Clinical Commissioning Policy Proposition: Doravirine for the treatment of HIV-1 in adults

Reference: NHS England 1822

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Contents

1 Executive Summary

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 HIV-1

Human immunodeficiency virus (HIV) is a virus that damages a type of white blood cell in the immune system called a CD4 cell. Damaging CD4 cells weakens the body's ability to fight off infection and disease, leaving people with HIV vulnerable to opportunistic infection. In some cases this can lead to acquired immunodeficiency syndrome (AIDS), which is the collective name given to several life-threatening illnesses that can develop when the immune system has become severely damaged by HIV.

HIV is transmitted through the body fluids of a person with a detectable level of the virus. Most people have flu-like illness several weeks after infection. After this, HIV may not cause any symptoms for a number of years, but it will still damage the immune system.

There is currently no cure for HIV, but, with treatment, most people with HIV will have near normal life expectancy and will not develop AIDS-related illness.

There are two main types of HIV – HIV-1 (the most common type in the UK) and HIV-2 (relatively uncommon in the UK). This policy proposition covers HIV-1 only as doravirine is not licensed for the treatment of HIV-2.

About current treatments

It is recommended that treatment with antiretroviral therapy is usually started immediately after a diagnosis of HIV to stop the virus replicating in the body. The standard of care is treatment with three drugs (known as triple therapy), typically involving two nucleoside reverse transcriptase inhibitors (NRTIs), plus one of the following: a non-nucleoside reverse transcriptase inhibitor (NNRTI), a protease inhibitor (PI), or an integrase inhibitor (INI). All drugs have the aim of stopping the virus replicating in the body, but have different processes for doing this.

About the new treatment

Typically, HIV treatment includes 3 different drugs, as described above. Doravirine is an NNRTI. It sticks to HIV reverse transcriptase (an HIV enzyme used to change HIV genetic code into DNA so that it can be injected into the CD4 cell) to prevent HIV DNA replicating. In the studies examined, doravirine has demonstrated that it is at least as clinically effective as the alternative treatments studied in the trials. It is available as a tablet containing doravirine only and as a tablet that contains doravirine and 2 nucleos(t)ide reverse transcriptase inhibitors (lamivudine and tenofovir disoproxil).

What we have decided

NHS England has carefully reviewed the evidence prepared by NICE on treating HIV-1 with doravirine. We have concluded that there is enough evidence to consider making the treatment available.

2 Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal to routinely commission doravirine.

This document also describes the proposed criteria for commissioning, proposed governance arrangements and proposed funding mechanisms.

For the purpose of consultation NHS England invites views on the evidence and other information that has been taken into account as described in this policy proposition.

A final decision as to whether doravirine for HIV-1 in adults will be routinely commissioned will be made by NHS England following a recommendation from the Clinical Priorities Advisory Group.

3 Proposed Intervention and Clinical Indication

Human immunodeficiency virus type 1 (HIV-1) is a virus that damages the CD4 cells of the immune system, leaving the body less able to fight off infection and disease. In some cases the damage caused to the immune system by HIV leads to acquired immunodeficiency syndrome (AIDS), which is the collective name given to several illnesses that can be life threatening for people with HIV. HIV cannot be cured, however, effective management of HIV reduces its impact on the immune system and can prevent people with the virus from developing AIDS.

Within a few weeks of infection, HIV may cause a flu-like illness with fever, headache, muscle aches and joint pain, sore throat and swollen lymph glands. This can last for a few weeks, after which there may be no specific signs or symptoms of HIV for a number of years. As the virus continues to destroy cells in the immune system, people with HIV may develop mild infections or other signs and symptoms, including fever, fatigue and weight loss. If untreated, HIV progresses to AIDS, which is characterised by certain conditions such as tuberculosis, cytomegalovirus, candidiasis, cryptococcal meningitis, toxoplasmosis, cryptosporidiosis, and different types of cancer, particularly

Kaposi's sarcoma and lymphoma. AIDS can be characterised by wasting syndrome, neurological complications such as dementia, and kidney disease.

HIV is transmitted from person to person through the body fluids of an infected person with a detectable viral load. It can affect people of any age, family origin, sex or sexual orientation.

Currently HIV is usually managed with a combination of three drugs including two nucleos(t)ide reverse transcriptase inhibitors (NRTIs; tenofovir disoproxil fumarate, tenofovir alafenamide, emtricitabine, abacavir, lamivudine) and either a protease inhibitor (PI; darunavir, atazanavir) boosted with ritonavir or cobicistat, a non-nucleoside reverse transcriptase inhibitor (NNRTI; rilpivirine, efavirenz), or an integrase inhibitor (INI; dolutegravir, elvitegravir/cobicistat, raltegravir). Doravirine is an NNRTI. NNRTIs inhibit HIV reverse transcriptase, which converts viral RNA into DNA. NNRTIs therefore shut down the ability of HIV to replicate and, in doing so, reduce a person's viral load of HIV.

Patients typically start on a 3-drug regimen and only move to another if there is lack of virological response, treatment failure, or tolerability issues. Additional issues include pill burden and dose frequency which may affect adherence. Considerations related to potential for drug-drug interactions are particularly relevant as people with HIV are living longer, which means they may become more likely to take medication for age-related comorbidities.

Drugs used to manage HIV can be taken as separate tablets that each contain one drug (for example, a tablet containing tenofovir disoproxil fumarate, a second tablet containing emtricitabine, and a third tablet containing dolutegravir) or as fixed dose combination tablets that contain two or three different drugs (for example, one tablet that contains tenofovir disoproxil fumarate, emtricitabine and efavirenz). Not all of the drugs used to manage HIV are available in fixed dose combination tablets. Doravirine is available in 2 different formulations. It is available as a tablet containing 100mg of doravirine alone, to be used in addition to a backbone of 2 NRTIs, as an alternative third agent in the treatment of HIV-1. It is also available as a fixed dose combination tablet containing 100mg of doravirine, 300mg of lamivudine and 300 mg of tenofovir disoproxil fumarate

(equivalent to 245mg of tenofovir disoproxil). The fixed dose combination tablet of doravirine is intended to be taken on its own without other antiretrovirals.

Doravirine is suitable for use in patients with HIV-1 who are new to treatment and those who are treatment experienced and wish to switch to doravirine. It is suitable for patients provided they do not have resistance to the NNRTI class and, in those taking the fixed dose combination tablet, provided they also do not have resistance to lamivudine or tenofovir. Doravirine can be taken with or without food.

4 Definitions

- **Adverse events**: unintentional and undesirable signs and symptoms reported during a study. Can be related to drugs used in the study or caused by other factors, such as natural progression of an existing condition
- **Antiretroviral therapy (ART)**: a combination of drugs that treat HIV
- **CD4 cell**: a type of white blood cell that kills viruses in the body
- **Integrase inhibitors (INIs)**: a class of antiretroviral drug that prevents HIV DNA being inserted into the DNA of CD4 cells
- **Non-nucleoside reverse transcriptase inhibitors (NNRTIs)**: a class of antiretroviral drug that stops HIV DNA being added to healthy CD4 cells
- **Nucleos(t)ide reverse transcriptase inhibitors (NRTIs)**: a class of antiretroviral drug that prevents the replication of HIV DNA, to which a third drug is added in antiretroviral therapy. 'NRTI' is used to denote nucleoside reverse transcriptase inhibitors (e.g. lamivudine and emtricitabine) and nucleotide reverse transcriptase inhibitors (e.g. tenofovir)
- **Protease inhibitors (PIs)**: a class of antiretroviral drug that prevents HIV from replicating
- **Viral load**: a measure of the number of viral particles in the body, reported as copies per millilitre of blood (copies/ml). Referred to as 'undetectable' when there are less than 50 copies of HIV-1 virus per ml of blood
- **Virological failure**: when the viral load in someone with HIV is greater than 200 copies/ml on 2 consecutive tests despite the use of antiretroviral therapy

- **Virologically suppressed**: when the level of HIV in the body is too low to be detected (also known as having an 'undetectable viral load'). This is usually when there are less than 50 copies of HIV-1 virus per ml of blood

5 Aims and Objectives

This policy proposition considered the evidence for doravirine for treating adults with HIV-1 infection.

The objectives were to:

- Review the evidence of effectiveness for doravirine.
- Define the eligibility criteria for doravirine.
- Define the commissioning arrangements required for doravirine.

6 Epidemiology and Needs Assessment

The latest available data shows that in 2017 85,537 people in England received treatment for HIV and 3,973 people were newly diagnosed with the condition (Country and PHE region HIV data tables, Public Health England, 2018). Around 99% of individuals on antiretroviral treatment for HIV are aged 18 and over, and around 98% of all people with HIV in the UK are on antiretroviral therapy (Public Health England, 2018).

It is estimated around 77,400 people in England would be currently eligible for treatment with doravirine under the terms of its marketing authorisation. However, the number of people who will receive treatment with doravirine in clinical practice will be determined by the availability and price of alternative treatment regimens.

7 Evidence Base

NHS England has concluded that there is sufficient evidence to support a proposal for the routine commissioning of this treatment for the indication.

The evidence for the efficacy of doravirine comes from the results of 3 studies funded by the company. Two are identically designed randomised controlled trials in a treatment naive population, the DRIVE-FORWARD (Molina et al. 2018) study which uses the doravirine standalone formulation, and the DRIVE-AHEAD (Orkin

et al. 2019) study which uses the combination dose formulation. The remaining study, DRIVE-SHIFT (Johnson et al. 2019), is an open label study in a treatment experienced population (a minimum of 6 months of viral suppression on their existing ART) who switched to doravirine combination formulation or remained on their existing ART. All the studies are non-inferiority trials, which means the studies aimed to demonstrate that doravirine is no less effective than comparator treatments. The studies were powered for non-inferiority based on the primary outcome, the proportion of participants with a HIV-1 RNA<50 copies/ml at week 48. While the studies are all 96 weeks long and these results are expected to be published subsequently, only data up to 48 weeks is currently available.

Effectiveness

Virological outcomes

Viral load is a measure of how much of the HIV virus there is in the blood, measured by the amount of HIV genetic material (RNA) present in the body. The measurement is given as the number of copies of the virus per millilitre of blood (copies/ml). If there are high levels of HIV in the blood, the risk of the person with HIV becoming ill from other infections increases. The aim of antiretroviral therapy is to reduce viral load to less than 50 copies/ml to lower the risk of the person with HIV acquiring other infections. In addition, when viral load is less than 50 copies/ml, the risk of HIV being passed on to another person is extremely low, even during unprotected sexual intercourse.

The DRIVE-FORWARD study showed that doravirine was as effective as darunavir and ritonavir in reducing HIV-1 RNA to below 50 copies per ml [84% vs 80% of people treated respectively, treatment difference 3.9% (95% CI -1.6 to 9.4)]. When the results for the primary outcome measure were stratified by baseline viral load, NRTI component, and CD4 T-cell count, the results continued to show a treatment difference 95% confidence interval that indicated non-inferiority. This pattern of results was also replicated when HIV-1 RNA less than 40 copies per ml and less than 200 copies per ml were reported, namely there was a treatment difference with 95% confidence intervals crossing zero, suggesting the drug has the same level of clinical effectiveness as comparator treatments in the trial.

The DRIVE-AHEAD study showed that doravirine/lamivudine/tenofovir disoproxil fumarate as a fixed dose combination tablet (DOR/3TC/TDF) was as effective as efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/FTC/TDF) in reducing HIV-1 RNA to below 50 copies per ml [84.3% vs 80.8% respectively, treatment difference 3.5% (95% CI, -2.0 to 9.0)]. Similar results were reported for individuals achieving HIV-1 RNA<40 copies/ml [83.8% v 79.7%, difference 4.1%, (95% CI, -1.5 to 9.7)], and HIV-1 RNA<200 copies/ml [86% vs 82.7% (difference not reported)].

The DRIVE-SHIFT study showed that a treatment experienced population with no history of virologic failure and with virologic suppression who switch to doravirine/lamivudine/tenofovir disoproxil fumarate as a fixed dose combination tablet (DOR/3TC/TDF) from a treatment (baseline) regimen consisting of a NRTI backbone plus a PI or INI or NNRTI had non-inferior results for proportion of individuals with HIV-1 RNA<50 copies per ml (406 [90.8%] at week 48 in DOR/3TC/TDF group, 211 [94.6%] at week 24 in existing ART group, difference -3.8% [95% CI -7.9 to 3.0]).

CD4 cell count

CD4 cells are white blood cells that fight infections in the body. The higher the number of CD4 cells in the body, the more capable the body is of fighting infection. A CD4 cell count of over 500 indicates that the body is able to effectively fight most infections. A CD4 cell count of below 200 indicates that the body is at high risk of developing serious illnesses. The HIV-1 virus kills CD4 cells, increasing the risk of the person with HIV developing serious illnesses.

The DRIVE-FORWARD study showed an average increase from baseline at week 48 in CD4 cell count of 193 cells per microlitre (µl) in the doravirine group compared to 186 per µl in the darunavir group (mean difference 7.1 per µl, 95% CI -20.8 to 35).

For the DRIVE-AHEAD study the average increase reported was 198 per µl for doravirine/lamivudine/tenofovir disoproxil fumarate as a fixed dose combination tablet (DOR/3TC/TDF) and 188 per µl for efavirenz/emtricitabine/tenofovir

disoproxil fumarate (EFV/FTC/TDF) (mean difference 10.1 per µl, 95% CI -16.1 to 36.3).

For the DRIVE-SHIFT study the mean increase in the number of CD4 cells from baseline at week 24 was 5 cells/mm^3 in the DOR/3TC/TDF immediate switch group (ISG), 18 cells/mm^3 in the baseline regimen delayed switch group (DSG), and at 48 weeks, 14 cells/mm^3 in the DOR/3TC/TDF ISG.

Safety and tolerability

Viral resistance

Viral resistance refers to when a virus is no longer affected by a drug that used to be effective against it. It means that a virus will continue to multiply despite the presence of a drug that would usually kill it. Viral resistance is caused by a mutation in a virus gene. Frequent mutations occur in the HIV-1 virus because it replicates very quickly and does not correct any mutations that occur when it replicates. The frequent mutations in the HIV-1 virus increases the risk of it becoming resistant to drugs.

Protocol defined virological failure (PDVF) defined as non-response (confirmed HIV-1 RNA of 200 copies or more per ml at week 24 or 36, or confirmed HIV-1 RNA of 50 copies or more per ml at week 48), or rebound (confirmed HIV-1 RNA of 50 copies or more per ml after initial response/HIV-1 RNA less than 50 copies per ml at any time during the study), was the primary measure of viral resistance in the studies. In all cases a confirmation of PDVF required 2 consecutive measures of HIV-1 RNA≥50 copies/ml at least 1 week apart.

In the DRIVE-FORWARD study 19 (5%) of individuals in the doravirine group had a PDVF compared to 24 (6%) in the darunavir group. Fifteen of these individuals had virological testing (7 doravirine, 8 darunavir). No genetic mutations associated with resistance to doravirine were identified and no phenotypic resistance to doravirine was observed. In the darunavir group, polymorphic mutations in the viral protease gene, but with no decrease in phenotypic susceptibility to darunavir, were observed in 3 individuals. No primary genotypic resistance mutations or

phenotypic resistance to any of the NRTI backbone treatments were identified in either group.

Five participants (2 in the doravirine group, 3 in the darunavir group) from the 93 who discontinued the DRIVE-FORWARD study for reasons other than PDVF had a HIV-1 RNA>400 copies per ml, sufficient for resistance testing. Of these, 1 who had discontinued treatment due to non-compliance developed resistance to doravirine and emtricitabine, and 1 who discontinued treatment due to a rash in the doravirine group was identified as phenotypically resistant.

In the DRIVE-AHEAD study 22 participants (6.0%) in the doravirine/lamivudine/tenofovir disoproxil fumarate as a fixed dose combination tablet (DOR/3TC/TDF) group and 14 (3.8%) in the efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/FTC/TDF) group met the criteria for PDVF. The majority of these (16/22 and 10/14, respectively) were due to viral rebound. Thirteen individuals in the DOR/3TC/TDF group and 10 in the EFV/FTC/TDF group who had PDVF had a successful genotype test. The number of individuals who had phenotypic testing were 13 and 9 respectively. Seven in the DOR/3TC/TDF group had developed a genotypic resistance to doravirine, 12 in the EFV/FTC/TDF had developed a genotypic resistance to efavirenz. Six individuals developed a phenotypic resistance to doravirine and 8 to efavirenz. Five of the individuals tested in the DOR/3TC/TDF group showed evidence of genotypic resistance and 5 showed phenotypic resistance to an NRTI. Five of the individuals tested in the EFV/FTC/TDF group showed evidence of genotypic resistance, and 4 of phenotypic resistance to an NRTI.

Thirty-five individuals in the DOR/3TC/TDF group and 50 in the EFV/FTC/TDF group in the DRIVE-AHEAD study discontinued the study for reasons other than PDVF. Of these, 9 had a successful genotype test and 9 a successful phenotype test in the DOR/3TC/TDF group. For the EFV/FTC/TDF group the corresponding numbers were 13 and 12 respectively. In those tested, no individuals in the DOR/3TC/TDF showed evidence of genotypic or phenotypic resistance to doravirine, or an NRTI. In the EFV/FTC/TDF group genotypic resistance, and phenotypic resistance to efavirenz, was found in 3 individuals.

In the DRIVE-SHIFT study 6 individuals in the immediate switch group (ISG), 1 in the baseline regimen delayed switch group (DSG), and 1 in the DSG after switching had a PDVF. Two in the ISG and 1 in the DSG had samples suitable for resistance testing. None in the ISG showed genotypic or phenotypic resistance to DOR, 3TC or TDF, the DSG participant showed genotypic and phenotypic resistance to 3TC and FTC at week 12. Viral resistance testing was undertaken in 1 participant in the DOR/3TC/TDF ISG and 2 in the baseline regimen DSG who had discontinued early without PDVF. None of these were found to have a genotypic or phenotypic resistance to any of the study drugs.

Blood lipids

Blood lipids are fats in the blood, such as fatty acids and cholesterol. The presence of elevated or abnormal levels of lipids or lipoproteins in the blood (hyperlipidaemia) increases the risk of developing heart disease, gall bladder disease and pancreatitis. HIV infection and treatment with some HIV medicines can increase the risk of hyperlipidaemia.

The DRIVE-FORWARD study reported that on average the level of LDL-cholesterol had decreased in the doravirine group at 48 weeks, and increased in the darunavir group, and the mean difference between the groups of -14.6 mg/dl was statistically significant ($p<0.0001$). HDL levels increased by a similar amount in both groups (3.9 mg/dl doravirine and 4.2 mg/dl darunavir). There was a statistically significant mean difference for non-HDL cholesterol in favour of doravirine (-19.4 mg/dl, 95% CI -23.3 to -15.4; $p<0.0001$).

The DRIVE-AHEAD study also reported the same outcomes. Mean change in LDL-cholesterol from baseline was -1.6 mg/dl with doravirine/lamivudine/tenofovir disoproxil fumarate as a fixed dose combination tablet (DOR/3TC/TDF) and 8.7 mg/dl with efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/FTC/TDF). Mean change in non-HDL-cholesterol was -3.8 mg/dl with DOR/3TC/TDF and 13.3 mg/dl with EFV/FTC/TDF. Mean difference on both these measures was statistically significant ($p<0.0001$). Mean total cholesterol and triglyceride concentrations fell in the DOR/3TC/TDF group (-2.0 and -12.4 mg/dl respectively) but increased in the EFV/FTC/TDF group (21.8 and 22.0 mg/dl respectively). Mean

levels of HDL-C increased in both groups, by 1.9 mg/dl for the DOR/3TC/TDF group and 8.5 mg/dl for the EFV/FTC/TDF group.

In the DRIVE-SHIFT study, at week 24, there was a statistically significant difference ($p<0.0001$) in the mean change in LDL-C and non-HDL-C between the immediate switch group (ISG) and baseline regimen delayed switch group (DSG) (LDL-C -16.5 mg/dl ISG, -1.9 mg/dl DSG, difference -14.7 mg/dl, 95% CI -18.9 to -10.4; Non-HDL-C, -24.7 ISG, -1.3 mg/dl DSG, difference -23.0 mg/dl, 95% CI -28.0 to -18.1). There were negative mean differences between the ISG and DSG for cholesterol, triglycerides, and HDL-C of -25.8 mg/dl, -42.9 mg/dl, and -3.0 mg/dl, respectively. In all instances, while specific p values were not reported, the 95% CI were all within a negative range, showing a statistically significant difference. These results are reported for participants receiving a ritonavir boosted protease inhibitor at study entry.

Adverse events

The DRIVE-FORWARD study reports that 80% of individuals who received doravirine had an all causes adverse event, and 31% had a treatment related adverse event. Nineteen (5%) had an all causes serious adverse event, and 1 (<1%) had a serious adverse event which was treatment related. Six (2%) patients had to discontinue treatment due to an adverse event, 4 (1%) due to a treatment related adverse event. The figures were similar in the darunavir group: 78% had an adverse event of any cause, 32% had a treatment related adverse event, 6% had an all causes serious adverse event, and 1 (<1%) had a treatment related serious adverse event. Twelve (3%) patients discontinued treatment due to an all causes adverse event, 8 (2%) due to a treatment related adverse event.

In the DRIVE-AHEAD study, the primary safety outcome measure, and adverse events of interest, was the proportion of participants with neuropsychiatric adverse events (dizziness, sleep disorders/disturbances, and altered sensorium). These all occurred statistically significantly less in the doravirine/lamivudine/tenofovir disoproxil fumarate (DOR/3TC/TDF) group compared to those on efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/FTC/TDF) (dizziness 8.8% compared to 37.1%, $p\leq0.001$; sleep disorders/disturbances 12.1% compared to 25.2%, $p\leq0.001$; and altered sensorium 4.4% compared to 8.2%, $p=0.033$). Any

adverse event, drug related adverse events, discontinues due to adverse event, and discontinues due to serious adverse events all occurred statistically significantly less in the DOR/3TC/TDF group than in the EFV/FTC/TDF group ($p<0.05$). Outside of neuropsychiatric events there were statistically significantly fewer skin/subcutaneous tissue disorders in the DOR/3TC/TDF group ($p<0.05$). There were no categories or individual adverse events that were statistically significantly ($p<0.05$) less common in the EFV/FTC/TDF group than the DOR/3TC/TDF group.

In the DRIVE-SHIFT study, by week 24, 68.9% in the immediate switch group (ISG) and 52.5% in the delayed switch group (DSG) had any adverse event, 19.5% and 2.2% respectively a drug related adverse event, and 2.9% and 3.6% a serious adverse event. Eleven (2.5%) in the ISG discontinued due to an adverse event, 1 (0.4%) in the DSG. Seven (1.6%) in the ISG discontinued due to a drug related adverse event, none in the baseline regimen. There were no deaths in either group. After switching at week 24, by week 48 126 (60.3%) people in the DSG had experienced any adverse event, 29 (13.9%) a drug related adverse event, and 4 (1.9%) a serious adverse event. There were 4 discontinues due to any adverse event, and 4 due to a drug related adverse event. There were no deaths.

8 Proposed Criteria for Commissioning

Doravirine will be routinely commissioned in line with cost-based, regional prescribing guidelines for the treatment of adults with HIV-1 who have no past or present evidence of resistance to the NNRTI class.

Stopping criteria

Following initiation, treatment with doravirine should be stopped, and an alternative ART regimen started, if the patient:

- Has a viral load of 200 copies/ml or more after 24 weeks on doravirine and 50 copies/ml or more after 48 weeks on doravirine, and the patient has been adhering to treatment

- Has a confirmed viral load above 200 copies/ml at any time after their viral load has been suppressed to below 50 copies/ml on doravirine, and the patient has been adhering to treatment

OR

- Experiences a serious adverse reaction to doravirine (as described in the summary of product characteristics)

Consider stopping doravirine if the patient becomes pregnant, as described in the summary of product characteristics.

9 Proposed Patient Pathway

Treatment with doravirine can be considered for adult patients who are naive to anti-retroviral treatment and those who are looking to switch treatment. Prescription and monitoring of doravirine is in line with the existing pathway for people with HIV who are on antiretroviral treatment and should be in line with cost based, regional prescribing guidelines.

10 Proposed Governance Arrangements

This policy should be used in conjunction with the most recent NHS Standard Contract for Specialised Human Immunodeficiency Virus Services (Adult) specification. The Standard Contract includes information on the composition of multidisciplinary teams (MDTs) for the assessment, monitoring and management of people with HIV.

11 Proposed Mechanism for Funding

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

12 Proposed Audit Requirements

Regional prescribing polices should be agreed by appropriate commissioners and shared with the HIV CRG.

All antiretroviral decisions, including rationale for drug choice, should be documented in the clinical notes.

Regular audit of prescribing against regional guidelines is expected.

13 Documents That Have Informed This Policy Proposition

The documents that have informed this policy proposition include a review of the clinical evidence available for doravirine and the following:

- NHS England (2018) Clinical Commissioning Policy: Immediate antiretroviral therapy for treatment of HIV-1 in adults and adolescents
- NHS England (2018) Clinical Commissioning Policy: Dolutegravir for treatment of HIV-1 infection (all ages)
- Public Health England (2018) National HIV surveillance data tables
- Public Health England (2017) Towards elimination of HIV transmission, AIDS and HIV-related deaths in the UK
- NHS England (2017) Clinical Commissioning Policy: Tenofovir alafenamide for treatment of HIV-1 in adults and adolescents
- NHS England (2015) Clinical Commissioning Policy: Elvitegravir/cobicistat/emtricitabine/tenofovir for treatment of HIV in adults
- NHS England (2013) Specialised Human Immunodeficiency Virus (HIV) Services (Adult)

The references included in the evidence review are listed in section 15 below.

14 Date of Review

This document will lapse upon publication by NHS England of a clinical commissioning policy for the proposed intervention that confirms whether it is routinely or non-routinely commissioned.

15 References

Johnson M, Kumar P, Molina, JM et al. (2019) Switching to Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate (DOR/3TC/TDF) Maintains HIV-1 Virologic Suppression Through 48 Weeks: Results of the DRIVE-SHIFT Trial. JAIDS: Journal of Acquired Immune Deficiency Syndromes, published ahead of print in April 2019, accessed on 14th May 2019 https://journals.lww.com/jaids/Abstract/publishahead/Switching_to_Doravirine_Lamivudine_Tenofovir.96395.aspx

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Orkin C, Squires K, Molina JM, et al. (2019) Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate is Non-inferior to Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate in Treatment-naive Adults With Human Immunodeficiency Virus-1 Infection: Week 48 Results of the DRIVE-AHEAD Trial. Clinical Infectious Diseases, volume 68, issue 4, pages 535-544

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