Medicines Management Programme

Managed Access Protocol – Odevixibat (Bylvay®) for the treatment of progressive familial intrahepatic cholestasis (PFIC) in patients aged six months or older

Medicine	Date of addition to Managed Access Protocol
Odevixibat (Bylvay®)	01/12/2024

Approved by	Professor Michael Barry, Clinical Lead, Medicines Management Programme	
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Table of Contents

List of Tables

List of abbreviations

BSEP Bile salt export pump
HSE Health Service Executive
HTH High Tech Hub
IBAT Ileal bile acid transporter
MAP Managed Access Protocol
MMP Medicines Management Programme
PCRS Primary Care Reimbursement Service
PFIC Progressive familial intrahepatic cholestasis
SmPC Summary of product characteristics

1.Odevixibat

Odevixibat (Bylvay®) is a reversible, potent, selective inhibitor of the ileal bile acid transporter (IBAT).

Odevixibat acts locally in the distal ileum to decrease the reuptake of bile acids and increase the clearance of bile acids through the colon, reducing the concentration of bile acids in the serum.

From 1 December 2024, four presentations of odevixibat are available on the High Tech Arrangement.

- Bylvay® 200 mcg capsules
- Bylvay® 400 mcg capsules
- Bylvay® 600 mcg capsules
- Bylvay® 1200 mcg capsules

1.1 Licensed indication

Odevixibat is indicated for the treatment of progressive familial intrahepatic cholestasis (PFIC) in patients aged six months or older.

1.2 Reimbursement

Reimbursement of odevixibat on the High Tech Arrangement is supported only for the licensed indication as outlined in section 1.1, in patients who meet the criteria outlined in this Managed Access Protocol (MAP). All criteria must be satisfied in order for reimbursement to be supported. Reimbursement is not supported for any other indication.

An application for reimbursement approval is required to be submitted on an individual patient basis. The *Odevixibat Reimbursement Application Form* should be completed and sent by secure email to the Health Service Executive (HSE)-Medicines Management Programme (MMP) at mmp@hse.ie.

The recommended dose of odevixibat is 40 mcg/kg administered orally once daily in the morning.

Table 1 outlines the strength and number of capsules that should be administered daily based on body weight to approximate a 40 mcg/kg/day dose. Please refer to the Summary of Product Characteristics (SmPC) for further prescribing information.

Table 1: Number of Bylvay® capsules needed to achieve the nominal dose of 40 mcg/kg/day

Body weight (kg)	Number of 200 mcg capsules		Number of 400 mcg capsules
4 to < 7.5	**1**	or	N/A
7.5 to < 12.5	**2**	or	1
12.5 to < 17.5	**3**	or	N/A
17.5 to < 25.5	**4**	or	2
25.5 to < 35.5	6	or	**3**
35.5 to < 45.5	8	or	**4**
45.5 to < 55.5	10	or	**5**
≥ 55.5	12	or	**6**

Capsule strength/number in **bold** is recommended based on predicted ease of administration.

Kg: kilogram; mcg: micrograms, N/A: not applicable

If an adequate clinical response has not been achieved after three months of continuous therapy, the dose may be increased up to 120 mcg/kg/day. Table 2 outlines the strength and number of capsules that should be administered daily based on body weight to approximate a 120 mcg/kg/day dose, with a maximum daily dose of 7,200 mcg per day. Please refer to the SmPC for further prescribing information.

Table 2: Number of Bylvay® capsules needed to achieve the nominal dose of 120 mcg/kg/day

Body weight (kg)	Number of 600 mcg capsules		Number of 1200 mcg capsules
4 to < 7.5	**1**	or	N/A
7.5 to < 12.5	**2**	or	1
12.5 to < 17.5	**3**	or	N/A
17.5 to < 25.5	**4**	or	2
25.5 to < 35.5	6	or	**3**
35.5 to < 45.5	8	or	**4**
45.5 to < 55.5	10	or	**5**
≥ 55.5	12	or	**6**

Capsule strength/number in **bold** is recommended based on predicted ease of administration.

Kg: kilogram; mcg: micrograms, N/A: not applicable

If a patient is recommended for reimbursement of odevixibat, reimbursement is supported in line with the licensed therapeutic dosage, i.e. initiation at the recommended dose of 40mcg/kg/day, up to a maximum daily dose of 7,200 mcg per day if required. Reimbursement of dosages in excess of the licensed therapeutic dosages (as outlined in Tables 1 and 2) is not supported.

See Section 3 for further details on Reimbursement criteria – Discontinuation.

1.3 Reimbursement price

The reimbursement prices of the presentations of odevixibat available on the High Tech Arrangement are outlined in Table 3. Commercial-in-confidence arrangements are in place with the marketing authorisation holder to reduce the net acquisition cost of odevixibat to the HSE.

Table 3: Reimbursement codes and prices for the presentations of odevixibat available on the High Tech Arrangement

Strength	Pack size	Code	Reimbursement price*
Bylvay® 200 mcg capsules	30	89352	€3,759.77
Bylvay® 400 mcg capsules	30	89353	€7,512.12
Bylvay® 600 mcg capsules	30	89354	€11,185.46
Bylvay® 1200 mcg capsules	30	89355	€22,490.69

mcg: micrograms
*Correct as at 1 December 2024

2.Reimbursement criteria – Initiation

This section outlines the criteria that must be satisfied in order for patients to be recommended for reimbursement of odevixibat for PFIC under the High Tech Arrangement.

2.1 Prescribers

Applications for reimbursement approval for odevixibat for the treatment of PFIC under the High Tech Arrangement will only be considered from consultant hepatologists and gastroenterologists registered with the Irish Medical Council, who are experienced in the management of PFIC, and who have agreed to the terms of this MAP and been approved by the HSE ('approved consultants').

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

The prescribing of Bylvay® for approved patients for the treatment of PFIC under the High Tech Arrangement will be confined to the approved consultants and their teams. The governance of the team on the High Tech Hub (HTH), including access, rests with the approved consultant.

2.2 Patient age

Applications for reimbursement approval will only be considered for individuals aged six months or older at the time of application. It is expected that applications will be received on behalf of paediatric patients.

2.3 Patient diagnosis

Clinicians must provide evidence of a documented diagnosis of PFIC as outlined in the following sections.

2.3.1 Patient history

For reimbursement approval, clinicians are required to provide a detailed patient history to support the diagnosis of PFIC, and include:

- Age at presentation with jaundice
- Age at presentation with abnormal liver function tests
- Presence of any extrahepatic manifestations, if relevant.

2.3.2 Genetic testing

For reimbursement approval, clinicians are required to submit evidence of documented genetic testing confirming the diagnosis of PFIC.

2.3.3 Liver function tests

For reimbursement approval, clinicians are required to submit recent liver function tests to support the diagnosis of PFIC.

2.3.4 Liver biopsy

For reimbursement approval, clinicians are required to submit a liver biopsy report to support the diagnosis of PFIC.

2.3.5 Liver ultrasound

For reimbursement approval, clinicians are required to submit a liver ultrasound report to support the diagnosis of PFIC.

2.4 Patient clinical status

In line with the SmPC for Bylvay®, applications for reimbursement approval will not be considered for individuals who meet any of the contraindications for treatment outlined in the SmPC.

2.4.1 Exclusion criteria

In line with the exclusion criteria from the pivotal PEDFIC 1 trial, the PEDFIC 2 trial, and the SmPC for Bylvay®, applications for reimbursement approval will not be considered for:

- Conditions, medications or surgical procedures that impair either gastrointestinal motility, or enterohepatic circulation of bile acids, including bile salt transport to biliary canaliculi which have the potential to reduce the efficacy of odevixibat
- Patients with pathologic variations of the ABCB11 gene that predict complete absence or lack of function of the bile salt export pump (BSEP) protein (i.e. patients with BSEP3 subtype of PFIC2)
- Patients with severe hepatic impairment (Child-Pugh C)
- Patients with body weight less than 4 kg
- Patient with past medical history or ongoing presence of other types of liver disease including, but not limited to, the following:
    - Biliary atresia of any kind
    - Alagille syndrome
    - Alpha 1-antitrypsin deficiency
    - Cystic fibrosis
    - Sclerosing cholangitis
    - Extrahepatic bile duct obstruction
    - Primary disorders of bile acid synthesis
    - Benign recurrent intrahepatic cholestasis, indicated by any history of normal serum bile acids
    - Suspected or proven liver cancer or metastasis to the liver on imaging studies
    - Histopathology on liver biopsy that is suggestive of alternate non-PFIC related aetiology of cholestasis
- Decompensated liver disease, coagulopathy, history or presence of clinically significant ascites, variceal haemorrhage, and/or encephalopathy.

2.5 Patient's medical treatment

2.5.1 Current medications

Clinicians must provide details of the patient's medical treatment at the time of application.

2.6 Baseline parameters

Clinicians are required to submit the following parameters, taken within one month of the date of application, in order to establish baseline levels prior to commencement of treatment with odevixibat:

- Serum bile acid levels
- Liver function tests
- Pruritus assessment.

3. Reimbursement criteria – Discontinuation

Odevixibat should be discontinued and reimbursement may no longer be supported after six months of continuous therapy in the absence of an adequate clinical response as outlined in section 3.2 below.

3.1 Follow-up data

Follow-up data will be requested by the MMP for audit purposes and provision of same is a condition of ongoing reimbursement. It is the responsibility of the approved consultant to ensure that the patient or their representative/guardian is aware that the provision of follow-up data is a condition of reimbursement, and that audits may occur during which their personal data will be reviewed.

Follow-up information should be submitted and sent by secure email to the MMP (mmp@hse.ie) when requested outlining:

- Serum bile acid levels
- Liver function tests
- Pruritus assessment
- Any changes to clinical history since initiation
- Whether odevixibat is to be continued or discontinued.

3.2 Assessment of clinical response

There should be an assessment of clinical response at months three and six followed by treatment discontinuation in the absence of an adequate response.

3.2.1 Assessment of clinical response after three months of treatment with odevixibat at 40 mcg/kg once daily dose

An adequate response to treatment is an improvement in at least two of the following parameters: serum bile acid levels, liver function tests and pruritus.

3.2.2 Assessment of clinical response after six months of treatment with odevixibat at doses up to 120 mcg/kg once daily dose

If an adequate clinical response has not been achieved after three months of continuous therapy, the dose may be increased up to 120 mcg/kg/day, with a maximum daily dose of 7,200 mcg per day.

Treatment should be discontinued in the absence of an adequate response following six months of continuous daily treatment with odevixibat. As above, an adequate response to treatment is an improvement in at least two of the following parameters: serum bile acid levels, liver function tests and pruritus.

4. Prescribing of odevixibat for approved patients

Please refer to the SmPC for Bylvay® for full prescribing information including monitoring and patient counselling requirements.

If a patient is recommended for reimbursement by the HSE-MMP, the High Tech prescription should be generated on the HTH. High Tech prescriptions which are not hub generated for odevixibat will not be eligible for reimbursement by the HSE Primary Care Reimbursement Service (PCRS). Only approved consultants and their teams will have access to generate prescriptions.