Clinical Commissioning Policy Proposition: Dolutegravir-rilpivirine for treating HIV-1 in adults

Reference: NHS England 1806

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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

HIV (human immunodeficiency virus) 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 infection. In some cases this can lead 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. 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 2 main types of HIV – HIV-1 (the most common type) and HIV-2 (relatively uncommon in the UK). This policy proposition covers HIV-1 only as dolutegravir-rilpivirine is not licensed for the treatment of HIV-2.

About current treatments

It is recommended that treatment with antiretroviral therapy (medicines used to treat HIV) is usually started immediately after a diagnosis of HIV to stop the virus replicating in the body. The standard of care is treatment with 3 drugs (known as triple therapy). All drugs have the aim of stopping the virus replicating in the body but have different ways to do this.

Typically, the 3-drug regimen will include 2 drugs known as 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).

About the new treatment

Typically, HIV treatment includes 3 different drugs, as described above. Dolutegravir-rilpivirine provides an alternative treatment with similar effectiveness in people whose disease is already virologically suppressed (that is, where levels of the virus are too low to be detected) but using 2 drugs instead of 3. It is a single tablet that contains both dolutegravir and rilpivirine.

Dolutegravir is an INI. It sticks to HIV integrase (an HIV enzyme used to insert HIV DNA into the DNA of the CD4 cells) and prevents HIV DNA being inserted into uninfected CD4 cells. Rilpivirine 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.

What we have decided

NHS England has carefully reviewed the evidence prepared by NICE on treating HIV-1 with dolutegravir-rilpivirine. 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 dolutegravir-rilpivirine. Dolutegravir and rilpivirine are available as separate tablets and as a single tablet that combines both drugs. This document relates to the use of the combined tablet only.

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 dolutegravir-rilpivirine for HIV-1 will be routinely commissioned will 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-1 cannot be cured, however, effective management of HIV-1 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 3 drugs including 2 nucleoside reverse transcriptase inhibitors (NRTIs; tenofovir disoproxil fumarate, tenofovir alafenamide, emtricitabine, abacavir, lamivudine) and either a protease inhibitor (PI; darunavir, raltegravir) boosted with ritonavir or cobicistat, a non-nucleoside reverse transcriptase inhibitor (NNRTI; rilpivirine, efavirenz) or an integrase inhibitor (INI; dolutegravir, elvitegravir/cobicistat, raltegravir, bictegravir).

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.

Current standard practice is to use a 3-drug regimen, however, using fewer drugs could bring advantages for patients. Using fewer drugs could reduce the number of drug-related adverse events and interactions with other medications being taken. It could also reduce the number of individual drugs or classes of drugs that the disease may become resistant to, saving more treatment options for the future.

Dolutegravir-rilpivirine is a single tablet regimen which allows treatment with 2 drugs rather than 3: dolutegravir (an INI), and rilpivirine (an NNRTI). It is a treatment option licensed for people whose disease is currently being controlled (HIV-1 RNA <50 copies/ml) with a stable antiretroviral regimen for at least 6 months, with no history of virological failure, and no known or suspected resistance to any NNRTI inhibitor or INI. As treatment with dolutegravir-rilpivirine does not involve the use of an NRTI, its use prevents the HIV virus becoming

resistant to NRTIs. This saves more treatment options for the future. Dolutegravir-rilpivirine also provides an alternative treatment option to NRTIs for people who have concerns about the toxicity of NRTIs.

The Summary of Product Characteristics (SPC) for dolutegravir-rilpivirine states that it is not recommended during pregnancy. For other contraindications to use, please refer to the SPC.

4 Definitions

- **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
- **Nucleoside reverse transcriptase inhibitors (NRTIs)**: a class of antiretroviral drug that prevents the replication of HIV DNA
- **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)
- **Virological failure/non-response**: 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. 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 the clinical effectiveness and safety of dolutegravir-rilpivirine for treating treatment-experienced adults with HIV-1.

The objectives were to:

- Define the evidence base upon which the commissioning criteria and arrangements for dolutegravir-rilpivirine are established
- Define the clinical commissioning criteria and commissioning arrangements for dolutegravir-rilpivirine.

6 Epidemiology and Needs Assessment

The latest available data shows that in 2017 there were around 85,500 people in England with a diagnosis of HIV (Public Health England, 2018). The overall prevalence of HIV in England was 1.6 per 1,000 people in 2016 (Public Health England, 2017) and around 4,000 people in England were newly diagnosed with the condition in 2017 (Public Health England, 2018).

In 2017 there were around 73,000 adults with HIV in England who were on antiretroviral treatment and had a viral load of less than 50 copies/ml (Public Health England, 2018). Taking into account the annual incidence of HIV, this number is likely to increase to 77,000 adults in 2018/19. It is estimated that around 84% of these people would meet the additional restrictions of the marketing authorisation for dolutegravir-rilpivirine (on a stable ART regimen for at least 6 months, with no history of virological failure, and with no known or suspected resistance to any NNRTI or INI). This suggests around 65,000 adults would be eligible for treatment with dolutegravir-rilpivirine in 2018/19, if they were to switch from their existing antiretroviral therapy. However, it is likely that fewer people would receive dolutegravir-rilpivirine in clinical practice, because of the eligibility criteria in section 8, and the availability 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 dolutegravir-rilpivirine comes from the pooled results of 2 identically designed randomised controlled trials known as the SWORD-1 and -2 studies (Llibre et al. 2018 and Aboud et al. TBC) and a substudy of the randomised controlled trials (McComsey et al. 2018). A paper of 2 case reports provided additional data on treatment adherence and caregiver burden (Suzuki et al. 2017). Evidence from the Aboud et al. paper that has not yet been published in a peer-reviewed publication. **This data has been considered by the policy working group based on a confidential draft of the article which was provided by the company. However, the publication of this evidence has been delayed and therefore will not be available in time for public consultation. Where there is confidential data, this information has been highlighted yellow.** It is anticipated that the manuscript will be published in a peer-reviewed journal before NHS England makes a final commissioning decision on dolutegravir-rilpivirine.

The SWORD studies were non-inferiority trials, which means the studies aimed to demonstrate that dolutegravir-rilpivirine is no worse than current antiretroviral therapies. Participants who were on antiretroviral therapy were either switched to dolutegravir-rilpivirine or continued with their existing treatment. Existing treatment varied, however, at baseline around 70% of participants were taking tenofovir disoproxil fumarate and/or emtricitabine and around half of the participants were taking an NNRTI as a third-agent. Llibre et al. 2018 (SWORD 1 and 2 studies) presents data comparing dolutegravir-rilpivirine with existing antiretroviral therapies for 48 weeks. After 48 weeks, participants in the dolutegravir-rilpivirine group were allowed to continue treatment up to 100 weeks, and those in the existing treatment arm who were virologically controlled were permitted to switch to dolutegravir-rilpivirine. Aboud et al. TBC presents data for participants that used dolutegravir-rilpivirine for 100 weeks and for participants who switched to dolutegravir-rilpivirine at 48 weeks.

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 number of participants with a viral load <50 copies/ml at week 48 in the SWORD studies (primary outcome) was statistically significantly non-inferior in the group that switched to dolutegravir-rilpivirine (94.7%) compared with the group that remained on their existing ART (94.9%, adjusted treatment difference of -0.2%, 95% CI -3.0 to +2.5, non-inferiority margin of 4%). Around 89% of the participants that switched to dolutegravir-rilpivirine had a viral load <50 copies/ml at week 100.

The number of participants with a virological non-response at week 48 in the SWORD studies was statistically significantly non-inferior in the group that switched to dolutegravir-rilpivirine (n=3, <1%) compared with the group that remained on their existing ART (n=6, 1%; adjusted treatment difference of -0.5%, 95% CI -1.4 to +0.5, non-inferiority margin of 4%). Around 3% of participants that switched to dolutegravir-rilpivirine had a virological non-response at week 100.

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.

There was an increase in median CD4 cell count from baseline to week 48 in the SWORD studies in both the group that switched to dolutegravir-rilpivirine (increase of 28.0 cells per µL) and the group that remained on their existing ART (increase

of 22.0 cells per µL). The statistical significance of the difference in these increases is not reported. By week 100, the median CD4 cell count in participants who had switched to dolutegravir-rilpivirine had increased by 33 cells per µL compared to baseline.

Health related quality of life and caregiver burden

Health related quality of life is the perceived quality of a person's daily life based on their health. This can include a person's physical and mental health. Two scales were used to assess health related quality of life in the included studies.

1. The HIV Treatment Satisfaction Questionnaire (HIVTSQs) measures satisfaction with treatment for people who have HIV. It is completed by participants and has 10 items. Scores range from 0 to 6 for each item. It provides an overall (total) score as well as subscores on lifestyle/ease and general satisfaction/clinical.

2. The Symptom Distress Module (SDM) measures distress linked to HIV or ART-related symptoms. It is completed by participants and has 20 items. Scores range from 0 to 4 for each item. It provides an overall score, known as the symptom bother score.

There was no statistically significant change in mean HIV Treatment Satisfaction Questionnaire total score in the SWORD studies for participants who switched to dolutegravir-rilpivirine compared with those that remained on their existing ART (baseline to week 48, p value not reported). There was also no statistically significant difference in the change in the mean general satisfaction/clinical subscore, however, there was a statistically significant greater increase in the mean lifestyle/ease subscore for participants who switched to dolutegravir-rilpivirine compared with participants who remained on their existing ART ($p<0.0001$).

There was a statistically significant greater decrease from baseline to week 48 in mean symptom bother score as measured by the Symptom Distress Module in the SWORD studies for participants who switched to dolutegravir-rilpivirine compared with participants who remained on their existing ART ($p<0.05$).

Burden on caregiver is the strain or load taken on by a person who cares for someone who is chronically ill. It can include physical, emotional, social and financial factors. When caring for someone with HIV, this may include helping them to take their medications at the correct time and taking them to healthcare appointments.

The Suzuki et al. (2017) case reports (n=2) stated that there was a reduced burden on caregivers when patients switched to dolutegravir-rilpivirine because the tablets could be taken without crushing or preparing them in an oral suspension, as required with their previous regimen.

Safety and tolerability

Bone density

Bone density is a measure of the amount of bone mineral in bone tissue. A decrease in bone density, also known as bone loss, is associated with a higher risk of bone fracture. Low bone density is also an indirect indicator of osteoporosis. Bone loss occurs faster in people with HIV than in people without HIV. Both the HIV infection and some HIV medicines may increase the rate of bone loss.

There was a statistically significant greater increase (improvement) in total hip bone mineral density in the SWORD substudy for the group that switched to dolutegravir-rilpivirine compared with the group that remained on their existing ART (baseline to week 48, difference in adjusted change of +1.29%, 95% CI 0.27 to 2.31, p=0.014).

There was a statistically significant greater increase (improvement) in lumbar spine bone mineral density in the SWORD substudy for the group that switched to dolutegravir-rilpivirine compared with the group that remained on their existing ART (baseline to week 48, difference in adjusted change of +1.32%, 95% CI 0.07 to 2.57, p=0.039) (McComsey et al. 2018).

There were statistically significant greater increases (improvements) in total hip T score (baseline to week 48, difference in adjusted change of +0.09%, 95% CI 0.02 to 0.16, p=0.016) and lumbar spine T score (baseline to week 48, difference in adjusted change of +0.12%, 95% CI 0.00 to 0.23, p=0.049) in the SWORD

substudy for the group that switched to dolutegravir-rilpivirine compared with the group that remained on their existing ART.

The 10 year probability of hip fracture in the SWORD substudy was reduced (improvement) for the group that switched to dolutegravir-rilpivirine (baseline to week 48, -0.08%) and increased for the group that remained on their existing ART (baseline to week 48, +0.03%). The 10 year probability of osteoporotic fracture in the SWORD substudy was reduced (improvement) in both the switch group (baseline to week 48, -0.12%) and non-switch group (baseline to week 48, -0.04%). The statistical significance of the difference in these changes was not reported.

There was a statistically significant greater reduction (improvement) in bone-specific alkaline phosphatase type, osteocalcin type, procollagen type 1 N-terminal propeptide, and type 1 collagen C-telopeptide from baseline to week 48 in the SWORD studies in the group that switched to dolutegravir-rilpivirine compared with the group that remained on their existing ART ($p<0.05$).

From baseline to week 100 there was a statistically significant decrease (improvement) in mean bone-specific alkaline phosphatase type, osteocalcin, and type 1 collagen C-telopeptide for participants who switched to dolutegravir-rilpivirine in the SWORD studies. There was a statistically significant increase (worsening) in mean procollagen type 1 N-terminal propeptide in the same group.

Renal function

Renal function is a measure of how well the kidneys are working. The kidneys filter toxins and waste products from the blood and release hormones to regulate blood pressure, produce red blood cells, and help the body absorb calcium. HIV can result in kidney disease and kidney failure (known as HIV-associated nephropathy). Some antiretroviral therapy can have a negative effect on the kidneys.

Changes in mean levels of cystatin C, retinol binding, beta-2-microglobulin, C-reactive protein, D dimer, fatty acid binding protein, glucose, interleukin-6,

soluble CD14, soluble CD163, soluble vascular cell adhesion molecule-1, and estimated glomerular filtration rate were reported at week 48 in the SWORD studies. The study paper stated that there was 'no consistent pattern of change' for these outcomes. The statistical significance of the differences in changes between the group that switched to dolutegravir-rilpivirine and the group that remained on their existing ART was not reported.

There was a statistically significant decrease (improvement) in median retinol binding protein/creatinine level from baseline to week 100 in participants in the SWORD studies who switched to dolutegravir-rilpivirine (p<0.001).

There was a statistically significant decrease (improvement) in median urine beta-2-microglobulin:creatinine from baseline to week 100 in participants in the SWORD studies who switched to dolutegravir-rilpivirine and who were on tenofovir disoproxil fumarate at baseline (p<0.001). There was no change in median urine beta-2-microglobulin:creatinine for participants who were not on tenofovir disoproxil fumarate at baseline.

Adverse events

Adverse events are unintentional and undesirable signs and symptoms reported during a study. Adverse events can occur in both the intervention and control groups of a study. They may be related to drugs being used in the study or they may be caused by other factors, such as natural progression of an existing condition. They can be mild or serious. If an event is thought to be related to the drugs being used in a study, it is known as a drug-related adverse event.

In the SWORD studies, at least 1 adverse event was reported by week 48 in 77% of the participants that switched to dolutegravir-rilpivirine and 71% of the participants that remained on their existing ART (statistical significance between groups not reported). By week 100, 88% of participants that switched to dolutegravir-rilpivirine had reported at least 1 adverse event.

The majority of adverse events in both groups in the SWORD studies were mild (grade 1). The most frequently reported adverse events at week 48 were nasopharyngitis (10% of both groups), headache (8% intervention, 5%

comparator), and upper respiratory tract infection (5% intervention, 7% comparator). Other adverse events by week 48 included diarrhoea (6% intervention, 5% comparator), back pain (3% intervention, 6% comparator), bronchitis (4% intervention, 3% comparator), influenza (2% intervention, 3% comparator), arthralgia (joint pain, 4% intervention, 2% comparator), insomnia (3% intervention, 2% comparator), depression (3% intervention, 1% comparator), anxiety (2% in both groups), and abnormal dreams (1% intervention, no cases in comparator group). By week 100, the most commonly reported adverse events in the intervention group were psychiatric disorders (17%), viral upper respiratory tract infection (15%), headache (12%), upper respiratory tract infection (10%), diarrhoea (9%), back pain (6%), bronchitis (7%), arthralgia (7%), syphilis (6%), and nasopharyngitis (2%).

Drug-related adverse events by week 48 in the SWORD studies were reported in 19% of participants in the intervention group and 2% of participants in the comparator group. Serious drug-related adverse events were reported in 1% of participants in the switch group and <1% in the non-switch group. The statistical significance of the differences in drug-related adverse events between the groups was not reported. By week 100, drug-related adverse events were reported in 20% of the participants that switched to dolutegravir-rilpivirine. It is not clear how many of these were drug related.

In the SWORD studies, there was 1 death (<1%) in both dolutegravir-rilpivirine and comparator groups (statistical significance not reported) by week 48. There were 2 further deaths (<1%) in the dolutegravir-rilpivirine group between week 48 and week 100. None of the deaths were considered to be related to 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.

Mean changes in total cholesterol, HDL cholesterol, calculated LDL cholesterol, triglycerides and total:HDL cholesterol from baseline to 48 weeks were reported in the SWORD studies. The statistical significance of the difference in changes between the group that switched to dolutegravir-rilpivirine and the group that remained on their existing ART was not reported.

Changes in total cholesterol, HDL cholesterol, LDL cholesterol, and total:HDL cholesterol from baseline to week 100 in the dolutegravir-rilpivirine group of the SWORD studies were reported to show 'no clinically relevant effect' (p values not reported).

Treatment adherence

Treatment adherence describes the extent to which someone acts on medical advice about their treatment. This can include taking the recommended dose of medication each day, taking medication at recommended times of day, and taking medication for a recommended period of time. Poor adherence to ART is associated with less effective suppression of the HIV-1 virus, resulting in a higher viral load of HIV in the body. A higher viral load of HIV increases the risk of a person becoming ill from other infections. Poor adherence to ART can also lead to permanent resistance of HIV to a particular drug or class of drugs.

Patient reported treatment adherence by week 48 in the SWORD studies was 97.9% in the group that switched to dolutegravir-rilpivirine and 98.3% in the group that remained on their existing ART. The statistical significance of the difference between the groups was not reported. Treatment adherence at week 100 was not reported.

The 2 participants included in the Suzuki et al. (2017) case reports maintained treatment adherence after switching to dolutegravir-rilpivirine.

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.

There were 3 reported cases of a viral mutation after the use of dolutegravir-rilpivirine for 100 weeks in the SWORD studies. At least one of the participants with a mutation did not show a decreased susceptibility to dolutegravir-rilpivirine, however, it was not reported whether the other 2 participants showed a decreased susceptibility or not. No cases of viral resistance were reported by week 48 in the group that remained on their existing ART.

8 Proposed Criteria for Commissioning

Dolutegravir-rilpivirine will be routinely commissioned as a fixed dose combination tablet in line with cost-based, regional prescribing guidelines, in the following circumstances:

- For adults with HIV-1 who:
    - Have disease that is virologically suppressed (<50 copies/ml), AND
    - Are on a stable ART regimen, and have been for ≥6 months, with no history of virological failure, AND
    - Do not have known or suspected resistance to any NNRTI or INI, AND
    - Do not have hepatitis B.

Approval for the use of dolutegravir-rilpivirine requires a multidisciplinary team (MDT) discussion, see section 10.

Stopping criteria

Treatment with dolutegravir-rilpivirine should be stopped, and an alternative ART regimen started, if the patient:

- Has a confirmed viral load above 200 copies/ml at any time after initiation of dolutegravir-rilpivirine

OR

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

9 Proposed Patient Pathway

Treatment with dolutegravir-rilpivirine can be considered for adult patients who have been on an existing antiretroviral regimen for at least 6 months. Prescription and monitoring of dolutegravir-rilpivirine 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

In accordance with the 2013/14 NHS Standard Contract for Specialised Human Immunodeficiency Virus Services (Adults), patients with HIV must have ongoing assessment, monitoring and management when starting, switching and remaining on antiretroviral therapies. This is to be undertaken by an appropriately qualified MDT with representation from, or access to, the following:

- Clinical leads with a minimum requirement of at least 2 of:
    - HIV physicians (at least 1 consultant)
    - Specialist HIV nurse
    - Specialist HIV pharmacist.
- Any of a range of other specialists involved in HIV care, routinely or to be co-opted as required, including:
    - Virologist
    - Psychologist
    - Paediatrician
    - In-patient medical staff
    - Adherence specialist
    - Social worker
    - Occupational therapist.
- Research representative or recruiting trials information with clear pathways for referral.

Services for patients with HIV must also provide specialist pharmacy services and

appropriate treatment adherence support for patients on antiretroviral therapies.

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

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

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 dolutegravir-rilpivirine and the following:

- 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
- NICE (2014) Chronic kidney disease in adults: assessment and management (CG182)
- 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

Aboud et al. TBC

Llibre J M, Hung C C, Brinson C et al. (2018) Efficacy, safety, and tolerability of dolutegravir-rilpivirine for the maintenance of virological suppression in adults with HIV-1: phase 3, randomised, non-inferiority SWORD-1 and SWORD-2 studies. Lancet vol 391 (10123): p839-849 and supplementary appendix

McComsey G A, Lupo S, Parks D et al. (2018) Switch from tenofovir disoproxil fumarate combination to dolutegravir with rilpivirine improves parameters of bone health. AIDS vol 32 (4): p477-485

Suzuki T, Hara N, Osa M, et al. (2017) Efficacy of switching to dolutegravir plus rilpivirine, the small-tablet regimen, in patients with dysphagia: two case reports. Journal of Pharmaceutical Health Care & Sciences vol 3: p23

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