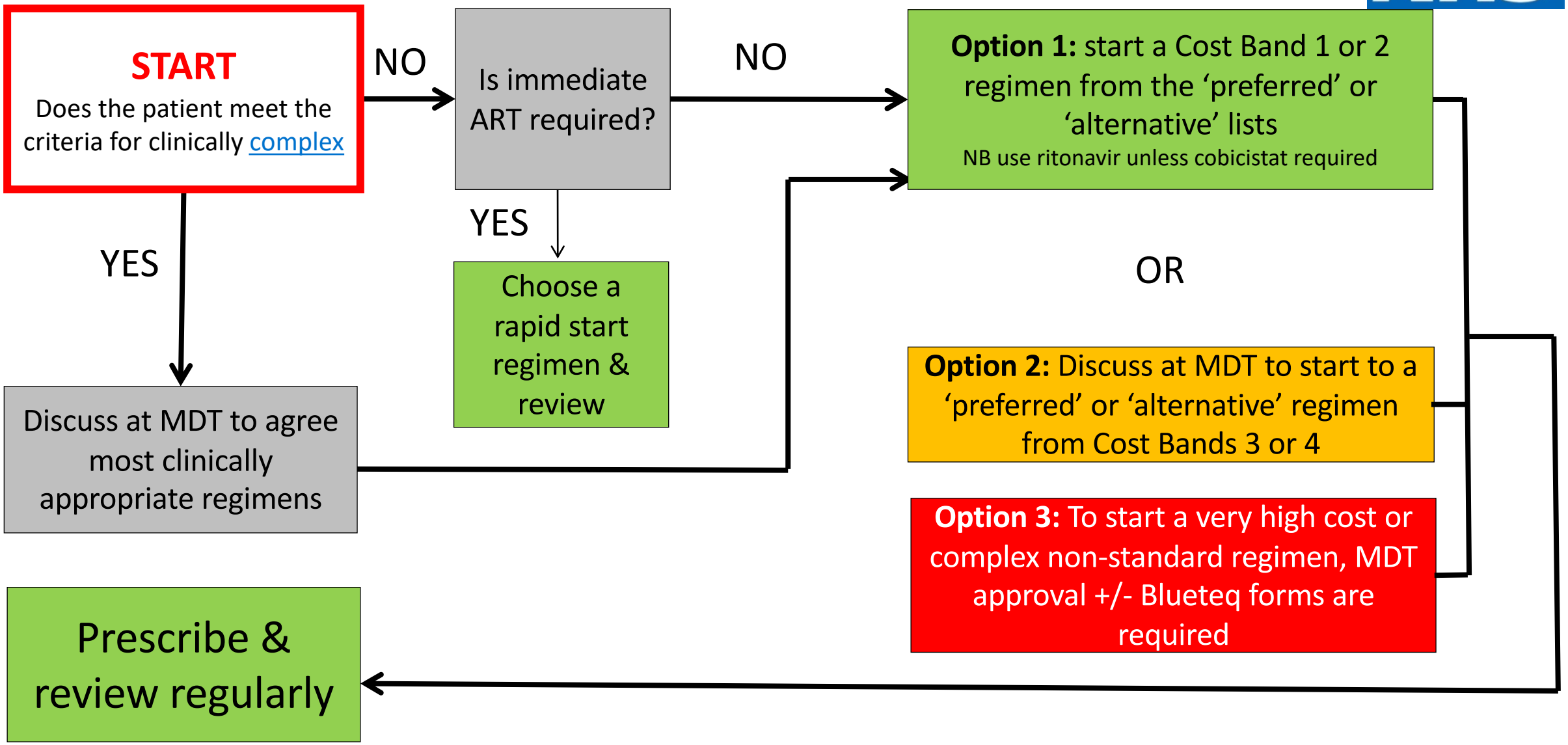
Alternative BHIVA-recommended regimens

#	Regimen	Age Adjustment (13 – 25)	HLA B*5701 positive	CD4 Count <200	Viral load >100,000	HIV RNA >500,000	Kidney function	Osteoporosis	Cardiovascular	Hepatitis B	Naïve and rapid treatment start	MDT/Allied Rx approval required
2.1	EFAVIRENZ [600mg] + EMTRICITABINE [200mg] + TENOFOVIR DISOPROXIL [245mg] - 1 tablet	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Not required
2.2	EMTRICITABINE [200mg] + TENOFOVIR DISOPROXIL [245mg] - 1 tablet NEVIRAPINE [400mg] - 1 tablet	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Not required
2.3	ABACAVIR [600mg] + LAMIVUDINE [300mg] - 1 tablet NEVIRAPINE [400mg] - 1 tablet	Yes	No	Yes	No	No	Yes	Yes	No	No	No	Not required
2.4	ABACAVIR [600mg] + LAMIVUDINE [300mg] - 1 tablet EFAVIRENZ [600mg] - 1 tablet	Yes	No	Yes	No	No	Yes	Yes	No	No	No	Not required
2.5	ATAZANAVIR [300mg] - 1 tablet LAMIVUDINE [300mg] - 1 tablet RITONAVIR [100mg] - 1 tablet	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	MDT required
2.6	ABACAVIR [600mg] + LAMIVUDINE [300mg] - 1 tablet ATAZANAVIR [300mg] - 1 tablet RITONAVIR [100mg] - 1 tablet	Yes	No	Yes	No	No	Yes	Yes	No	No	No	Not required
2.7	DARUNAVIR [800mg] - 1 tablet LAMIVUDINE [300mg] - 1 tablet RITONAVIR [100mg] - 1 tablet	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	MDT required
2.8	ABACAVIR [600mg] + LAMIVUDINE [300mg] - 1 tablet DARUNAVIR [800mg] - 1 tablet RITONAVIR [100mg] - 1 tablet	Yes	No	Yes	No	No	Yes	Yes	No	No	No	Not required
2.9	ABACAVIR [600mg] + LAMIVUDINE [300mg] - 1 tablet LOPINAVIR [200mg] + RITONAVIR [50mg] - 1 tablet	Yes	No	Yes	No	No	Yes	Yes	No	No	No	Not required
2.10	ATAZANAVIR [300mg] - 1 tablet COBICISTAT [150mg] - 1 tablet LAMIVUDINE [300mg] - 1 tablet	Yes	Yes	No	No	No	No	Yes	Yes	No	No	MDT required
2.11	ABACAVIR [600mg] + LAMIVUDINE [300mg] - 1 tablet ATAZANAVIR [300mg] - 1 tablet COBICISTAT [150mg] - 1 tablet	Yes	No	Yes	No	No	No	Yes	No	No	No	MDT required
2.12	COBICISTAT [150mg] - 1 tablet DARUNAVIR [800mg] - 1 tablet LAMIVUDINE [300mg] - 1 tablet	Yes	Yes	No	No	No	Yes	Yes	Yes	No	No	MDT required
2.13	ABACAVIR [600mg] + LAMIVUDINE [300mg] - 1 tablet COBICISTAT [150mg] - 1 tablet DARUNAVIR [800mg] - 1 tablet	Yes	No	Yes	No	No	Yes	Yes	No	No	No	MDT required
2.14	EMTRICITABINE [200mg] + TENOFOVIR DISOPROXIL [245mg] - 1 tablet ETRAVIRINE [200mg] - 1 tablet	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Not required
2.15	EMTRICITABINE [200mg] + TENOFOVIR DISOPROXIL [245mg] - 1 tablet LOPINAVIR [200mg] + RITONAVIR [50mg] - 2 tablets	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Not required
2.16	LAMIVUDINE [300mg] - 1 tablet LOPINAVIR [200mg] + RITONAVIR [50mg] - 2 tablets	Yes	Yes	No	No	No	Yes	Yes	No	No	No	MDT required
2.17	ABACAVIR [600mg] + LAMIVUDINE [300mg] - 1 tablet RALTEGRAVIR [600mg] - 2 tablets	Yes	No	Yes	No	No	Yes	Yes	No	No	No	Not required
2.18	ABACAVIR [600mg] + LAMIVUDINE [300mg] - 1 tablet RALTEGRAVIR [400mg] - 2 tablets	Yes	No	Yes	No	No	Yes	Yes	No	No	No	Not required
2.19	ABACAVIR [600mg] + LAMIVUDINE [300mg] - 1 tablet RILPIVIRINE [25mg] – 1 tablet	Yes	No	Yes	No	No	Yes	Yes	No	No	No	Not required
2.20	ABACAVIR [600mg] + LAMIVUDINE [300mg] - 1 tablet DORAVIRINE [100mg] - 1 tablet	No	No	Yes	No	No	Yes	Yes	No	No	No	MDT required
2.21	EMTRICITABINE [200mg] + TENOFOVIR ALAFENAMIDE [25mg] (Descovy) - 1 tablet NEVIRAPINE [400mg] - 1 tablet	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	MDT required
2.22	EFAVIRENZ [600mg] - 1 tablet EMTRICITABINE [200mg] + TENOFOVIR ALAFENAMIDE [25mg] (Descovy) - 1 tablet	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	MDT required
2.23	EMTRICITABINE [200mg] + TENOFOVIR ALAFENAMIDE [10mg] (Descovy) - 1 tablet LOPINAVIR [200mg] + RITONAVIR [50mg] - 2 tablets	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	MDT required
2.24	EMTRICITABINE [200mg] + TENOFOVIR ALAFENAMIDE [25mg] (Descovy) - 1 tablet ETRAVIRINE [200mg] - 2 tablets	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	MDT required

PEOPLE STARTING / RESTARTING ART

First-line or restart ART algorithm: NHS National ARV Algorithm Feb 2022

Eligibility for clinical trials should be considered at all visits

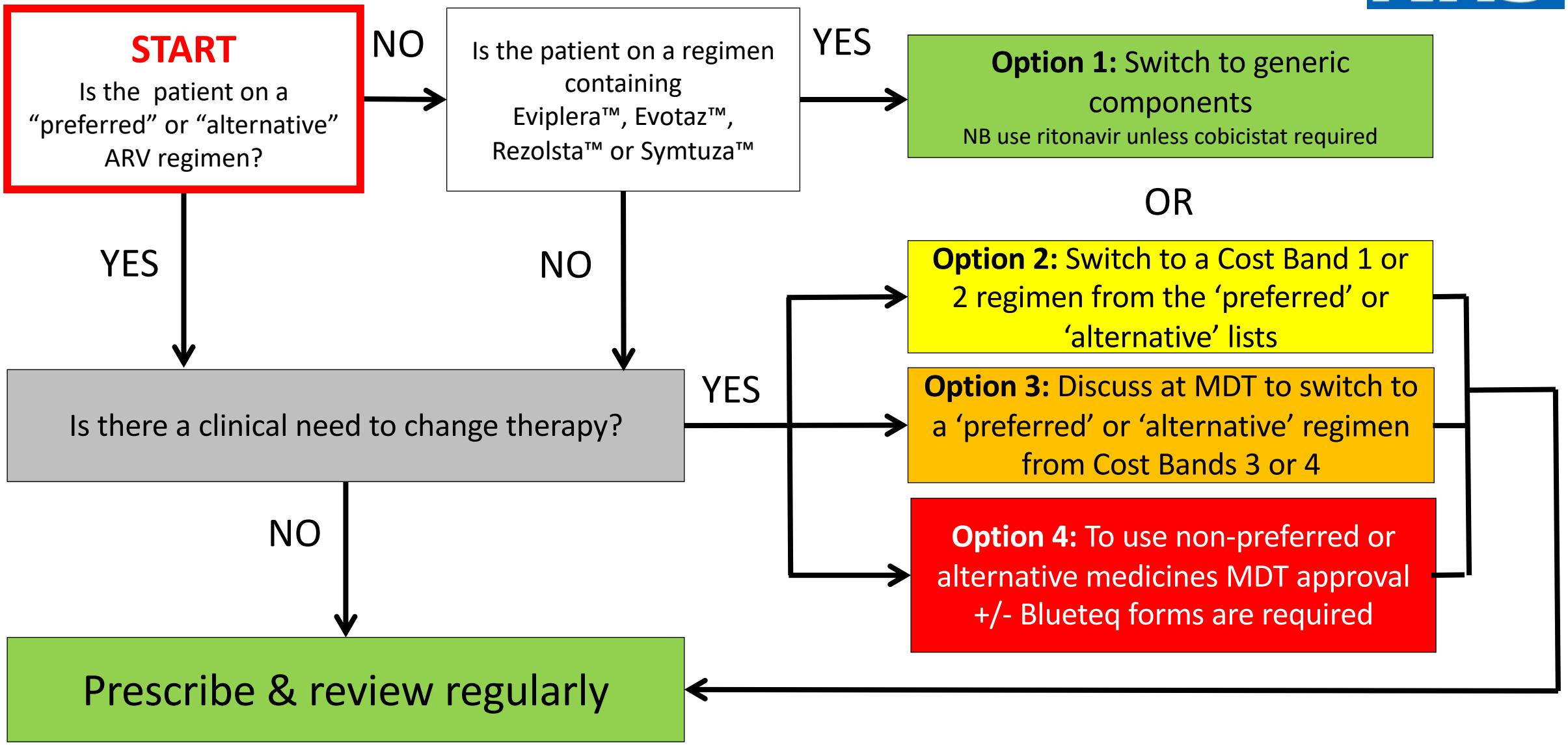


Immediate or rapid ART

- Where a patient wishes to initiate ART before usual baseline investigations are available, follow BHIVA guidance & the ‘quick start’ options on the national prescribing algorithm
- ‘Quick start’ options to be used first-line for patients who are treatment naïve and want a rapid treatment start before their HLA B*5701, Hepatitis status & baseline resistance results are available
- Prescribing should be reviewed against the first-line algorithm at next clinical review

PEOPLE ON STABLE ART

Patients Established on ART : NHS National ARV Algorithm Feb 2022
Eligibility for clinical trials should be considered at all visits



Switching: general principles

- Review all people on stable ART at next prescription, and at annual review, against the prescribing algorithm, clinical aid & toolkit to determine if regimen modification is required.
- Discuss patients on complex ART at MDT prior to undertaking any switch.
- For non-clinically urgent switches **remaining medication should be used first.**
- Many patients will be stable on alternative or non-recommended ART & it may be clinically appropriate to **continue** ART that may not be first choice today.
- Where a decision to continue alternative or non-preferred therapy is made, the rationale must be documented clearly.
- Each time a clinical need for switch occurs clinicians should use a clinically appropriate regimen in the lower cost bands in preference to those in higher cost bands.

Switching away from Symtuza, Rezolsta & Evotaz

- Discussing switch with patients on any PI regimen offers an opportunity to discuss other ART; the threshold for PI use may have altered since the initial decision
  - Switching to a more clinically appropriate regimen may be more expensive than switching to generic PI components but **clinical need should always take priority**
- **Ritonavir is the preferred booster** where there are no tolerability or drug interaction issues
- The thresholds for using particular products will vary significantly between units

  e.g. **Symtuza®**
  - Some units switched people on tenofovir-disoproxil/emtricitabine + darunavir + ritonavir to this STR based on historical marginal cost differences
  - In others most people on Symtuza have a clear indication for PI-based STR
- **Evotaz® & Rezolsta®**
  - Switch to generic PI + ritonavir (preferred) or cobicistat (if needed), or an appropriate alternative

Specific switch examples

Reasonable to continue	
Abacavir/lamivudine + 3rd agent	Where CV risk <10%, TDF unsuitable & the 3rd agent is not amenable to 2DR
Nevirapine	Where no toxicity or drug interaction concerns
Efavirenz	If no reported side effects including sleep & mood-related (review every visit) or previous switch yielded no benefit
Boosted PI	Where most clinically appropriate
Switch recommended	
Lopinavir/ritonavir	Unless necessary based on resistance and darunavir not suitable
Atazanavir/b + tenofovir-DF containing backbone	Additive renal toxicity; if no NRTI resistance, atazanavir/b + lamivudine superior to TDF/XTC + atazanavir/b in context of suppressed switch
Etravirine	Unless resistance or other reasons to avoid RPV or DOR
Maraviroc	Use should be reviewed in an MDT
PI or dolutegravir monotherapy	Review use in an MDT; intensification or switch recommended

Injectable cabotegravir/rilpivirine 1

- The agreed NHS price does not include VAT, extra staff/administration costs or pre-emptive oral bridging packs should these be deemed necessary
- People should be counselled that:
  - Known or suspected resistance to the either drug or detectable viraemia are exclusions
  - An initiation phase of 1m oral lead in followed by their first and second IM injection visits 1m apart = 3 visits in the first 3 months followed by 2-monthly clinic visits
  - Each injection visit involves two deep IM injections (1 into each buttock muscle) and is likely to require 30-60 minutes in clinic
  - Adherence is critical with a **maximum** of +/ 7 day window for late administration
  - In clinical trials, about 1 in 70 people at year 1 and 1 in 60 at year 2 on 2-monthly IM CAB/RPV experienced viral rebound despite 100% adherence, and most of these also developed resistance to one or both drugs
- Identifying people with adherence challenges plus viral suppression may be challenging

Injectable cabotegravir/rilpivirine 2

Initially, as injectables roll out, it is reasonable for services to limit access to

- Those most in need
  - People who express a major psychological impact of daily pill taking
  - People who describe a concerning adherence pattern but remain virally suppressed
  - People who describe a real risk of stopping ART if they continue oral therapy
  - People for whom a 1 in 70 virological failure rate at year 1, and 1 in 60 at year 2, outweighs the disadvantages to them of oral therapy
- Those already receiving injectable cabotegravir/rilpivirine as part of a clinical trial or compassionate access programme
- Clinics that have capacity and staffing to ensure repeated, safe administration is possible

Complex & not routinely commissioned list

- This guide describes some complex regimens that are no longer preferred or alternative but are used in certain situations as deemed necessary by the MDT
- This list is not exhaustive but demonstrates the costs of these regimens
- Eviplera®, Evotaz®, Rezolsta®, Symtuza® are not routinely commissioned as outlined in earlier slides