# Clinical Commissioning Policy: Bictegravir-emtricitabine-tenofovir alafenamide for the treatment of HIV-1 in adults

**NHS England Reference: 170131P**

# Clinical Commissioning Policy: Bictegravir-emtricitabine-tenofovir alafenamide for the treatment of HIV-1 in adults

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## Contents

## Policy Statement

NHS England will commission Bictegravir-emtricitabine-tenofovir alafenamide for the treatment of HIV-1 in adults in accordance with the criteria outlined in this document.

In creating this policy NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

This policy document outlines the arrangements for funding of this treatment for the population in England.

## Equality Statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

## Plain Language Summary

### About Human Immunodeficiency Virus type 1 (HIV-1)

Human immunodeficiency virus, or HIV, is the virus that causes Acquired Immunodeficiency Syndrome (AIDS). HIV attacks the immune system by destroying

CD4 positive (CD4+) T cells, a type of white blood cell that is vital for fighting infections. The destruction of these cells leaves people living with HIV vulnerable to other infections, diseases and other complications. HIV treatment with antiretroviral therapy (ART) has transformed the outlook for people living with HIV from that of a significantly shortened lifespan to a manageable long-term condition. Without treatment, HIV causes progressive damage to the immune system that ultimately results in serious ill health and death. ART prevents damage to the immune system through suppression of the HIV virus and reduces the risk of a wide range of serious complications which are more frequent in untreated, HIV-infected individuals.

See also, section 4 for additional definitions of terms used in this document.

**About current treatments**

Current standard HIV treatment involves ART which uses 3 drugs typically made up of 2 from a drug family called nucleos(t)ide reverse transcriptase inhibitors (NRTIs) plus 1 drug from 1 of 3 other drug types: a ritonavir/cobicistat-boosted protease inhibitor (PI/r), a non-nucleoside reverse transcriptase inhibitor (NNRTI) or an integrase inhibitor (INI). ART requires a very high level of patient adherence (ideally greater than 95%) to avoid drug resistance and once started should be continued lifelong. The effectiveness of ART is measured by its ability to reduce the amount of HIV in the blood (viral load) to undetectable levels on routine tests (usually to less than 50 copies per ml).

Treating HIV with ART has transformed the outlook for people living with HIV. ART allows most people with HIV to have a normal life expectancy. As a consequence, people living with HIV are more likely to develop age-related medical conditions. Careful management of those conditions alongside their HIV infection is important. HIV management involves life-long treatment with ART. As a result, HIV clinicians should aim to maximise tolerability and quality of life while minimising harm.

**About the new treatment**

Bictegravir-emtricitabine-tenofovir alafenamide (B/F/TAF) contains bictegravir which is a new treatment for HIV-1 from the INI group. Bictegravir is only available as a ‘3 in 1’ pill combined with 2 NRTIs (emtricitabine and tenofovir alafenamide). An

evidence review looked at how safe and effective B/F/TAF is compared to 2 other triple drug combinations first line, both based on 1 INI + 2 NRTI: dolutegravir, abacavir and lamivudine (DTG/ABC/3TC), and dolutegravir, emtricitabine and tenofovir alafenamide (DTG/F/TAF). The evidence review showed that B/F/TAF is as effective as the 2 treatments it was compared against.

The evidence review also looked at how safe and effective B/F/TAF is when switching from boosted protease inhibitor-based 3-drug regimens and DTG/ABC/3TC. The evidence showed the B/F/TAF is comparable to the treatments people were switched from in terms of maintaining HIV control and other important outcomes.

**What we have decided**

NHS England has carefully reviewed the evidence to treat HIV-1 with B/F/TAF prepared by NICE**.** We have concluded that there is enough evidence to consider making the treatment available in the circumstances stated in this policy

# 1 Introduction

Bictegravir is a HIV-1 integrase strand transfer inhibitor (INI), a type of antiretroviral drug designed to block the action of integrase, a viral enzyme that inserts the genome of the HIV-1 virus into the DNA of specific human white blood cells called T-helper cells. Integration is a vital step in HIV reproducing itself. Integrase inhibitors block the virus from integrating, effectively stopping it from replicating and causing further damage to the infected person's immune system.

B/F/TAF is a fixed dose combination of 3 drugs which includes bictegravir, emtricitabine and tenofovir alafenamide. It has a positive opinion from the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) for the treatment of adults infected with HIV-1 without present or past evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir.

B/F/TAF is a daily oral treatment containing 3 antiretroviral components in 1 tablet.

# 2 Definitions

**Antiretroviral therapy (ART):** This usually consists of a combination of 3 antiretroviral drugs. A backbone of 2 nucleoside reverse transcriptase inhibitors (NRTI) and a 3rd agent from 1 of the following classes of drugs: non-nucleoside reverse transcriptase inhibitors (NNRTI), ritonavir or cobicistat boosted protease inhibitors (PI/r) and integrase inhibitors (INI).

**Fixed dose combination (FDC):** tablets containing 2 or more HIV drugs including single tablets that combine a complete ART combination into 1 pill.

Integrase inhibitor (INI): a type of antiretroviral drug designed to block the action of integrase, a viral enzyme that inserts the genome of the HIV-1 virus into the DNA of specific human white blood cells called T-helper cells.

**NRTI backbone:** The 2 nucleo(s)tide reverse transcriptase inhibitors that are the basis of a combination antiretroviral treatment.

**Viral load:** HIV RNA levels in plasma are used to monitor response to ART. Patients on effective therapy sustain viral loads of <50 copies/ml (undetectable). Patients who fail to achieve an undetectable viral load or who experience a confirmed and

sustained viral load rebound to above 200 copies/ml are deemed to be experiencing virological failure.

## 3 Aims and Objectives

This policy considered: The evidence for B/F/TAF for treating adults with HIV-1 infection.

The objectives were to:

- Review the evidence of effectiveness for B/F/TAF
- Define the eligibility criteria for B/F/TAF.
- Define the commissioning arrangements required for B/F/TAF.

## 4 Epidemiology and Needs Assessment

In 2017, 85,537 (84,551 adults and 986 children) people were being seen for HIV care in England with 3,973 new cases of HIV diagnosed in the same year (Data from Public Health England (PHE) – National HIV surveillance data).

PHE also reported that 83,585 people in England were receiving antiretroviral therapy (ART) at the end of 2017, representing 98% of the population seen for HIV care in England. In 2017, more than a third (39%; 33,144/85,537) of people accessing HIV care in England were aged 50 years and above, compared with 17% in 2007. HIV is a lifelong condition and the prevalence of comorbidities, including cardiovascular (CV) disease, chronic kidney disease (CKD), mental health disorders and osteoporosis is higher in patients living with HIV (PLWHIV), compared with non-infected individuals (Bagkeris et al. 2018). HIV services should continue evolving to meet the changing needs of people living with HIV including the management of comorbidities and other complex health conditions.

The overall goal of treatment is HIV-1 viral suppression (maintaining an undetectable viral load level). British HIV Association Treatment guidelines (BHIVA) for adults currently recommend the following first-line treatment (Waters et al. 2016):

- One of the following NRTI backbones:

1. emtricitabine and tenofovir disoproxil fumarate (F/TDF): recommended for individuals who do not show established or significant risk factors for kidney or bone problems. OR

2. emtricitabine and tenofovir alafenamide (F/TAF): preferred option if the individual has established or significant risk factors for kidney or bone problems. OR

3. abacavir and lamivudine: alternative option, although an individual should not be given abacavir if there are contraindications e.g. HLA-B*5701 positive, hepatitis B co-infection or high risk of cardiovascular disease. AND

a third drug: of which the preferred options are atazanavir/ritonavir, or darunavir/ritonavir, or raltegravir or elvitegravir/cobicistat or rilpivirine, or dolutegravir. An alternative option is efavirenz.

## 5 Evidence Base

NHS England has concluded that there is sufficient evidence to support the routine commissioning of this treatment for the indication in certain circumstances (see Section 8 criteria for commissioning below).

**Summary of evidence – Previously untreated HIV-1**

NHS England considered evidence from 3 studies on the clinical effectiveness and safety of B/F/TAF for adults with previously untreated HIV-1. The 3 studies were all randomised controlled trials: Gallant et al. 2017 (n=629) which compared B/F/TAF with dolutegravir, abacavir and lamivudine (DTG/ABC/3TC), Sax et al. 2017a (n=645) and Sax et al. 2017b (n=98) both of which compared B/F/TAF with dolutegravir, emtricitabine and tenofovir alafenamide (DTG/F/TAF).

Sax et al. (2017b) was not sufficiently powered which means that the study did not include enough people for the statistical analysis to detect whether there were any statistically significant differences between B/F/TAF and DTG/F/TAF. Thus, the statistics reported should be treated as descriptive and interpreted with caution.

**Clinical effectiveness**

Gallant et al. (2017) reported that 48 weeks after beginning treatment, 92.4% of participants receiving B/F/TAF had less than 50 copies of HIV-1 per ml of plasma compared with 93% of those receiving DTG/ABC/3TC, with a treatment difference of -0.6% [(95% CI: -4.8 to 3.6) p=0.78] as a primary outcome. Both treatments worked equally well in reducing HIV-1 viral copies and the difference between them was not statistically significant. Both Sax et al. (2017a and b) studies also reported no statistically significant difference in the proportion of participants achieving less than 50 copies of HIV-1 per ml of plasma in those receiving B/F/TAF when compared with DTG/F/TAF. Sax et al (n=645) reported 89.4% of participants receiving B/F/TAF obtaining less than 50 copies of HIV-1 RNA per ml of plasma compared with 92.9% of those receiving DTG/F/TAF, treatment difference of -3.5% [(95% CI: -7.9 to 1.0) p=0.12], and Sax et al (n=98) with 97% of participants compared with 91% obtaining less than 50 copies of HIV-1 RNA per ml of plasma, treatment difference 6.4% [(95% CI: -6.0 to 18.8) p=0.17].

Gallant et al. (2017) reported an increase of 233 CD4 cells per microlitre (µl) (SD ± 185.2) of plasma in participants receiving B/F/TAF compared with an increase of 229 cells per µl (SD ± 188.8) in those receiving DTG/ABC/3TC. Both treatments worked equally well in increasing CD4 cell counts and the difference between them was not statistically significant difference (p=0.81). Both Sax et al. studies also reported no statistically significant difference in the increase of CD4 cells for participants receiving B/F/TAF when compared with DTG/F/TAF. Sax et al. (2017a) reported an increase of 180 cells per µl (SD ± 166.6) from baseline in participants receiving B/F/TAF compared with an increase of 201 cells per µl (SD ± 166.4) in those receiving DTG/F/TAF (p=0.10). Sax et al (2017b) showed an increase of 258 cells per µl (SD ± 221.7) in participants receiving B/F/TAF compared with an increase of 192 cells per µl (SD ± 242.0) in those receiving DTG/F/TAF giving a treatment difference, in least square mean, of 72 cells per µl [(95% CI: -30 to 174) p=0.16].

Secondary outcome evidence in Gallant et al. (2017) showed a decrease in hip bone density of -0.78% (SD ± 2.22) in participants receiving B/F/TAF compared with a decrease of -1.02% (SD ± 2.31) for those receiving DTG/ABC/3TC giving a non-

statistically different treatment difference of 0.238% [(95% CI: -0.151 to 0.626) p=0.23]. A non-statistically significant treatment difference was also reported for lumbar spine bone mineral density with a reduction of -0.83% (SD ± 3.19) for those receiving B/F/TAF and -0.60% (SD ± 3.10) for those receiving DTG/ABC/3TC, treatment difference -0.235% [(95% CI: -0.766 to 0.297) p=0.39].

Study drug adherence, as a subgroup analysis (<95% and ≥95% adherence) of participants who achieved less than 50 HIV-RNA copies per ml of plasma at week 48 after starting treatment, was reported by both Gallant et al. (2017) and Sax et al. (2017a). Gallant et al. stated that, of those participants who reported <95% adherence, 81% who received B/F/TAF and 86% who received DTG/ABC/3TC achieved a viral load below 50 HIV-RNA copies per ml (p=0.65). They also stated that, of those reporting ≥95% adherence, 97% who received B/F/TAF and 96% who received DTG/ABC/3TC achieved a viral load below 50 HIV-RNA copies per ml (p=0.66) showing no statistically significant differences in either subgroup. Sax et al. stated that, of those reporting <95% adherence, 84% who received B/F/TAF and 90% who received DTG/F/TAF achieved lower than 50 HIV-RNA copies per ml (p=0.35). They also stated that, of those reporting ≥95% adherence, 94% in both groups achieved lower than 50 HIV-RNA copies per ml (p=1.00) showing no statistically significant differences in either subgroup.

Gallant et al. (2017) and both Sax et al. (2017a and b) studies reported no treatment emergent resistance to B/F/TAF, DTG/ABC/3TC or DTG/F/TAF in the study participants.

**Safety**

Drug-related adverse events

Gallant et al (2017) which studied 629 people with previously untreated HIV-1 stated that 26% (n=82) of the 316 who received B/F/TAF and 40% (n=127) of the 315 who received DTG/ABC/3TC reported an adverse event. Sax et al. (2017a) which studied 645 people, reported 18% (n=57) of the 320 people who received B/F/TAF and 26% (n=83) of the 325 who received DTG/F/TAF.

Drug-related serious adverse events

Gallant et al (2017) stated that less than 1% of people who received either B/F/TAF or DTG/ABC/3TC reported a drug-related serious event.

Adverse events leading to discontinuation

Gallant et al (2017) stated that no-one who received B/F/TAF experienced an adverse event that led to discontinuation while 1% was reported in those who received DTG/ABC/3TC. Sax et al. (2017a) stated that 2% of people who received B/F/TAF experienced an adverse event that led to discontinuation while less than 1% reported discontinuation in those who received DTG/F/TAF.

Results suggest that B/F/TAF has a similar safety and tolerability profile to both DTG/ABC/3TC and DTG/F/TAF.

**Summary of evidence – Treatment switching**

NHS England considered evidence from 2 studies on the clinical effectiveness and safety of switching to B/F/TAF for virologically supressed HIV-1 infected adults from current suppressive antiretroviral therapy.

The 2 studies were both randomised controlled trials, Molina et al. 2018 (n=563), a non-inferiority trial, which compared B/F/TAF with dolutegravir, abacavir and lamivudine (DTG/ABC/3TC) and Daar et al. 2018 (n=577), an open label non-inferiority trial which compared B/F/TAF with boosted protease inhibitor-based regimen.

**Clinical effectiveness**

Molina et al. (2018) reported that 48 weeks after switching treatment, 93.6% of participants receiving B/F/TAF had less than 50 copies of HIV-1 per ml of plasma compared with 95% of those continuing to receive DTG/ABC/3TC, with a treatment difference of -1.4% [(95% CI: -5.5 to 2.6) p=0.59]. Both treatments worked equally well in maintaining HIV-1 viral copies below 50 per ml of plasma with no statistically significant difference between them. Daar et al. (2018) reported that 92.1% of participants receiving B/F/TAF maintained less than 50 copies of HIV-1 RNA per ml of plasma compared with 88.9% of those receiving boosted protease inhibitor-based regimens, treatment difference of 3.2% [(95% CI: -1.6 to 8.2) p=0.20] at 48 weeks

after switching. Again, both treatments worked equally well in maintaining HIV-1 viral copies below 50 per ml of plasma with no statistically significant difference between them.

Molina et al. (2018) reported a decrease of 31 CD4 cells per microlitre (µl) (SD ± 181.3) of plasma in participants receiving B/F/TAF compared with an increase of 4 cells per µl (SD ± 191.0) in those receiving DTG/ABC/3TC, treatment difference, in least square mean, of -35 cells/ µl [(95% CI: -67 to -3) p=0.031] at 48 weeks. After adjusting for baseline CD4 count the treatment difference was not statistically significant [-21 cells/ µl (95% CI: -51 to 9) p=0.18] indicating both treatments work equally well.

Secondary outcome evidence in Molina et al. (2018) showed a small increase in hip bone mineral density of 0.16% in participants receiving B/F/TAF compared with 0.30% for those receiving DTG/ABC/3TC giving a non-statistically different treatment difference (p=0.47). A non-statistically significant treatment difference was also reported for lumbar spine bone mineral density with an increase of 0.69% for those receiving B/F/TAF and 0.42% for those receiving DTG/ABC/3TC (p=0.33). This indicates that there is no difference between treatments for this outcome.

Study drug adherence, as a subgroup analysis (<95% and ≥95% adherence) of participants who achieved less than 50 HIV-RNA copies per ml of plasma at week 48 after switching treatment, was reported by Molina et al. (2018). Of those patients who reported <95% adherence (41/282 for the B/F/TAF arm and 64/282 for the DTG/ABC/3TC ARM), 93% (38/41) in the B/F/TAF arm achieved less than 50 HIV-RNA copies per ml of plasma compared to 88% (56/64) in the DTG/ABC/3TC arm (p=0.52). Similarly in those reporting ≥95% adherence, the proportion achieving less than 50 HIV-RNA copies per ml of plasma was 94% (226/240) in the B/F/TAF arm compared to 97% (211/217) in the DTG/ABC/3TC (p=0.17) showing no statistically significant differences in either subgroup.

Molina et al. (2018) reported no treatment emergent resistance to B/F/TAF or DTG/ABC/3TC in the study participants. Daar et al. (2018) reported no treatment emergent resistance to B/F/TAF but 1 was reported in a participant who was receiving ritonavir-boosted darunavir with abacavir plus lamivudine.

## Safety

### *Drug-related adverse events*

Molina et al (2018) stated that 8% (n=23) of the 282 who received B/F/TAF and 16% (n=44) of the 281 who received DTG/ABC/3TC reported a drug related adverse event (p=0.006). Daar et al. (2018) with 577 participants, reported 19% (n=54) of the 290 people who received B/F/TAF and 2% (n=6) of the 287 who received boosted protease inhibitor-based regimens (p value not reported).

### *Drug-related serious adverse events*

Both Molina et al (2018) and Daar et al (2018) stated that less than 1% of people who received B/F/TAF reported a drug-related serious event with none reported for those who received DTG/ABC/3TC or boosted protease inhibitor-based regimens.

### *Adverse events leading to discontinuation*

Molina et al (2018) stated that 2% of people who received B/F/TAF experienced an adverse event that led to discontinuation while 1% was reported in those who received DTG/ABC/3TC. Daar et al. (2018) also stated that 1% of people who received B/F/TAF experienced an adverse event that led to discontinuation while less than 1% reported discontinuation in those who received boosted protease inhibitor-based regimens.

Results suggest that B/F/TAF has a similar safety and tolerability profile to both DTG/ABC/3TC and boosted protease inhibitor-based regimens.

### *Patient reported outcomes*

Wohl et al. (2018) described patient reported outcomes from 2 prospective, randomised double-blind studies comparing the differences in HIV symptom scores in newly treated (Gallant et al. 2017) and HIV-1 supressed patients (Molina et al. 2018). Patient reported outcome measures were administered at baseline and weeks 4, 12, and 48. Treatment differences were assessed using unadjusted and adjusted logistic regression and longitudinal modelling techniques. Statistical significance was assessed using $p<0.05$. Across both populations, bothersome

symptoms were reported by fewer patients receiving B/F/TAF compared with DTG/ABC/3TC.

In treatment-naïve adults, there were statistically significant differences between B/F/TAF and DTG/ABC/3TC, with fewer reports of fatigue/loss of energy, nausea/vomiting, dizziness/light-headedness, and difficulty sleeping at 2 or more time points seen in the B/F/TAF group ($p<0.05$) in the adjusted logistic regression model. In the longitudinal models, there were statistically significant differences in the fatigue and nausea/vomiting domains with fewer reports in B/F/TAF group.

In HIV-1 supressed patients, there were statistically significant differences between B/F/TAF and DTG/ABC/3TC, with fewer reports of nausea/vomiting, sad/down/depressed, nervous/anxious, and poor sleep quality (from the PSQI) in the B/F/TAF arm at 2 or more time points in the adjusted logistic regression model, as well as in the longitudinal models.

# 6 Criteria for Commissioning

B/F/TAF will be routinely commissioned in HIV-1 infected adults **in line with cost-based, regional prescribing guidelines**:

1. if they meet the commissioning criteria as outlined in the NHS England commissioning policy: tenofovir alafenamide for treatment of HIV-1 in adults and adolescents. Ref: NHS England: 16043/P (see **Appendix I**)*; **OR***

2. if they require an unboosted integrase inhibitor-containing regimen but neither:

    - raltegravir; NOR
    - dolutegravir

    can be taken due to drug-drug interactions or poor tolerability/toxicity.

All patients for whom B/F/TAF is considered a treatment option must be considered in an HIV specialist treatment multidisciplinary team (MDT) meeting and the decision of the MDT recorded.

**Stopping criteria**

- Stop treatment with B/F/TAF if there is a non-response to treatment or tolerability issues and switch to an appropriate alternative antiretroviral therapy in line with cost-based, regional prescribing guidelines.
    - Non-response to treatment is measured as the occurrence of any of the following:
        - Sustained plasma HIV RNA levels greater than 200 copies per ml; or
    - Tolerability issues include: significant toxicities or side effects.

Should prices materially change and in particular should they increase, NHS England may need to review whether the policy remains affordable and may need to make revisions to the existing policy.

# 7 Patient Pathway

Commissioned HIV care and treatment providers who meet the NHS standard contract for specialised human immunodeficiency virus services (Adults) (B06/S/a) initiate and monitor HIV drug treatment. Prescription and monitoring of B/F/TAF fixed dose combination is in line with the existing patient pathway and should be in line with cost-based, regional prescribing guidelines.

# 8 Governance Arrangements

All patients identified who might benefit from starting B/F/TAF should be referred to and discussed at specialist HIV MDTs and the recommendation recorded in accordance with regional and locally agreed ART prescription guidance.

All patients identified who are currently on suppressive ART and might benefit from switching to B/F/TAF should be managed by regional and locally agreed best practice guidance for switching antiretroviral drugs in addition to being discussed at specialist HIV MDTs.

For patients deemed suitable for switch (see section 8) following medical review, this must be undertaken with a planned approach to ensure no drug wastage occurs.

(For guidance on role and responsibilities of MDT meetings see current HIV CRG guidance).

This includes the cohorts identified for routine commissioning as well as any exceptional cases.

## 9 Mechanism for Funding

Reimbursement for the use of ART for individuals meeting the criteria in this policy is provided via England Specialised Commissioning Teams. Antiretrovirals should be prescribed in line with NHS England Clinical Commissioning Policies in addition to agreed regional prescribing initiatives.

## 10 Audit Requirements

All patients identified who might benefit from B/F/TAF must be referred to and their treatment discussed in a HIV MDT. Recommendations for treatment must be recorded. Commissioners will review the audits..

## 11 Documents which have informed this Policy

The documents that have informed this policy include a review of the clinical evidence available for B/F/TAF. Additional evidence sources are listed in the table of references below.

## 12 Date of Review

This document will be reviewed when information is received which indicates that the policy requires revision.

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# APPENDIX I

**Clinical Commissioning Policy: Tenofovir Alafenamide for treatment of HIV 1 in adults and adolescents Reference: NHS England: 16043/P**

**1. Patients with definite contra-indications to TDF**

- Patient with confirmed osteoporosis on DEXA or a high risk of major fracture as determined by FRAX who have a definite contra-indication to TDF; or
- Patients with renal disease based on NICE definitions (chronic kidney disease stage G3, or chronic kidney disease stage G1/2 plus stage A3 proteinuria or nearing this threshold) or renal toxicity or other intolerance secondary to TDF (TAF does not have a licensed indication for CKD stage 4 or 5) who have a definite contra-indication to TDF; or
- Abacavir should be considered as an alternative to TDF unless there are specific contra-indications (HLA-B5701 positive status, cardiovascular disease or high estimated risk of cardiovascular disease in accordance with BHIVA guidelines, need for tenofovir-containing ART in HBV co-infected individuals).

**2. Patients with relative contra-indications to TDF**

- Patients approaching the thresholds of osteoporosis outlined above where abacavir is not a suitable alternative;
- Patients with renal markers approaching the thresholds where TAF is thought be more appropriate and abacavir not a suitable alternative;

**3. Stable patients switching from alternative ART regimens**

- Patients stable on elvitegravir/cobicistat/emtricitabine/TDF can switch to elvitegravir/cobicistat/emtricitabine/TAF, providing clinical assessment has deemed this clinically appropriate, without MDT discussion if it is cost-neutral or cost-saving switch; or
- Patients switching from alternative ARV regimens can switch to elvitegravir/cobicistat/emtricitabine/TAF where there is a clinical indication to do so, the switch is clinically appropriate and this had been discussed in an MDT.

- The rationale for switch must be explained to the patient and be clearly documented in the notes, available for audit.
- This should include a discussion about the potential need to switch back should the TAF-based product become more costly than the TDF equivalent (and the switch is clinically appropriate).

For clarification, stable patients refers to patients who are virologically stable, and patients who are clinically appropriate for switching are those that meet the criteria set out in criteria 1 and 2 of this policy. These criteria also apply to patients on emtricitabine/TDF or emtricitabine/rilpivirine/TDF from November 2016. A further addendum has been added to the end of this document to help with the identification of patients under each criterion applicable in this policy.

**Exclusions**

1. Patients with proven or suspected resistance to the component drugs in any TAF-containing FDC.

2. Use and reimbursement of TAF-based products by providers who are not commissioned by NHS England to provided HIV care and treatment services.

3. Any increase in the price of TAF-based products or price reduction in alternatives would require a review of this policy, as would any reduction in price of alternative combinations.

4. Patients for whom the drug is contra-indicated or data for use in that patient sub group does not exist to support the prescribing e.g.: HIV/HBV co-infection at the time of writing; these exclusions will likely change as more data becomes available.

This policy has been produced following completion of an evidence review for TAF as a new agent and its use in E/C/F/TAF. No further evidence reviews or new policies will be produced in relation to new combinations unless

a. the combination contains TAF and another new drug agent or formulation
b. new data emerges to demonstrate superiority over existing treatments, or

c. the combination requires investment which needs to be considered as part of annual prioritisation.

New policies will follow the process for policy development. In all other cases, where TAF is combined with routinely used ARVs, NHS England will review the evidence to demonstrate that new combination products are bio-equivalent to existing regimens and will then assess the cost impact of routine commissioning for specific, defined patient groups who will achieve additional benefit over existing treatments for the same or lower cost than current treatments. Following approval through the appropriate governance route, guidance will then be issued on the approved commissioning arrangements and this policy document updated as required.

In order that the patients most likely to benefit from treatment with TAF - as intended by the commissioning criteria - are selected, clinicians are provided with the following tool. This tool sets out the available peer reviewed published guidance.

**Renal Disease**

- For patients with CKD, the clinical criteria for TAF is based on the NICE classification for CKD and risk of CKD progression (fig1)(1)
- Where abacavir is not a suitable alternative, patients with moderately increased, high or very risk of CKD are most likely to benefit from a switch to TAF.
- For patients with moderate increased risk of CKD progression (CKD stage G1/2 + A2) and who might be considered for TAF under category 2, additional risk factors for CKD should be considered when considering eligibility for TAF. These include older age, diabetes, cardiovascular disease and hypertension. Other co-morbidities and concomitant nephrotoxic medication should be considered if associated with higher risk of CKD progression.
- TAF is not licensed for patients with eGFR <30ml/min (CKD stage G4 and G5)

**Bone disease**

- Published NICE guidance is available to guide assessment of bone disease and fracture probability (2, 3 and 4).

- National guidance recommends fracture probability should be assessed in postmenopausal women and men age 50 years or more who have risk factors for fracture, using FRAX (https://www.shef.ac.uk/FRAX/tool.aspx).
- National guidance recommends fracture probability should be assessed in postmenopausal women and men age 50 years or more, who have risk factors for fracture, using FRAX (https://www.shef.ac.uk/FRAX/tool.aspx). In individuals at intermediate risk, bone mineral density (BMD) measurement should be performed using dual energy X-ray absorptiometry and fracture probability re-estimated using FRAX. HIV infection should be considered a secondary risk factor for osteoporosis
- Where abacavir is not a suitable alternative, patients with osteoporosis or a high fracture probability (>10%) are most likely to clinically benefit from using TAF compared to TDF.
- TAF should be considered for HIV positive patients with osteoporosis and those with a high fracture probability (>10% either major osteoporotic or hip) (4) (category1)
- The HIV positive population most at risk include children and young people below the age of peak bone mass (aged approx. 25 years), those who have already had a low-trauma fracture, those who fall frequently, post-menopausal women and those on long term glucocorticoid therapy. These risk factors should be taken into account when considering TAF (category 2).

**Resistance**

- Current exclusion criteria include ‘Patients with proven or suspected resistance to the component drugs in any TAF-containing FDC’. For patients with the NRTI resistance mutation M184V, Descovy (TAF and emtricitabine) may be used if TAF is clinically indicated and patients meet the clinical criteria for commissioning as TAF is not currently available as a single drug formulation.