Clinical Commissioning Policy
Reimbursement for the use of generic and second line drugs for Pre Exposure Prophylaxis (PrEP) for the prevention of HIV (2112) [230402P]

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Commissioning Position

NHS England will routinely reimburse the drug costs associated with Pre Exposure Prophylaxis (PrEP) for the prevention of HIV as outlined in this document. This policy is for the use and reimbursement of bio-equivalent generic medicines licensed for PrEP. An additional licensed regimen is also included for a defined patient population as a second line option, based on the inclusion criteria defined within this policy. An exclusion to this policy is reimbursement for the use of the 'reference' antiretroviral medicine licenced for PrEP (Truvada ®).

The individuals eligible for the treatment will be those clinically assessed in local authority commissioned and approved sexual health services in line with the clinical guidance of https://www.bhiva.org/PrEP-guidelines.

Information about PrEP

PrEP is prescribed for people who do not have HIV but who are at risk of contracting the virus. The licensed PrEP regimen and standard of care is the use of antiretroviral drugs called tenofovir disoproxil[1] (TD) and emtricitabine (FTC) used in combination known as TD-FTC or TDF-FTC. A second line regimen, licensed for a limited population is tenofovir alafenamide (TAF) and emtricitabine (FTC) used in the combination known as TAF-FTC. Prescribers and service users select one of two dosing regimens for TD-FTC - daily or event based / on demand (depending on the risk factors experienced by the service user). TAF-FTC has only been evaluated as a daily dosing regimen.

PrEP is used as part of combination HIV prevention. In trials studying effectiveness of PrEP, the drug was given in addition to a comprehensive package of prevention services including HIV testing, risk-reduction counselling, condoms and sexually transmitted infection management. Of relevance in assessing the impact of PrEP are issues relating to uptake, adherence, sexual behaviour, drug resistance and cost-effectiveness.

The condition

Human Immunodeficiency Virus (HIV) is a virus that damages a type of white blood cell in the immune system called a CD4 cell. Damaged CD4 cells weakens the body's ability to fight off infection and disease, leaving people with HIV vulnerable to infection. In most cases if not treated this leads to acquired immunodeficiency syndrome (AIDS), which is the name given to several life-threatening illnesses that can develop when the immune system has become severely damaged by the HIV virus.

HIV is transmitted through the body fluids of a person with a detectable level of the virus (including semen, vaginal and anal fluids, blood and breast milk). Most people have a flu-like illness several weeks after infection. After this, HIV may not cause any symptoms for several years, but it will still weaken the immune system.

According to UK Health Security Agency (UKHSA) 'HIV testing, new HIV diagnoses, outcomes and quality of care for people accessing HIV services: 2021 report' (UKHSA.

[1] There are different tenofovir disoproxil salts in the different generics included. TD-FTC is an inclusive term. Those with fumarate are referred to as TDF-FTC and are also included in this policy

2021) in 2020 there were:

- 97, 740 people living with HIV, of whom
- 95% were diagnosed, of whom
- 99% were receiving HIV treatment, of whom
- 97% were virally supressed.
- In England, 8, 790 people were living with transmittable levels of HIV virus, which rose to 16, 040 when those not linked to care (290) and not retained in care (6,960) were included.
- 2, 630 new HIV diagnoses were made in 2020.
- From October 2017 to July 2020, over 24, 000 people had access to PrEP in England through the Impact Trial, most of whom identified as men who were gay or bisexual (96%).

The HIV Action Plan (2022-2025) for England aims to reduce HIV transmission, AIDS- and HIV-related deaths as well as reducing HIV-related stigma. To achieve these aims, a combination prevention approach will be implemented with a focus on prevent, test, treat and retain. PrEP is an important part of this strategy, focused on preventing HIV transmission in those identified as high risk.

Current treatments

Combination HIV prevention uses a mix of biomedical, behavioural and structural interventions to meet the needs of particular individuals and communities in efforts to reduce new infections. This includes sexual health and HIV screening, testing, partner notification, condoms, access to HIV and STI treatments. Use of antiretroviral drugs commonly used to treat those with diagnosed HIV play a key role in preventing HIV transmission in three ways:

- 'Treatment as prevention': This is when people with diagnosed HIV who are on effective treatment for 6 months or more and have an undetectable viral load, cannot transmit the virus. In addition, for the majority of people with HIV on effective treatment, they will experience near normal life expectancy and will not develop AIDS-related illness.
- Post exposure prophylaxis (PEP): This is when antiretroviral drugs are used for up to 1 month after possible exposure to HIV to prevent HIV infection occurring.
- Pre Exposure Prophylaxis (PrEP): This is when antiretrovirals are used before exposure to HIV as directed by qualified members of the sexual health team following a clinical assessment.

There is currently no vaccination or cure for HIV.

Marketing Authorisations

NHS England will confirm which approved products are available for use via the HIV drugs framework with emtricitabine/tenofovir disoproxil (200 mg/245 mg), having marketing authorisation for PrEP. This policy also includes a second-line licensed option of emtricitabine/tenofovir alafenamide (200mg/25mg) which has marketing authorisation for PrEP within a limited patient population of at-risk men who have sex with men, including adolescents (with body weight at least 35kg).

Evidence of Effectiveness

NHS England has previously considered the evidence base for PrEP. In 2016, NICE published an Evidence Summary [ESNM78] on the clinical effectiveness, safety, patient factors and resource implications of PrEP. This summary included a review of four randomised trials of Truvada (emtricitabine/tenofovir disoproxil 200 mg/245 mg) for pre-exposure prophylaxis (PrEP) of HIV in either HIV-negative men or transgender women who have sex with men, or HIV-negative individuals in a heterosexual partnership with a person already infected with HIV. The conclusion of the summary was that PrEP "reduced the relative risk of acquiring HIV infection by between 44% and 86% compared with placebo or no prophylaxis, which is equivalent to

approximate numbers needed to treat of between 13 and 68 per year."

NHS England also reviewed the published evidence from the DISCOVER trial which evaluated the clinical effectiveness and safety of tenofovir alafenamide and emtricitabine (25mg/200mg) in cis-gender males and transgender females in a randomised non-inferiority study compared to tenofovir disoproxil fumarate and emtricitabine. The conclusion was that "daily emtricitabine and tenofovir alafenamide shows non-inferior efficacy to daily emtricitabine and tenofovir disoproxil fumarate for HIV prevention, and the number of adverse events for both regimens was low. Emtricitabine and tenofovir alafenamide had more favourable effects on bone mineral density and biomarkers of renal safety than emtricitabine and tenofovir disoproxil fumarate."

In 2017, NHS England announced funding for the 3-year PrEP Impact implementation trial to address outstanding questions including the need for, uptake of, and duration of PrEP. By April 2020, over 21,000 individuals were enrolled on the trial with recruitment of up to 26,000 individuals by July 2020. Routine commissioning of PrEP services by local authorities commenced during 2020. NHS England has committed to reimburse agreed PrEP drug costs.

Safety

The marketing authorisations for each relevant drug product covers side effects, contra-indications and drug interactions. Prescribers should refer to the Summary of Product Characteristics (SPC) for additional information.

As of January 2022, TAF-FTC has a limited evidence base for use as PrEP therapy, evaluated in a single RCT study. The DISCOVER trial enrolled adults (≥ 18 years) cis-gender males and transgender females with an estimated glomerular filtration rate (eGFR) ≥ 60mL/min. The safety and implementation criteria for this policy therefore have been developed through the use of tenofovir alafenamide and emtricitabine as a HIV-1 treatment and the SmPC. Prescribers should engage patients in shared decision-making on the risk and benefits of second line PrEP therapy as they may fall outside the evaluated patient cohorts.

Implementation

PrEP Criteria

PrEP use will be supplied where all the following apply:

1. Local authority confirms it has commissioned a provider to offer PrEP services.
2. Decisions to offer PrEP are made by appropriately qualified members of the sexual health service following a clinical assessment where ongoing monitoring is in place. Clinical assessment and monitoring requirements should reflect national and local guidance.
3. Drug supply and data submission are required in accordance with contract terms set out by both local authorities and NHS England.
4. Generic TD-FTC is prescribed / supplied and approved in accordance with the appropriate provider arrangements for clinical governance and is the first-line therapy for PrEP.

Second line treatment:
If an individual is intolerant of, or there are contraindications to TD-FTC, then the regimen of TAF-FTC can be utilised if the individuals meet the following criteria:

1. PrEP criteria 1-3 (outlined above are met).
2. Individuals for second line treatment are confirmed eligible through a local[2] multi-disciplinary team (MDT) discussion.
3. Shared decision-making regarding the risks and benefits of second line PrEP therapy are discussed with the individual (see safety section and marketing authorisation sections).

[2] Services can determine the best approach for local MDT approval. A single lead centre with remote support to local services would be acceptable.

4. The individual cannot take the usual first-line PrEP therapy due to risk factors to TD-FTC use.

Risk factors for TD-FTC use:

- Individuals with a reduction in estimated glomerular filtration (eGFR[3] < 60 ml/min) and clinical assessment suggests that TAF-FTC would have a lower risk profile than TD-FTC **OR**
- Individuals with proven renal toxicity[4] with TD-FTC (acute or chronic) **OR**
- Individuals with osteoporosis who are at a high risk for fractures OR
- Individuals who are < 18 years[5] **OR**
- Individuals with an eGFR ≥ 60 ml/min in whom:
  - A progressive reduction in glomerular filtration rate[6] on TD-FTC is seen **AND**
  - Significant concurrent medical issues or monitoring/prescribing concerns which suggest TAF-FTC would have a lower risk profile to TD-FTC.

Exclusion criteria:

- Individuals with contraindications or the potential for significant drug interactions to TAF-FTC or TD-FTC as outlined in the Summary of Product Characteristics (SPC).

Effective from

July 2020, updated January 2023.

In April 2020, government announced funding for local authorities to support routine commissioning of PrEP services during 2020/21. NHS England had already committed to reimburse PrEP drug costs within routinely commissioned local authority PrEP services from the end of the trial.

Requirements and recommendations for data collection

Mandatory data collection will be via the existing epidemiological surveillance system operated by UKHSA to monitor population level sexually transmitted infections (STIs) and HIV: GUMCAD STI Surveillance System. Additional contractual data collection requirements to secure sufficient supply and support reimbursement will be set out in the local authority's service specification and the NHS England contract reporting requirements.

The second line treatment, TAF-FTC requires provider organisations to register all patients using prior approval software and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

Mechanism for funding

NHS England will reimburse drug costs for PrEP for eligible individuals as per the 2018 BHIVA recommendations within approved local authority commissioned PrEP services. To support data collection, Local Authority Providers are asked to complete and submit the appropriate dataset as outlined in the NHSE contract insert held within the Local Authority contracts.

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[3] This policy uses eGFR to define renal thresholds as this estimation of renal function as it is more frequently used in clinical practice. It is noted that Creatinine Clearance (CrCl) is used in the Summary of Product Characteristics (SPC). Prescribers should consider situations where eGFR is a poor approximation for renal function, such as in the extremes of body mass. Further details are available from the Medicines and Healthcare products and Regulation Agency (MHRA) 2019.

[4] Renal toxicity defined as a progressive, sustained decline in renal function or development of renal tubular acidosis, attributable to TD-FTC. Toxicity could also include development or worsening of existing proteinuria without another reversible or explained cause. It is expected that prescribers will consult renal specialists if there is diagnostic uncertainty.

[5] The efficacy and safety of TAF-FTC for PrEP in adolescents have not been evaluated in clinical studies. Based on the similarity of drug exposures, the efficacy and safety of TAF/FTCfor PrEP in adolescent men (aged 12 years and older with body weight at least 35 kg) who have sex with men and who adhere to daily dosing is expected to be similar to that in adults at the same level of adherence. The potential renal and bone effects with long-term use of TAF-FTC for PrEP in adolescents are uncertain.

[6] A reduction in eGFR of 15ml/min in the past 12 months or 25% reduction in eGFR in the past 12 months were determined to be significant threshold measures by the HIV Clinical Reference Group (CRG) working group.

Excluded from this policy is reimbursement for the use of the 'reference' antiretroviral medicine licenced for PrEP (Truvada ®) or any other drug not listed within this policy and used as PrEP. Any service costs associated with PrEP are also excluded as these are commissioned by local authorities. Reimbursement for drugs sourced outside of NHS England drug framework or issued via FP10s is also excluded from this policy.

Policy review date

This policy will be reviewed if required.

Links to other Policies

Policies relating to the treatment of HIV and 'treatment as prevention' can be found here.

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.

References

British Association for Sexual Health/ British HIV Association guidelines (BASHH/BHIVA) 2018. HIV pre-exposure prophylaxis (PrEP) [online]. Available at: https://www.bashhguidelines.org/media/1189/prep-2018.pdf. Accessed 10/10/21.

Medicines and Healthcare products and Regulation Agency (MHRA) 2019. Prescribing medicines in renal impairment: using the appropriate estimation of renal function to avoid the risk of adverse drug reactions [online]. Available at: https://www.gov.uk/drug-safety-update/prescribing-medicines-in-renal-impairment-using-the-appropriate-estimate-of-renal-function-to-avoid-the-risk-of-adverse-drug-reactions. Accessed 10/10/21.

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