Bylvay®
odevixibat

Reduction in serum bile acid and pruritus with Bylvay – a treatment for children with PFIC[1]

Bylvay has proven efficacy in children with progressive familial intrahepatic cholestasis (PFIC)[1]

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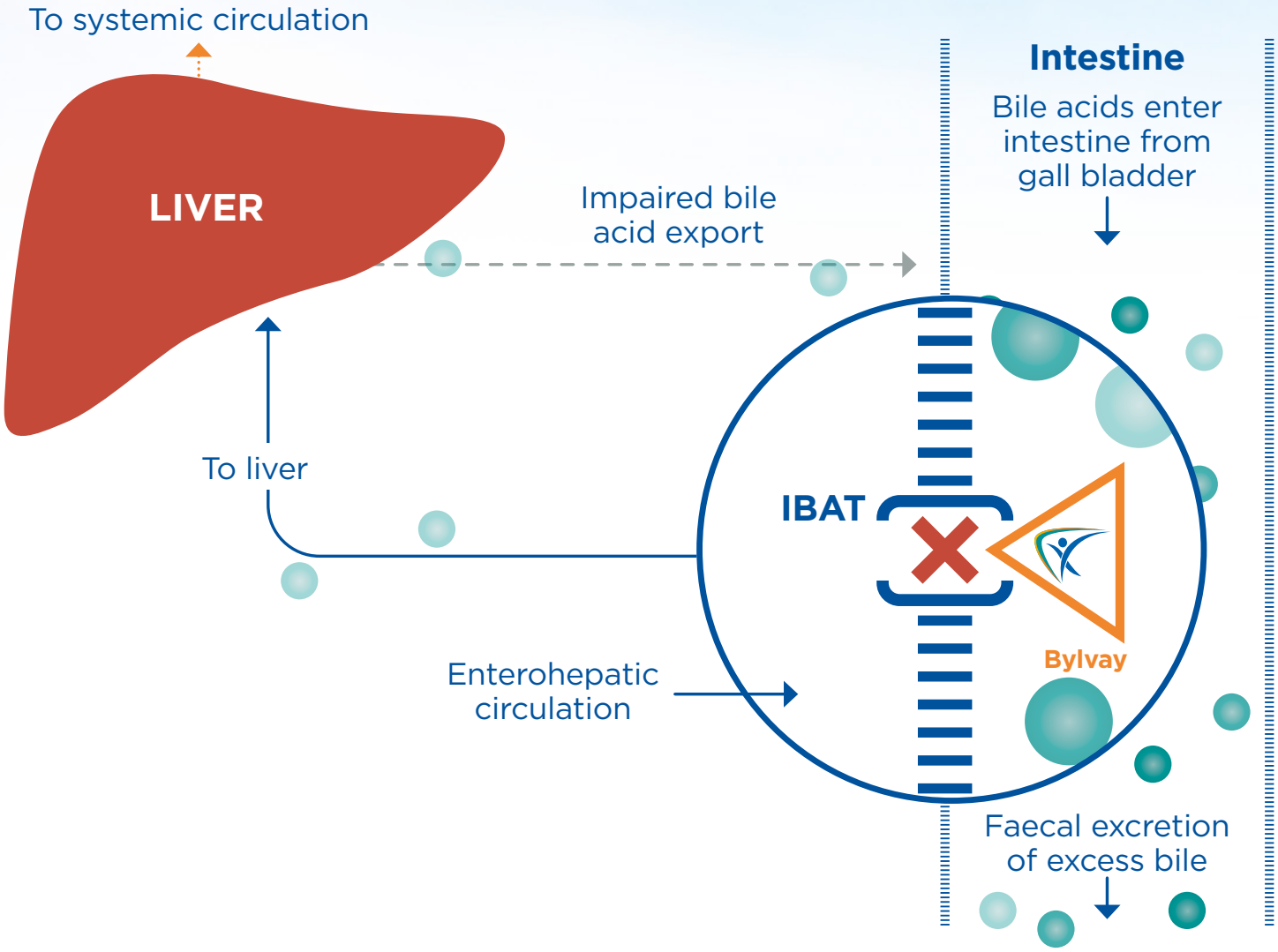
Instructions on how to access the prescribing and adverse event reporting information can be found on the final page.

Bylvay is indicated for the treatment of progressive familial intrahepatic cholestasis (PFIC) in patients aged 6 months or older[1]

1. Bylvay Summary of Product Characteristics.

Bylvay is the first licensed non-surgical biliary diversion treatment for PFIC

Bylvay is a reversible, selective ileal bile acid transporter (IBAT) inhibitor[1]



IBAT: ileal bile acid transporter; PFIC: progressive familial intrahepatic cholestasis

1. Bylvay Summary of Product Characteristics.

Progressive familial intrahepatic cholestasis (PFIC)

Bylvay delivers serum bile acid reductions, relief from pruritus, and gains in growth

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The first global phase 3 clinical trials in PFIC showed:[1-4]

Significantly more Bylvay-treated patients achieved serum bile acid (sBA) response at week 24 vs placebo (primary endpoint):[1]

- **43.5% (10/23)** of patients on Bylvay 40 µg/kg/day vs **0% (0/20)** of patients on placebo (p=0.0015)
- **21.1% (4/19)** of patients on Bylvay 120 µg/kg/day vs **0% (0/20)** of patients on placebo (p=0.0174)

Bylvay provides sustained relief from pruritus (exploratory endpoints)[1,5]

- **68% (52/77)** of children had clinically meaningful reductions in pruritus at 72 weeks vs baseline[5]
- Pruritus responders and their families benefited from significant improvements in the percentage of days needing help falling asleep, needing soothing, and sleeping with caregivers (all p<0.001)[6]

Over time, improvements in growth were observed in children treated with Bylvay (post hoc subgroup analysis)[4]

- Mean height and weight z-scores increased over time in Bylvay-treated patients vs baseline over 96 weeks[4]

Data from pooled analysis of PEDFIC-1 and PEDFIC-2 studies of odevixibat in PFIC. PEDFIC-1 was a double-blind, randomised controlled phase 3 trial where 62 patients aged 6 months to 18 years with PFIC1 or PFIC2 were randomised 1:1:1 to odevixibat 40 µg/kg/day (n=23), odevixibat 120 µg/kg/day (n=19) or placebo (n=20). Primary endpoints were change in pruritus over 24 weeks and serum bile acid response, defined as proportion of patients with at least a 70% reduction in fasting sBA levels from baseline to the end of treatment or who achieved a level ≤70 µmol/L at week 24. PEDFIC-2 included patients treated with either odevixibat or placebo during PEDFIC-1 and patients of any age with any time of PFIC2, with a body weight of more than or equal to 5 kg at screening. Patients on placebo in PEDFIC-1 were transferred to odevixibat in PEDFIC-2. All patients received odevixibat 120µg/kg/day in PEDFIC-2, which is an ongoing, open-label study

PFIC: progressive familial intrahepatic cholestasis; sBA: serum bile acid

1. Bylvay Summary of Product Characteristics. **2.** ClinicalTrials.gov. PEDFIC 1. NCT03566238. Available at: https://www.clinicaltrials.gov/study/NCT03566238. Last accessed November 2024. **3.** ClinicalTrials.gov. PEDFIC 2. NCT03659916. Available at: https://clinicaltrials.gov/study/NCT03659916. Last accessed November 2024. **4.** Thompson RJ, *et al.* Long-term efficacy and safety of odevixibat in patients with progressive familial intrahepatic cholestasis: results with 96 weeks or more of treatment. Poster presented at AASLD: American Association for the Study of Liver Diseases; November 4–8, 2022; Washington, DC, USA. **5.** Sturm E, *et al.* Outcomes with Odevixibat in patients with progressive familial intrahepatic cholestasis by level of pruritus reduction: pooled analysis from the PEDFIC trials. Poster presented at the 2022 NASPGHAN/CPNP/APGNN Annual Meeting, October 12–15, 2022; Orlando, FL, USA. **6.** Gupte G, *et al.* 2022 EASL International Liver Congress, June 22–28, 2022; London, UK.

Progressive familial intrahepatic cholestasis (PFIC)

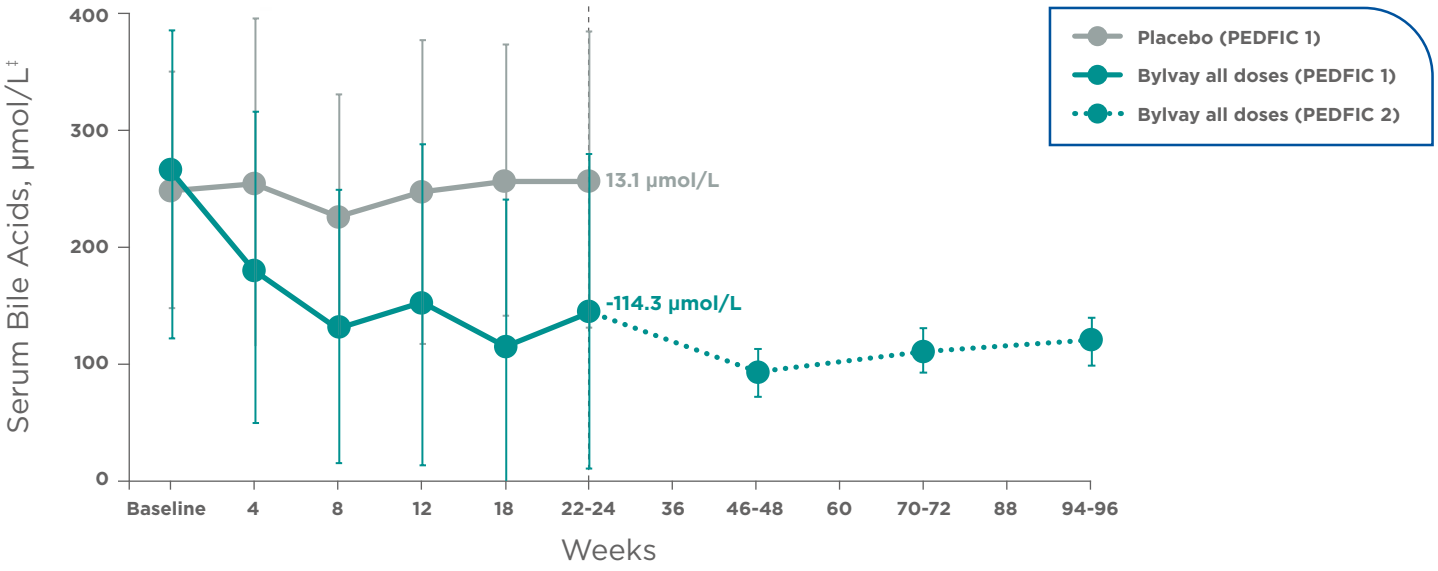
Bylvay offers early and sustained serum bile acid reduction

Serum bile acid levels correlate with liver toxicity effects[1]

Bylvay had a significant, clinically meaningful effect on sBA reduction vs placebo at 24 weeks*[2]

Bylvay 40 µg/kg/day: 43.5% (10/23);
Bylvay 120 µg/kg/day: 21.1% (4/19);
placebo 0% (0/20)
(p=0.0015 and 0.0174 vs placebo, respectively)

Change to serum bile acids over 96 weeks†[3,4]



Adapted from Thompson RJ, *et al.*

†All patients transition to Bylvay 120 µmol/L after 24 weeks when entering PEDFIC 2

‡ Error bars show SD and SE for measurements taken during the PEDFIC 1 and PEDFIC 2 studies, respectively

Bile acid reduction could prevent progressive liver damage and preserve native liver health[3,5–6]

- Lowering sBA is associated with less liver injury and higher native liver survival[6]
  - A sBA concentration below 102 µmol/L or a decrease of at least 75%, shortly after SBD, reliably predicted native liver survival of ≥15 years following SBD in PFIC2 patients (p<0.001)[7]

sBA: serum bile acid; SBD: surgical biliary diversion; SD: standard deviation; SE: standard error

*PEDFIC 1, Primary Endpoint: Proportion of patients with at least a 70% reduction in fasting sBA levels from baseline to the end of treatment or who achieved a level ≤70 µmol/L at week 24[2]

1. van Wessel DBE, *et al.* Hepatol. 2021;74:892–906.
2. Bylvay Summary of Product Characteristics.
3. Thompson RJ, *et al.* Lancet Gastroenterol Hepatol. 2022;7:830–42.
4. Thompson RJ, *et al.* Long-term efficacy and safety of odevixibat in patients with progressive familial intrahepatic cholestasis: results with 96 weeks or more of treatment. Poster presented at AASLD: American Association for the Study of Liver Diseases; November 4–8, 2022; Washington, DC, USA.
5. Gunaydin M, *et al.* Hepat Med. 2018;10:95–104.
6. Karpen SJ, *et al.* Hepatol Int. 2020;14:677–89.
7. Jones-Hughes T, *et al.* Orphanet J Rare Dis. 2021;16:255.

Progressive familial intrahepatic cholestasis (PFIC)

Bylvay sBA responses associated with native liver survival

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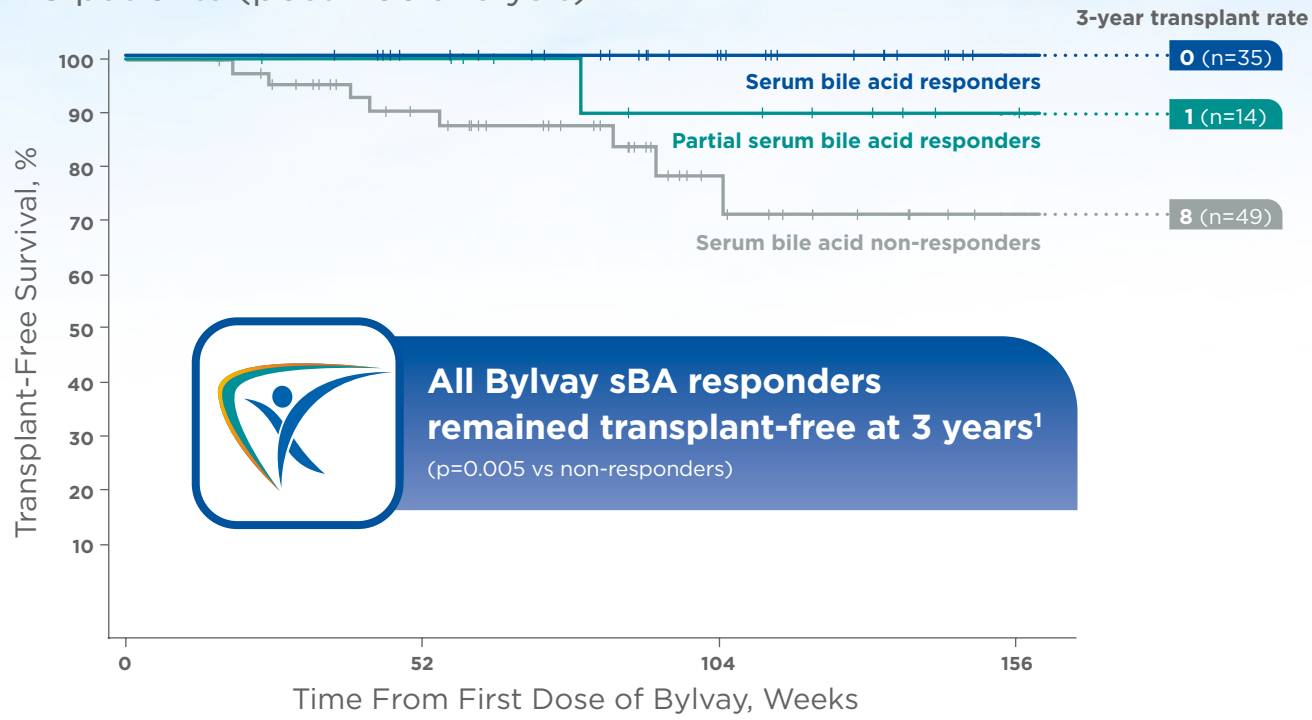
Native liver survival: long-term transplant-free survival rates in all types of PFIC patients (post-hoc analysis)[1]



Number at risk				
35	29	18	4	Serum bile acid responders
14	13	8	3	Partial serum bile acid responders
49	34	11	1	Serum bile acid non-responders

Adapted from Thompson, RJ *et al.*

Native liver survival can help preserve children's quality of life[2]

A review concluded PFIC patients living with native livers had HRQL scores comparable to healthy controls[2]

In contrast, patients with liver transplant had significantly lower mean school functioning scores (p=0.01) and suffered diarrhoea that could impact quality of life and catch-up growth[2]

Bylvay may also help children with PFIC1 to thrive after liver transplant[3]

Real-world data of 3 patients in post-transplant PFIC1 patients showed treatment with Bylvay reduced severe diarrhoea and improved concentration, weight gain and height compared to baseline[3]

HRQL: health-related quality of life; PFIC: progressive familial intrahepatic cholestasis; sBA: serum bile acid

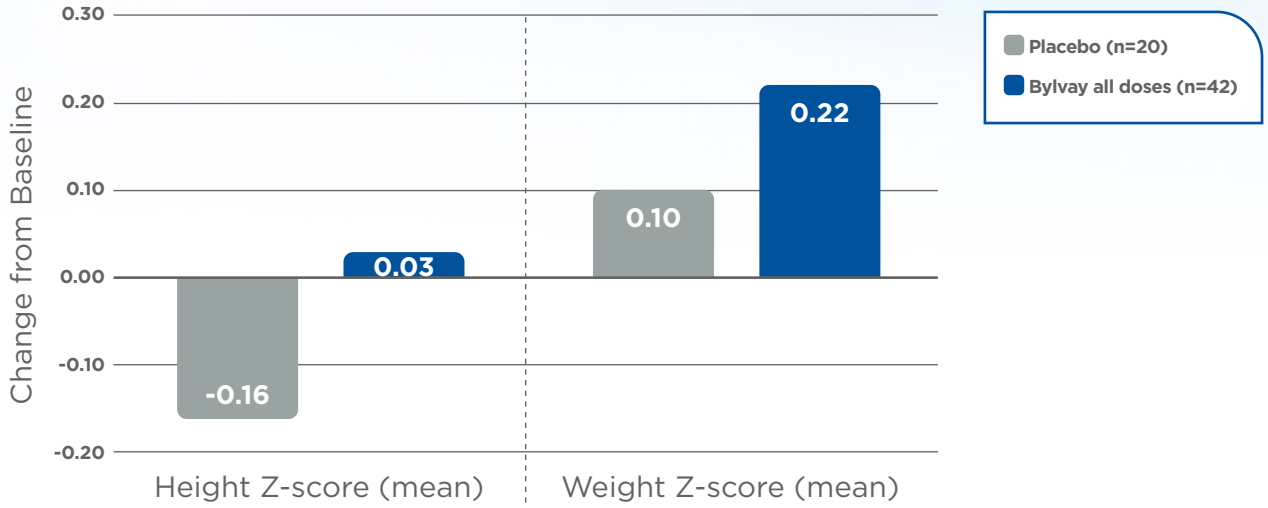
1. Thompson RJ, et al. JHEP Rep. 2023;5(8):100782.
2. Jones-Hughes T, *et al.* Orphanet J Rare Dis. 2021;16:255.
3. Vogel GF, *et al.* Odevixibat therapy in patients with FIC1-deficient progressive familial intrahepatic cholestasis and diarrhoea following liver transplantation that impacted daily activities: a retrospective case series. Poster presented at AASLD: American Association for the Study of Liver Diseases; November 4–8, 2022; Washington, DC, USA.

Progressive familial intrahepatic cholestasis (PFIC)

Over time, improvements in growth were observed in children treated with Bylvay

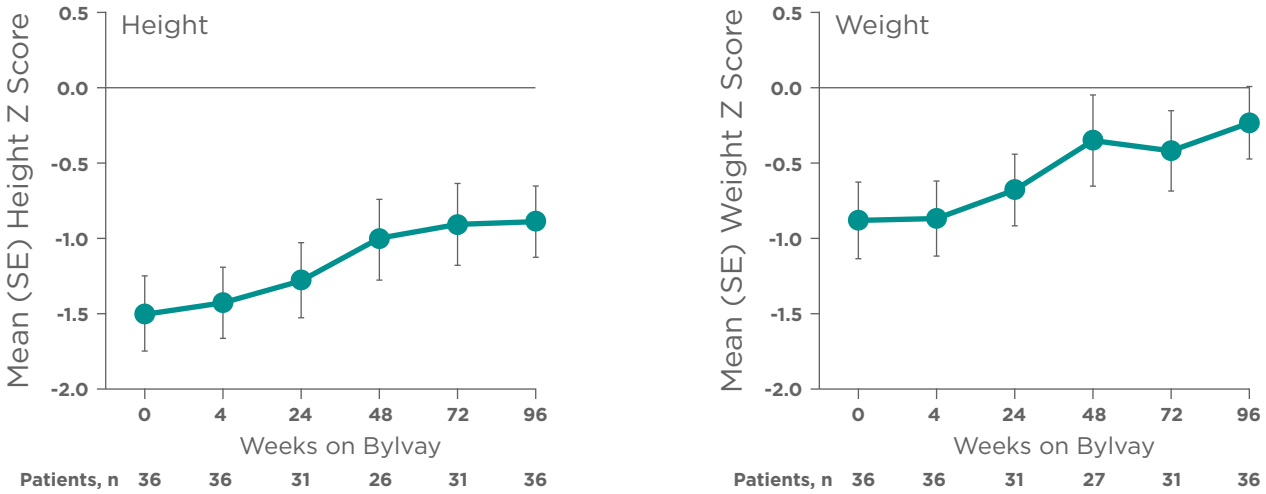
Patients with PFIC who received Bylvay experienced:

Gains in height and weight z-scores at 24 weeks (secondary endpoint, not significant)[1]



Adapted from the Bylvay SmPC.

In a subgroup pooled analysis of PEDFIC 1 and 2, sustained gains in growth with height and weight across 96 weeks[2]



Adapted from Thompson RJ, *et al.*

Improved height and weight indicate enhanced growth velocity and potential for catch-up growth in actively growing children[1]

SE: standard error

1. Bylvay Summary of Product Characteristics.

2. Thompson RJ, *et al.* Long-term efficacy and safety of odevixibat in patients with progressive familial intrahepatic cholestasis: results with 96 weeks or more of treatment. Poster presented at AASLD: American Association for the Study of Liver Diseases; November 4–8, 2022; Washington, DC, USA.

Progressive familial intrahepatic cholestasis (PFIC)

Sustained relief from pruritus

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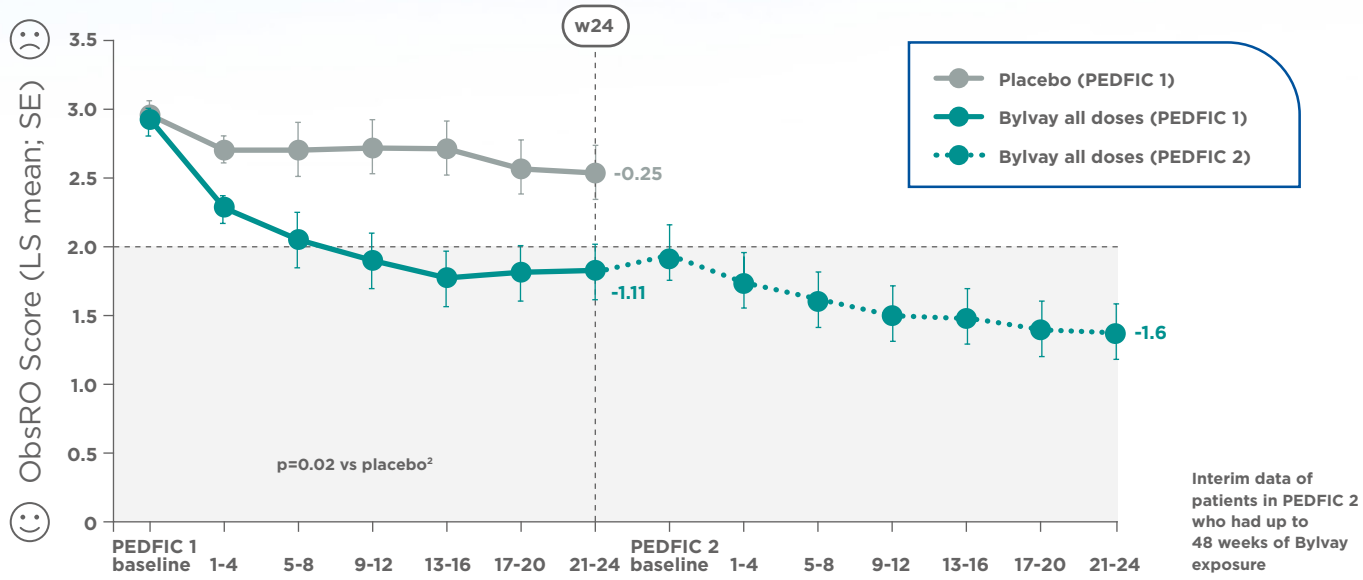
Bylvay delivered a clinically meaningful improvement in pruritus vs placebo at 24 weeks:*[1]

Bylvay 40 µg/kg/day: 58.3 % (n=23);
Bylvay 120 µg/kg/day: 47.7 % (n=19);
placebo 28.7 % (n=20)

Change in mean pruritus severity scores over 48 weeks[†2,3]



Adapted from Thompson RJ, *et al.* 2022 and Thompson RJ, *et al* 2023[2,3]

[†]All patients transition to Bylvay 120 µmol/L after 24 weeks when entering PEDFIC 2

*Proportion of positive pruritus assessments at the patient level over the 24-week treatment period, based on an observer-reported outcome (ObsRO) instrument.[1] Patients' pruritus was recorded by an observer twice daily (morning and evening).[1] Efficacy was assessed using an ObsRO scale from 0–4, with 0 being no itching.[1] An ObsRO score change of -1 point from baseline could be considered clinically meaningful[1]

68% of children had clinically meaningful reductions in pruritus at 72 weeks vs baseline (exploratory pooled analysis of PEDFIC 1 and 2)[4]

-1.5 average drop in ObsRO score[5]

ObsRO: observer-reported outcome; SE: standard error

1. Bylvay Summary of Product Characteristics.
2. Thompson RJ, *et al.* Lancet Gastroenterol Hepatol. 2022;7:830–42.
3. Thompson RJ, et al. JHEP Rep. 2023;5(8):100782.
4. Sturm E, *et al.* Outcomes with Odevixibat in patients with progressive familial intrahepatic cholestasis by level of pruritus reduction: pooled analysis from the PEDFIC trials. Poster presented at the 2022 NASPGHAN/CPNP/APGNN Annual Meeting, October 12–15, 2022; Orlando, FL, USA.
5. Dalgic B, *et al.* Relationships between decreases in serum bile acids, pruritus, and sleep disturbance scores with up to 72 weeks of Odevixibat treatment in patients with progressive familial intrahepatic cholestasis. Poster presented at the 2022 NASPGHAN/CPNP/APGNN Annual Meeting, October 12–15, 2022; Orlando, FL, USA.

Progressive familial intrahepatic cholestasis (PFIC)

Bylvay pruritus-responders and their families benefited from improvements in sleep patterns

In a post hoc pooled analysis of PEDFIC 1 and 2, Bylvay pruritus-responders and their families benefited from improved sleeping patterns vs baseline (all p<0.001)[1]

76%
fewer days
needing help to fall asleep[1]

75%
fewer days
needing soothing from a caregiver[1]

55%
fewer days
needing to sleep with a caregiver[1]

37%
fewer days
of scratching with bleeding[1]

Childhood sleep deprivation results in more than just tiredness

Severe sleep insufficiency in children has been linked to failure to thrive and delayed developmental milestones[2]

Decrease of disruptive sleep parameters in patients with ≥1 point ObsRO reduction*

*In the PEDFIC trials, cholestatic pruritus was measured using the PRUSCISION ObsRO scale, a validated 5-point scale: scores were recorded twice daily by an observer; all patients had a baseline score of ≥2 (medium to severe itching)[3]

ObsRO: observer-reported outcome

1. Gupte G, *et al.* 2022 EASL International Liver Congress, June 22–28, 2022; London, UK.
2. Fadzil A. Children. 2021;8:122.
3. Gwaltney C, *et al.* Adv Ther. 2022;39:5105–25.

Simple and flexible once-daily oral dosing[1]

Bylvay® odevixibat

Ability to provide efficacy at 40 µg/kg/day, and the flexibility to dose escalate to 120 µg/kg/day if an adequate clinical response has not been achieved after 3 months of continuous therapy.[1]

All capsules can be swallowed whole or can be opened and sprinkled onto food.

Bylvay is available in a 200, 400, 600 and 1200 µg capsule.

The larger 200 µg and 600 µg capsules are intended to be opened and sprinkled on food but may be swallowed whole.

The smaller 400 µg and 1200 µg capsules are intended to be swallowed whole but may be opened and sprinkled on food.

If the capsule is to be swallowed whole, the patient should be instructed to take it with a glass of water in the morning.

Body weight (kg)	**Total daily dose for 40 µg/kg/day** (µg)	**Total daily dose for 120 µg/day** (µg)
4 to <7.5	**200**	**600**
7.5 to <12.5	**400**	**1200**
12.5 to <17.5	**600**	**1800**
17.5 to <25.5	**800**	**2400**
25.5 to <35.5	**1200**	**3600**
35.5 to <45.5	**1600**	**4800**
45.5 to <55.5	**2000**	**6000**
≥55.5	**2400**	**7200**

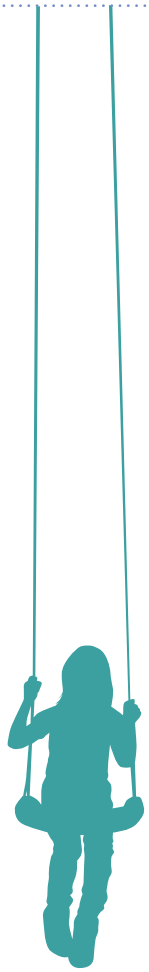
Maximum licensed dose = 7200 µg/day

For full dosing and administration information, please refer to SmPC.

1. Bylvay Summary of Product Characteristics.

Bylvay is well tolerated with a low adverse event (AE) rate

- Common AEs include diarrhoea, abdominal pain, haemorrhagic diarrhoea, soft faeces and hepatomegaly[1]
- Only 1% of patients discontinued Bylvay due to diarrhoea[1]
- Diarrhoea may lead to dehydration. Patients should be monitored regularly to ensure adequate hydration during episodes of diarrhoea[1]



AE: adverse event

1. Bylvay Summary of Product Characteristics.

Progressive familial intrahepatic cholestasis (PFIC)

Reduction in serum bile acid and pruritus with Bylvay – a treatment for children with PFIC[1]

Bylvay® odevixibat

Treat and relieve the symptoms of PFIC without invasive surgery by addressing the underlying cause of cholestasis[1]

Significantly more patients treated with Bylvay achieved a serum bile acid response at week 24 compared with placebo (p=0.003)*[2]

- **Bylvay-induced reductions** in sBA were significant and sustained to week 96 of treatment (p<0.001)[3]
- **Bylvay sBA responders had preserved native liver** for 3 years (ad hoc supplementary analysis)[4]
- **Bylvay supported clinically meaningful relief** from life-changing pruritus vs placebo[1]
- **Over time, improvements in growth were observed in children treated with Bylvay**[4]

BYLVAY: Indicated for the treatment of PFIC in **patients aged 6 months or older**[1]

*__Serum Bile Acid Response__ defined as serum bile acids ≤70 µmol/L at week 24 or a reduction from baseline to week 24 of ≥70%

PFIC: progressive familial intrahepatic cholestasis; sBA: serum bile acid

1. Bylvay Summary of Product Characteristics.
2. Thompson RJ, *et al.* Lancet Gastroenterol Hepatol. 2022;7:830–42.
3. Thompson RJ, *et al.* Long-term efficacy and safety of odevixibat in patients with progressive familial intrahepatic cholestasis: results with 96 weeks or more of treatment. Poster presented at EASL: European Association for the Study of the Liver; June 21–24, 2023; Vienna, Austria.
4. Thompson RJ, *et al.* JHEP Rep. 2023;5(8):100782.

Prescribing information

Bylvay® odevixibat

▼ This medicinal product is subject to additional monitoring.

Click here to access Bylvay prescribing and adverse event reporting information

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