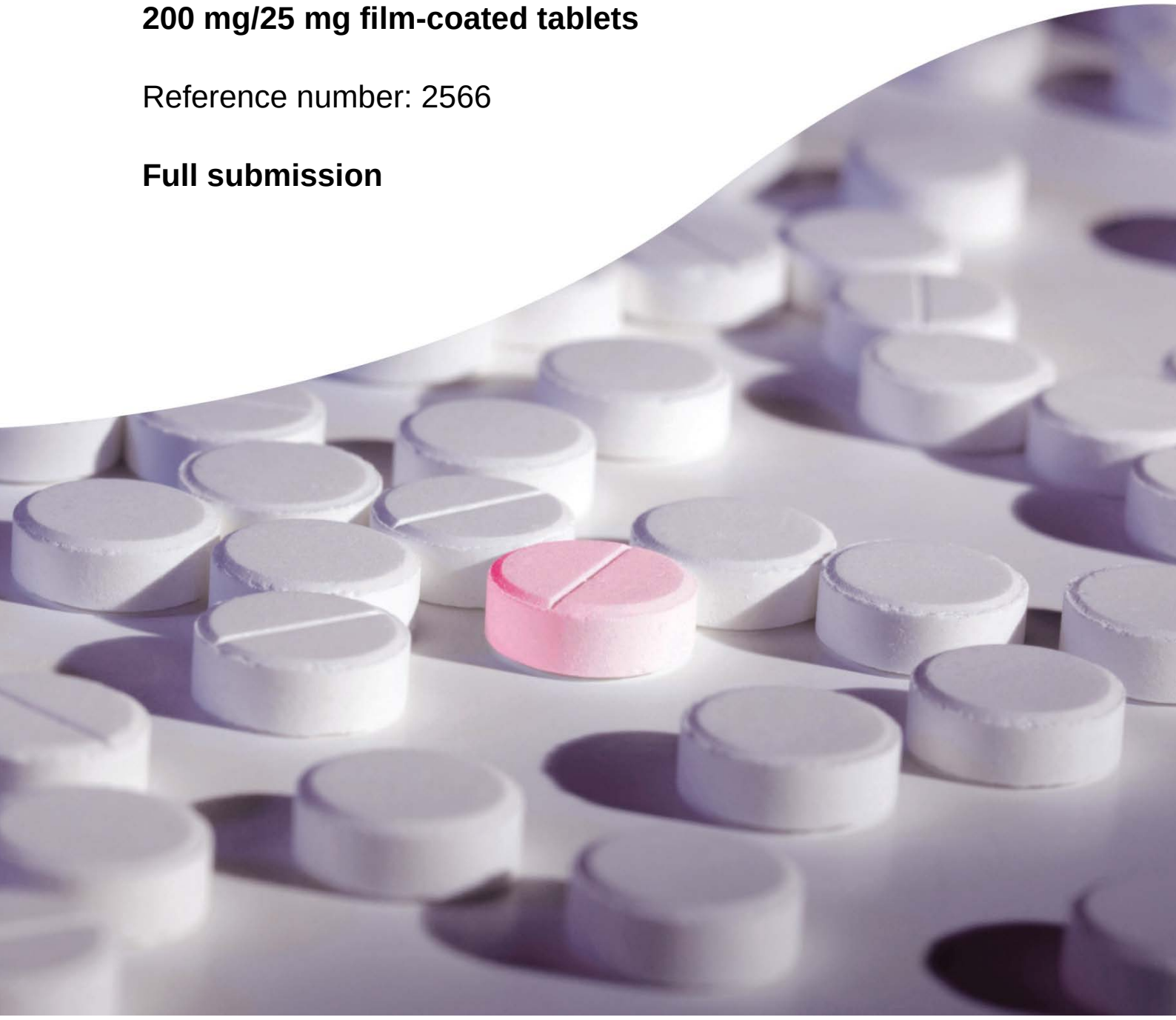
AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

AWMSG Secretariat Assessment Report

Emtricitabine/tenofovir alafenamide (as fumarate) (Descovy®) 200 mg/25 mg film-coated tablets

Reference number: 2566

Full submission



PAMS
Patient Access to Medicines Service
Mynediad Claf at Wasanaeth Meddyginiaethau

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This assessment report will be considered for review three years from the date of the Final Appraisal Recommendation.

AWMSG Secretariat Assessment Report
Emtricitabine/tenofovir alafenamide (as fumarate) (Descovy®) 200 mg/25 mg film-coated tablets

1.0 Key facts

Assessment details	Descovy® is indicated for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in at-risk men who have sex with men, including adolescents (with body weight at least 35 kg). Clinical expert opinion and the marketing authorisation holder (Gilead Sciences Ltd) suggest that Descovy® should be considered for a subpopulation of the licenced indication, where people are unable to take emtricitabine/tenofovir disoproxil (FTC/TD) due to concerns of renal or bone issues (see section 2.2).
Current clinical practice	Currently the management of PrEP to reduce the risk of sexually acquired HIV-1 infection is by as-needed FTC/TD. FTC/TD may present renal or bone adverse events in those with existing kidney or bone susceptibilities and therefore PrEP with FTC/TD may not be an option for these people. Apart from FTC/TD, Descovy® is the only other licensed option for PrEP. Clinical expert opinion suggests there is an unmet need in Wales for people with renal and bone complications who are currently unable to receive FTC/TD, and Descovy® could provide a vital option for PrEP.
Clinical effectiveness	The main evidence comes from DISCOVER, a 48-week trial of Descovy® versus Truvada® for PrEP, and a follow up study of DISCOVER participants providing 96-week comparative results. In addition, data were available from an open-label study for those who had already received 96 weeks of randomised, blinded treatment in the DISCOVER study, providing results for a total of 144 weeks of Descovy® treatment.
Cost-effectiveness	No cost-effectiveness evidence is included in this submission.
Budget impact	It is estimated that 60 people will receive treatment with Descovy® in Year 1 increasing to 64 people in Year 5. The base case suggests an additional cost of £277,469 in Year 1 increasing to £295,967 in Year 5. The base case also predicts no resource use implications. However, there is uncertainty around the projected budget impact, as the eligible people estimates are predominantly

	based on clinician expert opinion. The resource use considerations are also limited in scope.
Additional factors to consider	The need for advice for Descovy® has been identified by clinical experts in Wales. AWTTC was instructed to prepare this report by AWMSG Steering Committee in November 2022. Gilead Sciences Ltd provided some supporting information to aid this appraisal. Descovy® is included in the NHS England clinical commissioning policy for PrEP.

This assessment report is based and an evidence search conducted by AWTTC on 9 January 2023 and supporting information from Gilead Sciences Ltd.

2.0 Background

2.1 Condition and clinical practice

Human immunodeficiency virus (HIV) is a retrovirus that infects cells in the human immune system, such as $CD4^+$ lymphocytes, causing their destruction which results in the progressive suppression of the host immune system[1]. Untreated HIV is a progressive disease leading to the development of acquired immunodeficiency syndrome (AIDS)[1]. The number of people seen by NHS Wales for HIV treatment was 2,163 in 2021[2]. Over the three years of 2019–2021, the annual average number of new HIV diagnoses was in 62 men and in 25 women per year. For people where the probable exposure category was known, 60% of cases were due to sex between men and 38% due to heterosexual contact in 2021[2].

The British HIV Association/British Association for Sexual Health and HIV (BHIVA/BASHH) guidelines recommends emtricitabine/tenofovir disoproxil (FTC/TD) should be offered as pre-exposure prophylaxis (PrEP) to men who have sex with men (MSM, aged 15 years and older), transgender men and transgender women who are at elevated risk of HIV acquisition through condomless anal sex[3]. Daily FTC/TD should also be offered to heterosexual men and women who are at increased risk of HIV acquisition. Between 2015 and 2021, new diagnosis of HIV decreased by 75% in Wales. PrEP was introduced in 2017 and is considered to have been a significant factor in this reduction[4].

The BHIVA/BASHH guidelines refer to the possibility of kidney disease with FTC/TD in those with pre-existing kidney disease or risk factors and a risk of bone loss in those with pre-existing risk factors or demonstrated osteoporosis[3]. FTC/TD is recommended in combination with safer sex practices (and is established practice) for PrEP in NHS Wales for those at high risk of HIV infection[5]. In 2018 there were an estimated 19,500 people receiving PrEP in the UK. In Wales, 1,280 individuals were prescribed PrEP between July 2017 and September 2019[4]. While the significant social restrictions imposed at times during the Covid-19 pandemic did have a negative impact on use of PrEP, usage recovery has been swift and 1,302 individuals were prescribed PrEP in 2021[4].

In those unable to use PrEP (i.e. due to intolerance, renal or bone toxicity associated with FTC/TD) best standard care may include voluntary testing, risk counselling and the promotion of condoms[6]. The effectiveness of these interventions has been

variable[6]. The need for advice for Descovy® has been identified by clinical experts in Wales. AWTTC was instructed to prepare this report by the AWMSG Steering Committee in November 2022. Gilead Sciences Ltd provided some supporting information to aid this appraisal.

2.2 Medicine

Descovy® is a combination of emtricitabine and tenofovir alafenamide (TAF). Truvada® is a combination of emtricitabine and tenofovir disoproxil fumarate. Generic versions of Truvada®, also licensed for PrEP, exist in which tenofovir disoproxil (TD) is present as an alternative salt e.g. maleate, succinate and phosphate in addition to generic versions with the fumarate salt[3]. For the purpose of this report generic Truvada® is referred to as emtricitabine/tenofovir disoproxil (FTC/TD). The branded medicine, Truvada® has been used in the trials described in this report. FTC/TAF is referred to as Descovy® .Emtricitabine and tenofovir are nucleotide reverse transcriptase inhibitors of HIV which inhibit viral replication in cells[7]. TAF and TD salts are prodrugs of tenofovir[8]. TAF provides higher intracellular levels of the active metabolite tenofovir diphosphate and lower circulating levels of tenofovir relative to TD. TAF offers the potential for an improved safety profile compared with TD[8].

NHS England is responsible for the commissioning of PrEP in England[9] and their updated clinical commissioning policy states Descovy® can be used as a second line option for a subpopulation of people who are eligible for PrEP but are intolerant of, or have contraindications to, FTC/TD. This should be when an individual cannot take the usual first-line PrEP therapy due to risk factors to FTC/TD use. Risk factors for the use of FTC/TD are:

- a reduction in estimated glomerular filtration rate (eGFR < 60 ml/min) and clinical assessment suggests that Descovy® would have a lower risk profile than FTC/TD, or;
- proven renal toxicity with FTC/TD (acute or chronic), or;
- osteoporosis and high risk for fractures, or;
- an eGFR ≥ 60 ml/min where: a progressive reduction in glomerular filtration rate on FTC/TD is seen (reduction in eGFR of 15 ml/min in the past 12 months or 25% reduction in eGFR in the past 12 months) and there are significant concurrent medical issues or monitoring/prescribing concerns which suggest Descovy® would have a lower risk profile compared to FTC/TD, or;
- adolescents who are < 18 years[9].

2.3 Comparators

In the identified subpopulation of people who are eligible for PrEP but have renal or bone susceptibilities (preventing use of FTC/TD) best standard care would include voluntary testing, risk counselling, the promotion of condoms and clinically appropriate monitoring as required.

2.4 Guidance and related advice

- Welsh Government. HIV action plan for Wales 2023-2026. 2023[4].
- NHS Clinical Commissioning Policy: Reimbursement for the use of generic drugs for pre-exposure prophylaxis (PrEP) for the prevention of HIV. April 2023[9].
- National Institute for Health and Care Excellence (NICE). NG221: Reducing sexually transmitted infections. 2022[10].
- Provision of pre-exposure prophylaxis (PrEP) for HIV prevention in Wales. April 2020[5].

- BHIVA/BASHH guidelines on the use of HIV pre-exposure prophylaxis (PrEP). 2018[3]. (These guidelines are under review, publication date to be confirmed).

The All Wales Medicines Strategy Group (AWMSG) has previously recommended the use of emtricitabine/tenofovir alafenamide (Descovy®) in combination with other antiretroviral agents for the treatment of adults and adolescents (aged 12 years and older with body weight at least 35 kg) infected with HIV-1[11].

AWMSG previously recommended the use of FTC/TD in combination with safer sex practices for PrEP to reduce the risk of sexually acquired HIV-1 infection in adults at high risk. Adults at high risk include the following populations:

- men who have sex with other men (MSM) and transgender people having sex with men who are engaging in condomless anal sex.
- heterosexual and same-sex, HIV-1 negative partners who are in relationships with HIV-1 positive partners whose viral replication is not suppressed.
- other heterosexuals considered to be at high risk[5].

2.5 Prescribing and supply

AWTTC is of the opinion that, if recommended, Descovy® is appropriate for specialist only prescribing within NHS Wales for the indication under consideration (PrEP is currently only available through sexual health clinics). However, as part of the HIV Action Plan for Wales 2023–2026 it is outlined that primary care and specialist sexual health services should develop and implement a shared care model to improve access and delivery of PrEP[4].

3.0 Clinical effectiveness

The evidence considered in this appraisal is from a phase III study (DISCOVER) evaluating the efficacy and safety of Descovy® versus Truvada® for HIV prevention[7]. In DISCOVER, all participants received at least 48 weeks of randomised, blinded treatment. Further evidence was available after DISCOVER participants had all completed 96 weeks of blinded treatment[12]. At the end of 96 weeks participants who had initiated treatment in the DISCOVER study were able to continue Descovy® treatment in an open-label study, providing evidence after 144 weeks of treatment[13].

3.1 DISCOVER study

DISCOVER was a randomised, double-blind, multi-centred, non-inferiority study of Descovy® versus Truvada® in cisgender men who have sex with men (MSM) and transgender women who have sex with men[7]. Participants (N = 5,399) with a median age of 34 years, had a high risk of acquiring HIV based on their self-reported sexual behaviour or recent history of sexually transmitted infections. The primary endpoint was incident HIV infection, analysed when all participants had been followed for at least 48 weeks and when at least 50% had been followed up for 96 weeks. Six secondary bone density and renal safety endpoints were evaluated at 48 weeks[7]. Descovy® was non-inferior to Truvada® for the primary endpoint: the upper limit of the 95% confidence interval (CI) of the HIV incidence rate ratio (the rate for Descovy® divided by the rate for Truvada®) was 1.15 which was less than the prespecified non-inferiority margin of 1.62[7]. At the endpoint 22 participants were diagnosed with HIV, 7 of whom were in the Descovy® group and 15 of whom were in the Truvada® group (see Table 1)[7].

3.2 Follow up study at 96 weeks

Clinical outcomes for participants from the DISCOVER study were further analysed when all had completed 96 weeks of follow up[12]. Results showed little change compared to the DISCOVER result in the number of participants infected and the incident HIV infection rate for Descovy® remained non-inferior to that for Truvada® (see Table 1). The same safety endpoints measured in DISCOVER were also measured at 96 weeks and are discussed in the safety section, 3.2. The number of participants discontinuing at 96 weeks was 587 out of 2,694 (22%) for those receiving Descovy® and 543 of 2,693 (20%) for people who received Truvada®[12].

3.3 Open-label study

All participants who had commenced the DISCOVER study and had completed the 96 weeks of randomised, blinded treatment could opt to receive Descovy® for a further 48 weeks in the open label phase[13]. The number of participants who continued on Descovy® after 96 weeks was 2,080 of the 2,694 initially randomised to Descovy® and 1,933 of these were still on the treatment at Week 144. Eight people had acquired HIV in the blinded phase by 96 weeks and a further three acquired HIV in the open label phase in the following 48 weeks[13].

Table 1. Incident HIV infection rate in DISCOVER study and the 96-week follow up[7,12]

Endpoint	Time since baseline	Descovy®	Truvada®	Statistical significance (95% CI)
Incident HIV infection (Primary endpoint)	≥ 48 weeks*	7 infections per 4,370 PY	15 infections per 4,386 PY	Ratio of 0.47 (0.19 to 1.15)
Incident HIV infection	96 weeks	8 infections per 5,029 PY	15 infections per 5,052 PY	Ratio of 0.54 (0.23 to 1.26)
PY: person-year; CI: confidence interval. *Primary endpoint was determined when all participants had completed at least 48 weeks of treatment.				

3.4 Safety information

Emtricitabine and tenofovir are primarily excreted by the kidneys, and renal failure, renal impairment, elevated creatinine, hypophosphataemia and proximal tubulopathy have been reported with the use of tenofovir disoproxil for treating HIV infection[14].

In the 96-week follow up of the DISCOVER study, Descovy® was superior to Truvada® for a group of secondary safety endpoints assessing bone density and renal parameters (with the exception of the urine protein to creatinine ratio) (see Table 2)[12]. At the end of the open label phase mean increases in hip and spine bone mineral density from baseline to 144 weeks in the Descovy® arm (in N = 2,080 of 2,694 participants) were 0.54% and 1.02%. Median eGFR increased by 2.6 l/min from baseline to 144 weeks[13].

Table 2. Secondary safety endpoints in 96-week follow up of DISCOVER study[12]

Endpoint	Descovy®	Truvada®	Statistical significance
Mean change in hip bone mineral density from baseline (measured in 383 participants)	0.6%	−1.0%	P < 0.0001
Mean change in spine bone mineral density from baseline (measured in 383 participants)	1.0%	−1.4%	P < 0.0001
Change in beta microglobulin to creatinine ratio measured in N = 5,353 participants	−14.6%	14.2%	P < 0.0001
Retinol binding protein to creatinine ratio measured in N = 5,372 participants	0.2%	21.4%	P < 0.0001
Participants with medicine emergent urine protein to creatinine ratio > 22.6 mg/mmol	1%	1.3%	P = 0.22
Total participants with urine protein to creatinine ratio > 22.6 mg/mmol	27/2,694 (1.0%)	36/2,693 (1.3%)	N/A
Change in creatinine clearance (eGFR) in N = 5,387 participants	3.7 ml/min	−0.4 ml/min	P < 0.0001
eGFR: estimated glomerular flow rate.			

Subgroup analysis showed that after 96 weeks of treatment for participants aged 50 years and older the increase in eGFR for those on Descovy® was lower (1.2 ml/min) than in the total Descovy® study population (3.7 ml/min). The corresponding change in this older group with Truvada® was −3.2 ml/min versus −0.4 ml/min in the total Truvada® study population. People with moderate renal impairment (eGFR 60 to < 90 ml/min) in the Descovy® arm had a larger increase in eGFR of 4.7 ml/min versus 3.7 ml/min in the total Descovy® study population. Those with moderate renal impairment in the Truvada® arm had an increase of 1.0 ml/min compared to a decrease of 0.4 ml/min in the total Truvada® study population[12].

After 96 weeks of treatment both Descovy® and Truvada® arms had few serious adverse events, occurring in less than 1% of participants. Renal events leading to discontinuation of treatment occurred for two Descovy® participants and six Truvada® participants. Both treatments showed decreases in median lipid changes from baseline (fasting total cholesterol, LDL cholesterol, HDL cholesterol) and the decreases were statistically significantly larger for Truvada® than for Descovy®[12]. Approximately 50% of participants were overweight or obese (body mass index > 25 kg/m^2). After 96 weeks of treatment the median weight gain was 1.7 kg for Descovy® participants versus 0.5 kg for Truvada® participants (p < 0.0001)[12]. Results from the open label phase showed that Descovy® participants gained a median 2.3 kg over 144 weeks (nearly three years of treatment)[13].

3.5 Ongoing studies

The company has identified a study, PURPOSE 1[15] which will include Descovy® as a treatment for PrEP. PURPOSE 1 will involve a phase 3 blinded controlled study (lasting at least 52 weeks) in which adolescent girls and young women at risk of HIV infection will receive one of three active treatments: lenacapavir or Descovy® or

Truvada® as PrEP. This study will not involve participants from the UK due to low levels of HIV-1 infection. The study is estimated to complete in July 2027[15].

3.6 AWTTC critique

- Clinical experts in Wales contacted AWTTC to highlight the unmet need for people currently eligible for FTC/TD for PrEP but where contraindications such as renal and bone susceptibilities prevent its use. FTC/TD (as Truvada®) was the first licensed option for PrEP to reduce the risk of sexually acquired HIV-1 infection and has been available to eligible people in Wales since 2017. Descovy® was licensed for PrEP in 2022 and offers an alternative option to FTC/TD.
- AWTTC contacted the marketing authorisation holder for Descovy® to request a full submission for the appraisal of PrEP by AWMSG. Gilead Sciences Ltd confirmed they were not in a position to provide a submission due to a lack of resources. Due to the unmet need in Wales AWMSG Steering Committee instructed an appraisal using information in the public domain; Gilead Sciences Ltd agreed to work with AWTTC where possible.
- The DISCOVER and 96-week follow up study showed Descovy® met its primary endpoint and was non-inferior to Truvada® as PrEP for HIV prevention. Renal and bone endpoints were statistically superior for Descovy® versus Truvada® but differences were small. There were also differences in median lipid changes from baseline; both treatments showed decreases although Descovy® use was associated with smaller cholesterol decreases than found with Truvada®, and with larger weight gain. In addition, comparative data were only available for a 96-week comparison; further long-term data would help confirm these findings.
- The results of the DISCOVER study appear to be in line with other studies. A pooled analysis of 26 clinical trials of HIV treatment showed improvement in biomarkers for renal dysfunction for TAF versus TDF but the comparative incidence of clinically significant renal events was not clear. There were no cases of renal tubulopathy in participants receiving TAF versus 10 cases in those receiving TDF and fewer people on TAF (0.05%) versus TDF (0.5%) discontinued due to renal adverse events[16].
- Clinical experts in Wales confirm the findings of the pivotal study are in line with their experience i.e. both FTC/TD and Descovy® are used in the treatment of HIV and therefore there is significant clinical experience of both treatments (although noting the differences in the two populations and the risk/benefits). Renal, bone, weight and lipid effects are included in the Summary of Product Characteristics (SPCs) for both treatments. Experts highlighted to AWTTC that despite small differences in the renal endpoints in the study these are clinically significant. This is also reflected in the respective SPCs where FTC/TD is not recommended for PrEP for individuals with creatinine clearance < 60 ml/min but this contraindication is not present for Descovy® (no dose adjustment of Descovy® is required in adults or adolescents with creatinine clearance > 30 ml/min). Furthermore, they consider the differences in cardiovascular results is typical of that seen in practice where FTC/TD may have a more desirable effect on weight and cholesterol but experts did not consider that use of Descovy® would typically be associated with cardiovascular risk.
- Current management of people with renal and bone susceptibilities can result in increased monitoring and/or switching to off-label event-based dosing of FTC/TD or moving to best supportive care. There is wide diversity in the duration of PrEP use: some people use daily prophylaxis for short periods of

risk and some use daily prophylaxis continuously for several years. People also use PrEP as event-based dosing (off-label). Long term follow-up of people taking PrEP is needed to understand the long-term effects in this population, including for bone health, particularly in those who started PrEP before reaching peak bone mass. It is unknown whether the increase in bone mineral density in those taking Descovy® versus those receiving FTC/TD will lead to reduced fracture risk later in life[7].

- It is agreed that Descovy® should be considered within a subpopulation of its licensed indication, i.e. people who are at risk of HIV infection but cannot take FTC/TD as PrEP due to renal or bone susceptibilities. The criteria considered by NHS England is referred to in section 2.2 and clinical experts in Wales agree these criteria are also applicable to NHS Wales.
- Transgender men and cisgender women were not included in the DISCOVER study, however the mechanism of protection and pharmacokinetics of Descovy® are not expected to differ. Additional studies are planned to assess efficacy in cisgender women who are at risk of HIV through vaginal intercourse[15].
- People less than 18 years old, those with a history of osteoporosis or fragility fractures; and those with impaired renal function, (eGFR <60 mL/min) were excluded from the DISCOVER study. The efficacy and safety of Descovy® for PrEP in adolescents have not been evaluated in clinical studies. Based on the similarity of drug exposures, the efficacy and safety of Descovy® for 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 Descovy® for PrEP in adolescents are uncertain[9,17].
- The HIV Action Plan for Wales 2023-2026 should be noted. Wales has an ambition to end new cases of HIV by 2030. The plan sets out five priority areas for action with prevention being one of them. Increasing the awareness of and access to PrEP is included as part of the prevention strategy. In addition, funding from Public Health Wales has meant that an app designed to help PrEP users take their medication more effectively, is now more widely available and in multiple languages, including Welsh[4].

4.0 Cost-effectiveness

4.1 Context

A cost-effectiveness analysis has not been submitted.

4.2 Review of published evidence on cost-effectiveness

A literature review conducted by AWTTC identified one cost-utility analysis (CUA) and threshold analysis, focused on Descovy®[18]. The aim of these analyses, conducted using data from the United States, was to compare the costs and effects of Descovy® with FTC/TD, and to identify how much more payers should be willing to pay for the improved safety profile associated with Descovy®. The analysis, reported in US dollars, used the 2018 Federal Supply Schedule Price for Descovy®, $16,600 per annum. For FTC/TD it was assumed that the price competition arising from the imminent introduction of generics would result in a cost equivalent to 50% of that of Descovy® (i.e. $8,300 per annum). Safety data were collected from an age-stratified population of 123,610 MSM without HIV and from studies of people with HIV. These

data were used to forecast end-stage renal disease (ESRD) cases, fractures, costs, quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios (ICERs) over a 5-year time horizon. The adverse events profiles related to fractures and ESRD in these analyses were intentionally biased in favour of Descovy®, and they excluded atherosclerotic cardiovascular disease effects, which reportedly further biased the analyses in favour of Descovy®.

The CUA resulted in an ICER exceeding $7 million/QALY gained. The threshold analysis suggested that, when applying a willingness to pay (WTP) of $100,000/QALY, the maximum justifiable price for Descovy® was $8,670/annum. This represented a maximum justifiable mark-up over FTC/TD of $370 per annum, and a required price reduction of $7,930 per year for Descovy® to be considered a cost-effective treatment option. Sub-analysis focused on patients considered to be at higher risk of ESRD and fracture (i.e. patients aged > 55 years) produced an ICER which exceeded $3 million/QALY and a maximum justifiable price of $8,970/annum. This represented a maximum justifiable mark-up over FTC/TD of $670/annum, and a required price reduction of $7,630 per year for Descovy® to be considered a cost-effective treatment option.

The CUA was characterised by a number of limitations, including a short time horizon, which has implications in terms of capturing longer-term health effects and costs, and lack of discounting. Additionally, the costs used in these analyses are US based and the WTP threshold applied is higher than that applied in UK HTA. Consequently, the results of these analyses cannot be considered directly transferable to this current assessment. Moreover, the comparator used in these analyses (FTC/TD) would not be applicable in the analysis of Descovy® as a second line option for patients who are eligible for PrEP but are intolerant of or have contraindications to FTC/TD. The comparator for second line use would be best supportive care (BSC). The literature review did not identify any studies relevant to the cost-effectiveness of Descovy® versus BSC.

5.0 Budget impact

5.1 Context and methods

An AWTTC generated budget impact analysis estimates 60 people will receive Descovy® in Wales in Year 1, increasing to 64 people in Year 5. Year 1 estimates are based on Welsh clinical expert opinion. Welsh prescribing data, intelligence from Public Health Wales, and Welsh PrEP prescribing targets have informed estimates of how the number of people likely to receive Descovy® will increase on a yearly basis[4,19]. The comparator used in the analysis is BSC, which has no associated medicine acquisition cost. Based on the SPC, people are modelled to receive one Descovy® 200 mg/25mg film-coated tablet, once daily[17]. The list price for Descovy® is taken from the Monthly Index of Medical Specialities[20]. Sensitivity analyses explore the impact of alternative assumptions for the proportion of people eligible for PrEP who are not suitable for FTC/TD.

5.2 Results

The budget impact is presented in Table 3. It is estimated that introducing Descovy® would lead to an overall cost of £277,469 in Year 1, increasing to £295,967 in Year 5. Sensitivity analyses exploring the impact of varying the proportion of people not suitable for FTC/TD by applying the lower and upper estimates provided by Welsh

clinical experts results in a budget impact between £194,229 and £360,710 in Year 1 increasing to between £212,727 and £379,208 in Year 5.

Table 3: Budget impact for Descovy® for pre-exposure prophylaxis of HIV

Net costs	Year 1	Year 2	Year 3	Year 4	Year 5
Subpopulation of eligible people (people unable to receive FTC/TD due to renal or bone issues)	64	64	64	64	64
Uptake of new medicine (approx.)	94%	95%	97%	98%	100%
Number of patients receiving Descovy®	60	61	62	63	64
Medicine acquisition costs in a market without new medicine	£0	£0	£0	£0	£0
Medicines acquisition costs in a market with new medicine (based on list price*)	£277,469	£282,094	£286,718	£291,343	£295,967
Net medicine acquisition costs	£277,469	£282,094	£286,718	£291,343	£295,967
Numbers may not compute due to rounding					

It is estimated that the introduction of Descovy® will have no net resource implications, as monitoring requirements are assumed to be equivalent for those receiving Descovy® and best supportive care.

5.3 AWTTC critique

- There is uncertainty around the projected budget impact, as the eligible people numbers are based on mid-point estimates provided by Welsh clinician experts. However, sensitivity analyses explore the impact of varying the number of people who would be eligible for Descovy® to reflect the lower and upper estimates provided by clinical experts. The company alternatively suggest that approximately 1% of those eligible for PrEP are likely to be unable to receive FTC/TD. This alternative assumption produces a lower budget impact of £101,739 in Year 1, increasing to £110,988 in Year 5. AWTTC does not consider this estimate to be more plausible than the base case.
- The base case assumes that all patients who receive Descovy® in each year receive two six-month prescriptions. There is uncertainty around this assumption. An alternative scenario, where approximately half of the patients receive two six-month prescriptions and the other half receive just one six-month prescription results in a lower projected budget impact of £213,438 in Year 1, increasing to £227,667 in Year 5.

- The comparator used in the base case is BSC. However, clinical experts in Wales suggest that some people with renal susceptibilities may be prescribed FTC/TD PrEP on an as-required basis following a benefit-risk assessment. If it is assumed that approximately 50% of people receive BSC and the remaining receive FTC/TD PrEP for six months (each year), the introduction of Descovy® results in a budget impact of £263,177 in Year 1, increasing to £280,772 in Year 5, when the list price for FTC/TD PrEP is applied. The net resource implications arising from the introduction of Descovy® in this scenario lead to a saving of £3,349 in Year 1, increasing to £3,573 in Year 5. This is a consequence of reduced monitoring[21]. People receiving FTC/TD PrEP are assumed to require one additional ultrasound scan per annum, and four additional urinalyses and renal function tests than those people receiving BSC or Descovy®.
- The budget impact considerations are limited in scope. Monitoring costs are simplified in the analysis and resources use relating to adverse events are not included. People receiving Descovy® require renal and bone status monitoring, body weight assessments, and blood lipids and glucose levels are tested for, as appropriate. However, these assessments are generally undertaken during routine clinic visits, and the additional costs associated with blood tests would not substantially increase the budget impact. According to Welsh clinical experts those receiving BSC attend the same number of clinic visits as those on preventative treatment. Given the low cost associated with these blood tests, the simplification of the resource use analysis is not likely to influence budget impact-based decision-making.
- Patients receiving BSC are at an increased risk of HIV infection. The cost associated with treating HIV is not accounted for in the analysis. The analysis is therefore potentially limited in scope.

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