IPSEN

Intended for UK Healthcare Professionals only.

Bylvay® ▼
odevixibat

Progressive Familial Intrahepatic Cholestasis (PFIC)

Could PFIC be the hidden cause of cholestasis and pruritus in your adult patients?

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

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

1. Bylvay Summary of Product Characteristics.

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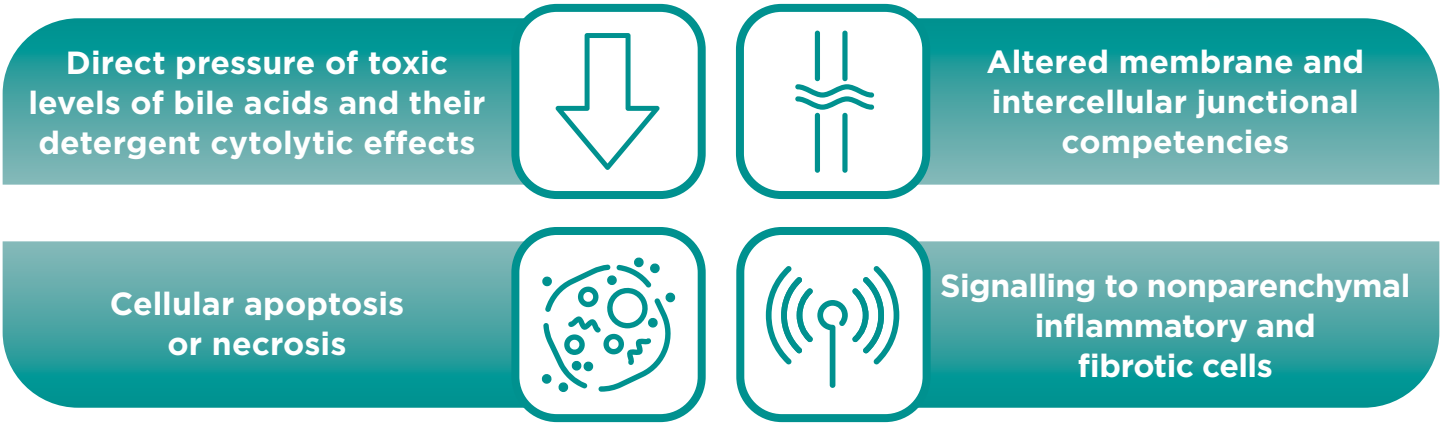
Adult-onset PFIC and the cholestatic patient

- PFIC is a rare and treatable genetic condition often assumed to be exclusively diagnosed in children but can also have an adult onset[2,3]
- PFIC is characterised by cholestatic disease with elevated serum bile acids and often pruritus[2,3]
- Toxic effects associated with raised serum bile acids can lead to permanent liver damage (fibrosis and cirrhosis) and ultimately end stage liver disease[3-5]

Mechanisms for hepatocyte and cholangiocyte harm due to elevated bile acids in the hepatobiliary system include:[4]



- In paediatric patients with PFIC, lowering serum bile acids is associated with higher native liver survival (avoidance of liver transplant) for up to 3 years[6]

Check serum bile acid levels as part of your diagnostic investigations in cholestatic patients

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The science is evolving

Today, PFIC is associated with a broadening collection of genetic defects linked to bile transport and signalling mechanisms.[2,5]

Evolving spectrum of known and potential PFIC gene defects[7-9]

	PFIC 1	PFIC 2	PFIC 3	PFIC 4	PFIC 5	PFIC 6	PFIC 7	PFIC 8-12
Protein Deficiency	FIC 1	BSEP	MDR3	TJP2	FXR	OST-A	USP53	**Ongoing research continues to highlight links to new genes e.g. KIF12, ZFYVE19, SEMA7A, SLC51A, VPS33B**
Mutated Gene	*ATP8B1*	*ABCB11*	*ABCB4*	*TJP2*	*NR1H4*	*MYO5B*	*USP53*	

Although genetic screening for adults is not always conclusive, PFIC genetic defects are being identified in a widening variety of adult cholestatic patients.[2,5,10] Adult-onset cases of PFIC are often heterozygotic, i.e. only have one mutant allele.[10]

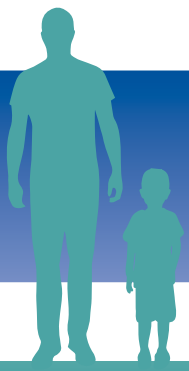
In a recent study, ~ 1 in 4 patients with adult-onset cholestatic liver disease had a PFIC related genotype[10]

28% **Incidence of PFIC gene variants in a cohort of 356 patients with adult-onset liver disease[10]**

Patients were only screened for 3 of the 12 known PFIC gene variants:[10]

ABCB4 **ABCB11** **ATP8B1**

Adults:
Milder, more sporadic or insidious phenotypes



Children:
Aggressive and known paediatric onset

Identifying patients with adult onset PFIC

Adult onset PFIC is a **clinical** diagnosis. Cholestatic patients with **elevated serum bile acids** and **pruritus** signal the need for further investigation.[2,3]

Further investigate these patients if they have high sBA and pruritus:

Idiopathic cholestasis[3,11-13]

May be difficult to definitively diagnose, but symptoms can include:

- Jaundice
- Pruritus
- Diarrhoea
- Abnormal hepatic lab parameters
- Evidence of liver disease progression

Secondary cholestasis

- **Intrahepatic cholestasis of pregnancy** (ICP)[11]
- **Drug induced liver injury**/acute failure due to cholestasis, not obstruction[11]
- **Hormonal-induced cholestatis** (triggered by menopause or birth control)[11,14]
- **Family history of cholecystectomy,** with or without history of ICP
- **Sero-negative primary biliary cirrhosis**[15,16]
- **Autoimmune hepatitis,** including antimitochondrial or antinuclear antibodies[15,16]

Episodic cholestasis[17]

- Mild presentation
- Ambiguous or overlapping PFIC genetics

Assessments to support a diagnosis of adult onset PFIC

1. **Common symptoms:** especially pruritus and jaundice, along with the presence of gastrointestinal symptoms, like diarrhoea[3]
2. **Hepatic biomarkers:** particularly elevated serum bile acids, Alkaline phosphatase (ALP) and bilirubin[3,17]
3. **Hepatic imaging:** ultrasound and cholangiography can exclude extrahepatic obstructions and identify liver damage[3,18-20]
4. **Genetic testing:** can support diagnosis, however, it is not always conclusive as adult patients are unlikely to have classic genetics and support from a geneticist may be required.[3,17]

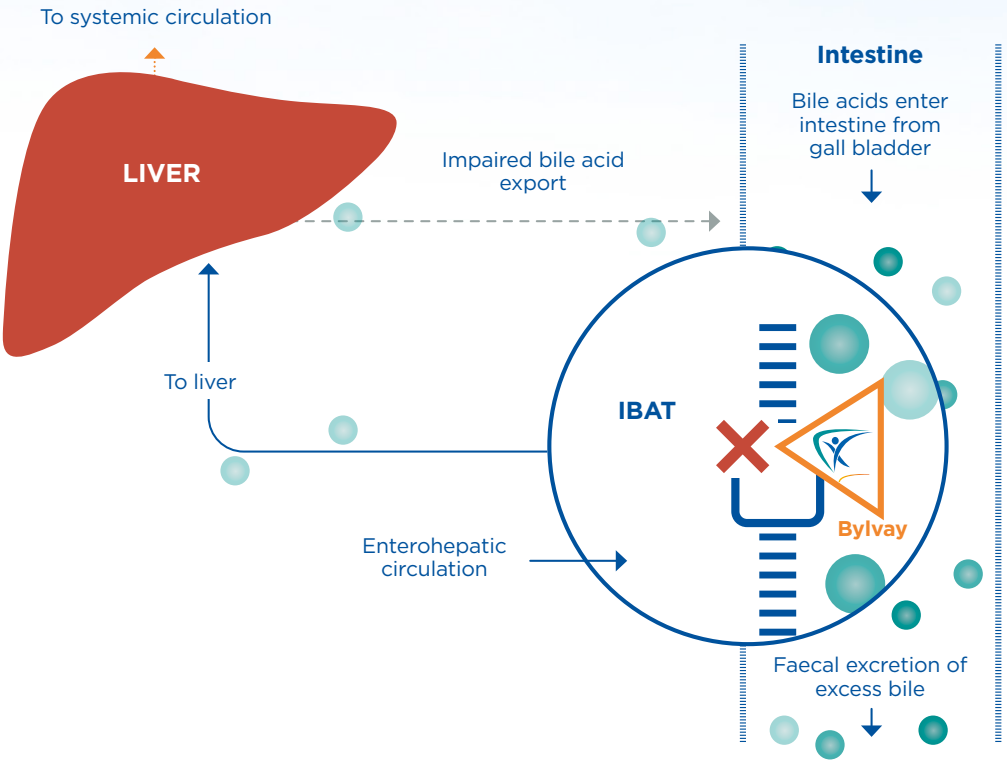
Progressive familial intrahepatic cholestasis (PFIC)

BYLVAY is the first non-surgical bile diversion treatment for all PFIC types

In clinical studies compared with placebo, Bylvay (odevixibat):[1,21]

- ☑ significantly reduces serum bile acids
- ☑ relieves the burden of pruritus
- ☑ improves parameters linked to liver health

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



In adults with cholestatic disease & pruritus, screen for elevated serum bile acids..

Consider adult-onset PFIC as part of your differential diagnosis

References: 1. Bylvay Summary of Product Characteristics. **2.** Bedoyan SM, *et al.* Expert Opin Pharmacother. 2022;23:1771–79. **3.** Gunaydin M, *et al.* Hepat Med. 2018;10:95–104. **4.** Karpen SJ, *et al.* Hepatol Int. 2020;14:677–89. **5.** Henkel SAF, *et al.* World J Hepatol. 2019;11(5):450–63. **6.** Clemson C, *et al.* Native liver survival in odevixibat serum bile acid responders: data from the PEDFIC studies in patients with progressive familial intrahepatic cholestasis. Presented at AASLD: American Association for the Study of Liver Diseases; November 4–8, 2022; Washington, DC, USA. **7.** Goldberg A and Mack CL. Clin Liver Dis. 2020;15:105–9. **8.** OMNIM.org. Phenotypic Series - PS211600. Available at https://www.omim.org/phenotypicSeries/PS211600. Last accessed October 2024. **9.** ProteinAtlas.org. SLC51A. Available at https://www.proteinatlas.org/ENSG00000163959-SLC51A. Last accessed October 2024. **10.** Nayagam J, *et al.* Hepatol Commun. 2022;6:2654–64. **11.** Hilscher MB, *et al.* Mayo Clin Proc. 2020;95:2263-79. **12.** Srivastava A. J Clin Exp Hepatol. 2014;4:25-36. **13.** Pollock G and Minuk GY. J Gastroenterol Hepatol. 2017;32:1303-09. **14.** Zu Y, *et al.* Front Pharmacol. 2021;12:761255. **15.** Chascsa DM and Lindor KD. Clin Liver Dis. 2018;22:589- 601. **16.** Zen Y, Hübscher SG, Nakanuma Y. Bile duct diseases. In: Burt AD, Ferrell LD, Hübscher SG, eds. MacSween's Pathology of the Liver. 7th ed. 2018:515-593. **17.** Bull LN, Thompson RJ. Clin Liver Dis. 2018;22:657-669. **18.** Davit-Spraul A, *et al.* Orphanet J Rare Dis. 2009;4:1. **19.** Ranucci G, *et al.* Dig Liver Dis. 2022;54:40-53. **20.** Feldman AG, Sokol RJ. Nat Rev Gastroenterol Hepatol. 2019;16:346-360. **21.** Thompson RJ, *et al.* Lancet Gastroenterol Hepatol. 2022;7:830–42.

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Prescribing Information

▼ This medicinal product is subject to additional monitoring.

Click here to access Bylvay prescribing and adverse event reporting information

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