

Clinical Commissioning Policy: Tenofovir Alafenamide for treatment of HIV 1 in adults and adolescents

Reference: NHS England: 16043/P



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Contact Details for further information england.specialisedcommissioning@nhs.net

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Clinical Commissioning Policy: Tenofovir Alafenamide for treatment of HIV 1 in adults and adolescents

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Policy Statement

NHS England will commission tenofovir alafenamide for HIV 1 in adults and adolescents 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 anti-retroviral therapy

Treating HIV with anti-retroviral therapy (ART) has transformed the outlook for people living with HIV. ART allows most people with HIV to live a normal life - with a normal life expectancy.

As people get older, some medical concerns become very important. These include:

- heart disease
- kidney problems
- bone problems.

Some HIV drugs have side effects that affect these medical problems which happen as people get older.

Until a cure is found, ART is a life-long treatment - with most people taking ART for decades.

- This means it is very important to minimise long-term side effects
- At the same time we need to make sure ART is still effective.

About the new treatment

An evidence review looked at how safe and effective a medicine was.

- The medicine is called tenofovir alafenamide or TAF.
- It was compared to another drug called tenofovir disoproxil fumarate or TDF.
- Like TDF, TAF is an effective drug. TAF appears to have a lower risk of kidney and bone side effects in the short-term. However, we do not know if it is lower in the long-term.
- TAF is used in combinations with other HIV drugs. In this case, we looked at the combination known as elvitegravir/cobicistat/emtricitabine/TAF or E/C/F/TAF but there are other combinations using TAF that will become available soon. The evidence review will provide some of the information we need when we look at new combinations in future. The review also looked at the cost of the drugs.

The review also looked at the cost of the drugs.

What we have decided

NHS England has carefully reviewed the evidence for TAF in E/C/F/TAF. We have concluded there is enough evidence to consider making this available as a treatment option for HIV positive patients:

- Who cannot take the usual first line HIV drug treatments
- Who already take a drug that combines elvitegravir/cobicistat/emtricitabine with TDF
- Who have defined renal or bone problems or who have medical reasons why they cannot take other HIV drugs.

Section amended from original – please see explanatory note below.

A further assessment has been undertaken in relation to two other TAF containing products - rilpivirine/emtricitabine/TAF and emtricitabine/TAF. NHS England has

concluded that the clinical evidence, commissioning criteria and impact assessment applies to these TAF containing products from November 2016.

1 Introduction

HIV treatment (antiretroviral therapy, ART) has improved greatly over the last two decades and standard of care now involves triple therapy, typically with two nucleos(t)ide reverse transcriptase inhibitors (NRTIs) plus one of the following: a ritonavir/cobicistat-boosted protease inhibitor (PI/r), a non-nucleoside reverse transcriptase inhibitor (NNRTI) or an integrase inhibitor (INI).

ART requires good adherence (perhaps >95%) to avoid drug resistance and once commenced should be continued lifelong. Development of new ARV medicines often focuses on improvements in tolerability, reductions in toxicity and drug to drug interactions.

Effectiveness of ART is measured by its ability to reduce viral load to undetectable levels on routine tests (usually to less than 50 copies/mL). In England in 2014, 95% of patients on treatment had a viral load of less than 200 copies/mL.(Skingsley et al 2015). Current standard treatment is therefore effective for very many people. New drug treatments therefore need to demonstrate clinical and cost effectiveness and improved safety profiles compared to current standard treatments.

Tenofovir alafenamide (TAF) received an EU license for treatment in HIV-1 infected adults and adolescents in November 2015 as a component of the fixed dose combination (FDC) Genvoya® (cobicistat, elvitegravir, emtricitabine and tenofovir alafenamide). This policy considers the use of tenofovir alafenamide as part of that combination antiretroviral therapy for the treatment of HIV 1 in adults and adolescents infected with HIV-1 immunodeficiency virus-1 (HIV-1). Adolescents are defined as children 12 years of age or older and with a body weight in excess of 35kg.

Currently TDF is available as a single drug product, as part of a dual formulation with emtricitabine (Truvada®), and in three FDCs: Atripla® (efavirenz, emtricitabine, TDF) Eviplera® (rilpivirine, emtricitabine, TDF) and Stribild® (cobicistat, elvitegravir, emtricitabine, TDF).

TAF was approved in the EU based on studies showing similar efficacy but an improved safety profile compared with TDF.

The manufacturer has offered TAF at a commercially confidential price. Assuming that TAF is provided at the same price or lower than that offered to NHS England and agreed with the Commercial Medicines Unit, the availability of TAF as a treatment option would potentially benefit patients who would otherwise be treated with TDF but for whom TDF was previously contraindicated because of underlying renal or bone disease. It will also be of wider short-term benefit to the NHS in terms of commissioning for value programmes.

It is anticipated that when additional TAF containing fixed dose combination products receive regulatory approval and become available the evidence review and commissioning criteria for TAF will be updated. HIV drugs are not currently reviewed by NICE to determine their clinical and cost effectiveness.

Section amended from original – please see explanatory note below.

Two further fixed dose combinations using TAF have since received market authorisation, emtricitabine/TAF, Descovy® and emtricitabine/rilpivirine/TAF, Odefsey®. This policy additionally considers the use of tenofovir alafenamide as a bioequivalent of TDF as part of these fixed dose combinations antiretroviral therapy for the treatment of HIV 1 in adults and adolescents infected with HIV-1 immunodeficiency virus-1 (HIV-1).

2 Definitions

The key terms used in this policy and their definitions are:

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 one 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): Single tablets that combine a complete ART combination into one pill.

NRTI backbone: The two NRTIs that are the basis of a combination. Two backbones are currently recommended for first line therapy: abacavir plus lamivudine (alternative in current guidelines (Churchill et al 2016); available as separate tablets or in a combination pill and TDF plus emtricitabine (preferred in current guidelines (Churchill et al 2016); available as separate tablets or in a combination pill); Both of these backbones are available in some 'all in one' tablets combined with other drugs.

Viral load: HIV RNA levels in plasma are used to monitor response to ART. Patients on effective therapy sustain viral load <50 copies/ml (undetectable). Patients who fail to achieve an undetectable viral load or who experience a confirmed viral load rebound to above 50 copies/ml are deemed to be experiencing virological failure.

First-line therapy: The first combination that someone is prescribed. Efavirenz is a recommended first line 3rd agent, given in combination with either tenofovir and emtricitabine or lamivudine and abacavir, and for reasons of clinical effectiveness and cost is the preferred first line option. (see section 5)

Second-line therapy: The use of alternative 3rd agents where efavirenz cannot be used for reasons of potential or actual intolerance or transmitted HIV drug resistance.

Alternative 3rd agents include: the NNRTI rilpivirine, the INIs raltegravir, elvitegravir/cobicistat and dolutegravir, and the PI/rs darunavir/ritonavir or cobicistat and atazanavir/ritonavir or cobicistat. Drug selection depends on side effects profile, tolerability, resistance profile, drug-drug interactions and cost.

Intolerance: when patients either (i) experience side effects, or (ii) have been assessed to be at high risk of side effects.

Stable patients: patients who have a sustained undetectable viral load on ART and who are not experiencing side effects.

3 Aims and Objectives

This policy aims to identify the evidence and cost implications of routine commissioning of a TAF-containing product for treatment of HIV 1 in adults and adolescents.

The objectives are to enable access to TAF where its use is supported by clinical evidence and where it is demonstrated to represent good value.

This policy aims to identify those patients who would benefit from E/C/F/TAF. This includes a defined group of people in whom TDF is contraindicated or who are currently taking the regimen elvitegravir/cobicistat/emtricitabine with TDF.

Section amended from original – please see explanatory note below.

It has now been confirmed that this TAF policy applies to the use of TAF containing products (emtricitabine/TAF and emtricitabine/rilpivirine/TAF) for patients meeting the clinical criteria.

4 Epidemiology and Needs Assessment

The HIV epidemic continues to pose a public health risk in England. By the end of 2014, an estimated 103, 700 (CI 97,500-112,700) people were living with HIV in the

UK; of whom 17% (18,100) were undiagnosed and unaware of their infection (Skingsley et al 2015). Whilst HIV-1 remains a life-threatening disease, effective antiretroviral therapy (ART) means it can be managed as a chronic long term condition and treatment outcomes in the England are good and compare very favourably to other European countries. In 2014 there were 78,317 HIV positive patients attended HIV services in England (85,489 in the UK), of whom 70,641 (91%) were receiving ART (Skingsley et al 2015). Of those receiving ART 95% had sustained viral suppression. There continues to be just over 6000 patients newly diagnosed with HIV in the UK per year and thus the number of patients attending HIV services and requiring ART continues to rise, (approximate 5% increase from 2013 to 2014). In the UK in 2010, 57,867 patients were on ART, rising to 76,462 patients in 2014. Ensuring patients continue to receive good and effective care but at the same time ensuring best use of resources is of high importance.

British HIV Association Treatment guidelines for adults currently recommend the following first-line (Churchill et al 2016):

- **NRTI backbone:** tenofovir disoproxil fumarate and emtricitabine is the preferred option.
- **Third drug:** preferred options are atazanavir/ritonavir, or darunavir /ritonavir, or raltegravir or elvitegravir/cobicistat or rilpivirine, or dolutegravir. An alternative option is efavirenz. At the time of writing efavirenz is the least expensive 3rd agent so despite its alternative standing in the BHIVA guidelines it is a preferred option in regional prescribing pathways.

These guidelines remain under regular review for any new outcome data, the expiry of patents for standard of care drugs and the availability of new drugs. Where new drugs become available they need to have similar or better efficacy and safety profiles than current ARVs and should either be cost comparative or contribute significantly to commissioning for value programmes.

Tenofovir is a safe and widely used ARV. Evidence shows the new compound offers some additional benefits in the short term in terms of reduced toxicity for particularly **ly** patient groups; in addition the proposed pricing structure may contribute substantially

to commissioning for value programmes in the short-term. The likely significant price reductions as generic versions of TDF come to market must also be considered.

5 Evidence base

Tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF) are both pro-drugs of tenofovir. TDF is already one of the most widely used HIV drugs, especially in combination with emtricitabine. Both TAF and TDF need to be converted inside cells to the active version of tenofovir (tenofovir diphosphate). The difference between the two pro-drugs is that TDF is converted to tenofovir in the plasma which then enters cells to undergo the activation step; TAF, however, mainly enters cells in the TAF form and is then broken down to tenofovir followed by conversion to the active form. TAF results in similar active levels in cells but with much lower plasma concentrations of tenofovir, thought to be the main predictor of tenofovir-associated toxicity. Renal impairment and reduced bone mineral density are the most important reported tenofovir toxicities and TAF, by virtue of the lower plasma tenofovir levels, is associated with lower rates of abnormal markers (serum creatinine, estimated GFR, markers of proteinuria) for both side effects compared with TDF. TAF-based regimens are at least as effective as TDF-based treatments for first-line treatment and for treatment switch. TAF is associated with a less favourable lipids profile than TDF with greater rises in total-, LDL- and HDL-cholesterol; numerical differences are, however, small and when compared as cobicistat, elvitegravir, emtricitabine, TDF vs elvitegravir/cobicistat/emtricitabine/TAF the average total: HDL-cholesterol ratio is the same for both. A summary of the trials investigating TAF-based HIV treatment follows:

Studies of TAF vs TDF in FDCs with elvitegravir/cobicistat/emtricitabine

- The safety and efficacy of TAF compared to TDF has been assessed in one phase 2 RCT (Sax et al 2014), in two phase 3 RCTs in ART naïve patients and in one phase 3 RCT in stable patients switching to TAF.
- GS-104 and GS-111 compared elvitegravir/cobicistat/emtricitabine/TDF FDC with elvitegravir/cobicistat/emtricitabine/TAF [E/C/F/TAF] FDC for first-line HIV treatment. In terms of efficacy, the TAF-based regimen was

non-inferior to TDF-based treatment at 48 weeks (Sax et al 2015). There were low rates of resistance in both arms. The TAF-based group had significantly reduced impact on a range of biomarkers for renal and bone toxicity. Both FDCs are effective across a range of baseline viral loads.

- In GS-109 patients who were suppressed on TDF-based combinations either continued treatment or switched to E/C/F/TAF FDC. Individuals switching treatment were as likely to maintain viral suppression (97% vs 93%) and experienced significant improvements in biomarkers for renal health. Bone mineral density at the spine and hip increased in the TAF group (Mills et al 2015).

In summary TAF is tolerated well and is an effective nucleoside reverse transcriptase inhibitor for the treatment of HIV-1 infection when used in combination antiretroviral therapy. TAF is associated with improved renal and bone markers compared to TDF.

6 Criteria for Commissioning

The criteria below sets out when TAF, as part of the TAF-containing combination product, will be routinely commissioned.

As TAF (compared to TDF) offers clinical benefit for specific patients groups with defined renal, bone or drug contra-indications, these criteria will be relevant to future consideration of use of TAF (compared to TDF) when it is included in combinations with other widely used drugs:

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;
- All patients with relative contra-indications to TDF must be discussed at MDT.

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).

Section amended from original – please see explanatory note below.

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 provide 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.

7 Patient Pathway

Commissioned HIV care and treatment providers who meet the service specification initiate and monitor HIV drug treatment. Prescription and monitoring of TAF containing fixed dose combination products is in line with the existing patient pathway.

8 Governance Arrangements

All patients identified who might benefit from starting TAF as a part of the fixed dose combination products cobicistat/elvitegravir/emtricitabine/TAF, will in most cases be referred to and discussed at specialist HIV MDTs and the recommendation recorded in accordance with regional/locally agreed ART prescribing guidance.

All patients identified who are currently on cobicistat/elvitegravir/emtricitabine/TDF, and who might benefit from switching to cobicistat/elvitegravir/emtricitabine/TAF, should be managed by regional/locally agreed best practice guidance for switching ARVs. Those switching from other products should be discussed at MDT (see section 6).

For patients deemed suitable for switch (see section 6) 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 HIV CRG guidance February 2016).

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

Section amended from original – please see explanatory note below.

The governance arrangements outlined above as applicable to all routinely commissioned fixed dose combination products containing TAF (namely cobicistat/elvitegravir/emtricitabine/TAF, emtricitabine/TAF and emtricitabine/rilpivirine/TAF).

9 Mechanism for Funding

Reimbursement for use of ART for individuals meeting the criteria in this policy is provided via specialised commissioning teams.

10 Audit Requirements

1. Patients on cobicistat/elvitegravir/emtricitabine/TAF referred to MDT
2. Estimated GFR changes in patients commencing TAF-based ART
3. Patients with contraindications to other NRTI backbones switched to F/TAF

11 Documents which have informed this Policy

B06/S/a Specialised Human Immunodeficiency Virus (HIV) Services (Adult) – service specification

B06/S/b Specialised Human Immunodeficiency Virus (HIV) Services (Children) – service specification

12 Date of Review

Section amended from original – please see explanatory note below.

This document was reviewed in November 2016 following the routine commissioning decision around the fixed dose combination products containing emtricitabine/TAF and emtricitabine/rilpivirine/TAF, and the addition of a tool to support identification of appropriate patients under the clinical criteria outlined in this policy.

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

References

Churchill D, Waters L, Ahmed N *et al.* BHIVA guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy 2015. Accessed 5th February 2016 at <http://www.bhiva.org/documents/Guidelines/Treatment/2015/2015-treatment-guidelines.pdf>

Mills A, Arribas JR, Andrade-Villaenueva J *et al.* Switching from tenofovir disoproxil fumarate to tenofovir alafenamide in antiretroviral regimens for virologically suppressed adults with HIV-1 infection: a randomised, active-controlled, multicentre, open-label, phase 3, non-inferiority study. *Lancet ID* 2015; 16: 43-52.

Sax P, Zolopa A, Brar I *et al.* 2014. Tenofovir alafenamide vs tenofovir disoproxil fumarate in single tablet regimens for initial HIV-1 therapy: a randomised phase 2 study. *J Acquire Immune Defic Syndr*, 67(1), pp. 52-58

Sax PE, Wohl D, Yin MT *et al.* Tenofovir alafenamide versus tenofovir disoproxil fumarate, coformulated with elvitegravir, cobicistat, and emtricitabine, for initial treatment of HIV-1 infection: two randomised, double-blind, phase 3, non-inferiority trials. *Lancet* 2015; 385: 2606-15.

Skingsley A, Kirwan P, Yin Z *et al.* HIV new diagnoses, treatment and care in the UK 2015 report: data to end 2014. October 2015. Public Health England, London.

APPENDIX

Section amended from original – please see explanatory note below.

Tool to support identification of patients who meet the clinical criteria outlined in this policy (16043/P Tenofovir Alafenamide for treatment of HIV-1 in adults and adolescents)

Clinical criteria for commissioning

Section 6 of the commissioning policy for tenofovir alafenamide (published July 2016) states the following clinical criteria for use of TAF

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;

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 <30 (CKD stage G4 and G5)

ACR* and GFR [†] categories and risk of adverse outcomes			ACR categories (mg/mmol)		
			A1	A2	A3
			<3 Normal to mildly increased	3 – 30 Moderately increased	>30 Severely increased
GFR categories (ml/min/1.73m ²)	G1	≥90 Normal and high	No CKD in the absence of markers of kidney damage.		
	G2	60 – 89 Mild reduction related to normal range for a young adult			
	G3a	45 – 59 Mild/moderate reduction			
	G3b	30 – 44 Moderate/severe reduction			
	G4	15 – 29 Severe reduction			
	G5	<15 Kidney failure			
Increasing risk →					Increasing risk ↓
* ACR: albumin:creatinine ratio † GFR: glomerular filtration rate					

Fig 1: Classification and prognosis of CKD by GFR and albuminuria categories (NICE CKD guidelines 2015)(1) Green: moderate risk; amber: high risk; red: very high risk. Adapted from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group (2013) KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney International (Suppl. 3):1-150*

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.

References

1. NICE, Clinical guidance CG182. Chronic kidney disease in adults: assessment and management (last updated Jan 2015).
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2. NICE, Clinical guideline CG146. Osteoporosis: assessing the risk of fragility fracture. August 2012. <https://www.nice.org.uk/guidance/cg146/chapter/1-Guidance>
3. NOGG. National osteoporosis guideline group: Guideline for the diagnosis and management of osteoporosis in postmenopausal women and men from the age of 50 years in the UK (updated March 2014).
[https://www.shef.ac.uk/NOGG/NOGG Pocket Guide for Healthcare Professionals.pdf](https://www.shef.ac.uk/NOGG/NOGG_Pocket_Guide_for_Healthcare_Professionals.pdf)
4. NOGG: National osteoporosis guideline group: Osteoporosis – clinical guidelines for prevention and treatment. Updated Jan 2016.
<https://www.guidelines.co.uk/nogg/osteoporosis>

**Change Notice for Published Specifications and Products
developed by Clinical Reference Groups (CRG)**

Amendment to the Published Products

Product Name

Clinical Commissioning Policy: Tenofovir Alafenamide for treatment of HIV 1 in adults and adolescents

Ref No

CRG Lead

Janette Harper

Description of changes required

Describe what was stated in original document	Describe new text in the document	Section/Paragraph to which changes apply	Describe why document change required	Changes made by	Date change made
<p>What we have decided NHS England has carefully reviewed the evidence for TAF in E/C/F/TAF. We have concluded there is enough evidence to consider making this available as a treatment option for HIV positive patients:</p> <ul style="list-style-type: none"> • Who cannot take the usual first line HIV drug treatments • Who already take a drug that combines elvitegravir/cobicistat/emtricitabine with TDF • Who have defined renal or bone problems or who have medical reasons why they cannot take other HIV 	<p><i>In addition to existing text:</i> November 2016 Addendum: A further assessment has been undertaken in relation to two other TAF containing products - rilpivirine/emtricitabine/TAF and emtricitabine/TAF. NHS England has concluded that the clinical evidence, commissioning criteria and impact assessment applies to these TAF containing products from November 2016.</p>	<p>Executive Summary – What we have decided</p>	<p>Additional products commissioned under the existing policy</p>	<p>Janette Harper</p>	<p>January 2017</p>

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drugs.					
Introduction to the condition and references licencing of TAF containing products, specifically Genvoya.	<i>In addition to existing text:</i> November 2016 Addendum: Two further fixed dose combinations using TAF have since received market authorisation, emtricitabine/TAF, Descovy® and emtricitabine/rilpivirine/TAF, Odefsey®. This policy additionally considers the use of tenofovir alafenamide as a bioequivalent of TDF as part of these fixed dose combinations antiretroviral therapy for the treatment of HIV 1 in adults and adolescents infected with HIV-1 immunodeficiency virus-1 (HIV-1).	Introduction	Additional products commissioned under the existing policy	Janette Harper	January 2017
Policy aims and objectives, to identify evidence and cost implications of routine commissioning of a TAF-containing product for treatment of HIV 1 in adults and adolescents. Access to TAF (specifically E/C/F/TAF combination) restricted to where its use is supported by clinical evidence and where it is demonstrated to represent good value.	<i>In addition to existing text:</i> November 2016 Addendum: It has now been confirmed that this TAF policy applies to the use of TAF containing products (emtricitabine/TAF and emtricitabine/rilpivirine/TAF) for patients meeting the clinical criteria.	Aims and Objectives	Additional products commissioned under the existing policy	Janette Harper	January 2017
The criteria when TAF, as part of the TAF-containing combination product, will be routinely commissioned. 1) Patients with definite contraindications to TDF Summary of contraindications – Confirmed osteoporosis; high risk of major fracture determined by	<i>In addition to existing text:</i> November 2016 Addendum: 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	Criteria for Commissioning	Clarification required as to intention of the commissioning criterion around stable patients, to remove confusion where existing policy	Janette Harper	January 2017

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<p>FRAX; Renal disease based on NICE definitions; renal toxicity or other intolerance secondary to TDF; cardiovascular disease or high estimated risk of cardiovascular disease.</p> <p>2) Patients with relative contraindications 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;</p> <p>3) Stable patients switching from alternative ART regimens Stable patients providing clinical assessment has deemed this clinically appropriate, without MDT discussion if it is cost-neutral or cost-saving switch; Patients switching from alternative ARV regimens where there is a clinical indication to do so, the switch is clinically appropriate and this had been discussed in an MDT.</p>	<p>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.</p>		<p>could be interpreted that any patient that was stable could be switched to TAF containing products for cost saving purposes. The intention of the policy was that switching of patients should only be for patients where there is a clinical criteria as outlined in criteria one and two, and stable referred to the virological stability of the patient only.</p>		
<p>All patients identified who might benefit from starting TAF as a part of the fixed dose combination products cobicistat/elvitegravir/emtricitabine/TAF, will in most cases be referred</p>	<p><i>In addition to existing text:</i> November 2016 Addendum: The governance arrangements outlined above as applicable to all routinely commissioned fixed dose combination products containing TAF (namely</p>	<p>Governance Arrangements</p>	<p>Additional products commissioned under the existing policy</p>	<p>Janette Harper</p>	<p>January 2017</p>

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<p>to and discussed at specialist HIV MDTs and the recommendation recorded in accordance with regional/locally agreed ART prescribing guidance.</p> <p>All patients identified who are currently on TDF containing regimens who might benefit from switching to E/C/F/TAF combination, should be managed by regional/locally agreed best practice guidance for switching ARVs. Those switching from other products should be discussed at MDT.</p>	<p>cobicistat/elvitegravir/emtricitabine/TAF, emtricitabine/TAF and emtricitabine/rilpivirine/TAF).</p>				
<p>This document will be further reviewed when information is received which indicates that the policy requires revision.</p>	<p><i>In addition to existing text:</i> This document was reviewed in November 2016 following the routine commissioning decision around the fixed dose combination products containing emtricitabine/TAF and emtricitabine/rilpivirine/TAF, and the addition of a tool to support identification of appropriate patients under the clinical criteria outlined in this policy.</p>	<p>Date of Review</p>	<p>Additional products commissioned under the existing policy</p>	<p>Janette Harper</p>	<p>January 2017</p>
<p>No current appendix</p>	<p>Appendix added providing tools and further guidance to support the identification of patients within the cohort where TAF containing products are deemed to be of most clinical benefit – bone and renal disease, for definitive and relative contraindications and resistance.</p>	<p>Appendix</p>	<p>Inclusion of tools to help identify the relevant cohort of patients for treatment with TAF containing products.</p>	<p>Janette Harper</p>	<p>January 2017</p>