Medicines Management Programme

Managed Access Protocol – Fostemsavir for the treatment of adults with multidrug resistant HIV-1 infection for whom it is not possible to construct a suppressive anti-viral regimen.

Medicine	Date of addition to Managed Access Protocol
Fostemsavir (Rukobia®)	9/12/2024

Approved by	**Professor Michael Barry, Clinical Lead, MMP**	
Date approved	Version 1.0	28/11/2024

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List of abbreviations

ART	Antiretroviral Therapy
ARV	Antiretroviral
EPAR	European Public Assessment Report
HIV-1	Human Immunodeficiency Virus Type 1
HSE	Health Service Executive
MAP	Managed Access Protocol
MDR	Multidrug Resistant
Mg	Milligrams
MMP	Medicines Management Programme
PCRS	Primary Care Reimbursement Service
RNA	Ribonucleic acid
SmPC	Summary of product characteristics

1. Fostemsavir for the treatment of multidrug resistant HIV-1 infection

Rukobia® contains fostemsavir. Fostemsavir is a human immunodeficiency virus type 1 (HIV-1) gp120-directed attachment inhibitor. Fostemsavir is a prodrug without significant antiviral activity that is hydrolysed to the active moiety, temsavir, upon cleavage of a phosphonooxymethyl group in vivo. Temsavir binds directly to the gp120 subunit within the HIV-1 envelope glycoprotein gp160 and selectively inhibits the interaction between the virus and cellular CD4 receptor, thereby preventing viral entry into, and infection of, host cells.

From December 2024, one presentation of fostemsavir is available under Hospital Pricing Approval:

- Rukobia® 600 mg prolonged-release tablets.

1.1 Licensed indication(s)

Fostemsavir (Rukobia®), in combination with other antiretrovirals (ARVs), is indicated for the treatment of adults with multidrug resistant (MDR) HIV-1 infection for whom it is otherwise not possible to construct a suppressive anti-viral regimen.

1.2 Funding

Funding of fostemsavir for the treatment of MDR HIV-1 is supported only for patients with MDR HIV-1 for whom it is otherwise not possible to construct a suppressive anti-viral regimen, who meet the criteria outlined in this managed access protocol (MAP). All criteria must be satisfied in order for funding to be supported.

An application for funding approval is required to be submitted on an individual patient basis. The *Fostemsavir Application Form* should be completed and sent by secure email to the Health Service Executive (HSE)-Medicines Management Programme (MMP) at mmp@hse.ie. See section 2.1 Submission of Applications for further detail.

Table 1 outlines the licensed dosage of fostemsavir for MDR HIV-1. Please refer to the Summary of Product Characteristics (SmPC) for further prescribing information.

Table 1 Licensed dosage of fostemsavir

Medicine	Route of administration	Dose
Fostemsavir	Oral	600 mg twice daily

mg: milligrams

If a patient is recommended for funding of fostemsavir, this is supported up to the maximum licensed dosage specified in Table 1. Funding of dosages in excess of the licensed therapeutic dosages (as outlined in Table 1) is not supported. Fostemsavir should be given in combination with at least one other ARV medicine. See Section 3 for further details on Discontinuation Criteria.

1.3 Price

The ex-factory price of the presentation of fostemsavir that falls under the scope of this MAP is outlined in Table 2. A commercial-in-confidence arrangement is in place with the marketing authorisation holder to reduce the net acquisition cost of fostemsavir to the HSE.

Table 2 Ex-factory price for fostemsavir available under Hospital Pricing Approval

Strength (pack size)	Ex-factory price*
Rukobia® 600 mg (60)	€2,940.12

mg: milligrams
*Correct as at 26/11/2024.

2. Approval criteria – Initiation

This section outlines the criteria that must be satisfied in order for patients to be recommended for funding of fostemsavir for MDR HIV-1.

2.1 Submission of applications

Applications for approval of funding for fostemsavir for the treatment of MDR HIV-1 will only be considered from consultants , with specialist registration with the Irish Medical Council in the speciality of infectious diseases or genitourinary medicine, practicing in a designated centre, and who have agreed to the terms of this MAP and been approved by the HSE ('approved consultants'). The designated centres are as follows:

- Cork University Hospital
- Beaumont Hospital
- Mater Misericordiae University Hospital
- St James's Hospital
- St Vincent's University Hospital
- University Hospital Galway
- University Hospital Limerick.
- University Hospital Waterford

The National Programme in Infectious Diseases and OPAT will assist the MMP in identifying designated centres as required.

Approved consultants are responsible for ensuring that the patient or their representative/guardian is aware that the application for funding approval is being made on their behalf.

It is expected that patients who may be eligible for treatment with fostemsavir for MDR HIV-1 will be reviewed at a multidisciplinary team conference prior to an application being submitted.

2.2 Patient age

Applications for funding approval will only be considered for individuals aged 18 years and older at time of application.

2.3 Patient diagnosis

For a positive recommendation, clinicians are required to confirm a diagnosis of MDR HIV-1 at the time of application. For the purposes of this MAP, MDR HIV-1 can be defined as having phenotypic or genotypic resistance to at least two of the standard ARV drug classes:

- Nucleoside reverse transcriptase inhibitor
- Non-nucleoside reverse transcriptase inhibitor
- Protease inhibitor
- Integrase inhibitor.

It is usually established by at least one major resistance mutation within each drug class, present in genotypic resistance testing.

2.3.1 Genetic testing

A confirmed diagnosis of MDR HIV-1 is a condition of funding approval.

- The application should include a copy of a test confirming a diagnosis of HIV-1.
- A copy of a genotypic resistance test confirming MDR HIV-1 should be included with the application for funding approval. This should indicate the presence of at least one major resistance mutation within at least two of the standard ARV drug classes.

2.4 Patient clinical history/status

Funding approval will only be supported in MDR HIV-1 when patients:

- Cannot construct a fully-active regimen with existing ARVs due to previous intolerance to ARVs, contraindications to ARVs, drug-drug interactions, and other relevant clinical factors.
- Have at least one fully active and available drug in two or fewer ARV classes.

It is expected that patients will be experiencing virological failure with their existing antiretroviral therapy (ART) (i.e. HIV-1 ribonucleic acid [RNA] > 200 copies /mL).

Fostemsavir must be administered in combination with at least one additional ARV in order for funding approval to be supported.

2.4.1 Virological failure with existing ART regimens

When reviewing the application, the MMP require evidence to validate that the patient is experiencing virological failure with the current ART regimen, where relevant. Virological failure is indicated by an elevated viral load, i.e. HIV-1 ribonucleic acid (RNA) > 200 copies /mL.

2.4.2 Cannot construct a fully-active regimen with existing ARVs due to previous intolerance to ARVs, contraindications to ARVs, drug-drug interactions and other relevant clinical factors

When reviewing the application, the MMP require evidence to validate that the patient has experienced intolerance to the existing ART regimen, or that existing ART regimens are not clinically advisable.

2.4.3 Have at least one fully active and available drug in two or fewer ARV classes

When reviewing the application, the MMP require evidence to validate that there is at least one fully active and available drug, in two or fewer ARV classes, suitable for administration in combination with fostemsavir. Clinicians are required to provide details of the proposed treatment regimen including fostemsavir. Patients must be treated with at least one additional ARV agent in combination with fostemsavir in order for approval of funding to be supported.

2.4.4 Exclusion criteria

Applications for funding approval will not be considered for individuals who meet any of the contraindications for treatment as outlined in the relevant SmPC.

In line with the SmPC, approval of funding will not be considered in patients with HIV-1 Group 1 subtype CRF01_AE strains.

2.5 Patient's medical treatment

When reviewing applications, the MMP may request evidence to validate that the patient has been in receipt of ART, e.g. printout of dispensed medicinal products.

3. Discontinuation criteria

The approved consultant should routinely monitor patient response to fostemsavir. Treatment with fostemsavir should be discontinued in the following circumstances:

- Limited or loss of response, as determined by the viral load compared to baseline, measured at six-monthly intervals from initiation of the fostemsavir-containing regimen. Viral load > 200 copies /mL is considered inadequate virological suppression.
- Emergence of treatment resistance to fostemsavir, as evidenced by genotypic resistance testing.
- Intolerable adverse events or other safety concerns.

4. Medicines management

Please refer to the relevant SmPC for Rukobia® for full prescribing information including monitoring and patient counselling requirements. Sites must ensure a local policy is in place for appropriate medicines management taking into consideration information outlined in the SmPCs and conditions of the marketing authorisation.