

Help your patients  
rise above cholestatic  
pruritus so they can

# LIV IT UP

## FDA APPROVED FOR PFIC

LIVMARLI is indicated for the treatment of cholestatic pruritus in patients 12 months of age and older with progressive familial intrahepatic cholestasis (PFIC).

Limitations of Use: LIVMARLI is not recommended in a subgroup of PFIC type 2 patients with specific *ABCB11* variants resulting in nonfunctional or complete absence of bile salt export pump (BSEP) protein.<sup>1</sup>

### IMPORTANT SAFETY INFORMATION

#### CONTRAINDICATIONS

LIVMARLI is contraindicated in patients with prior or active hepatic decompensation events (eg, variceal hemorrhage, ascites, or hepatic encephalopathy).

#### WARNINGS AND PRECAUTIONS

**Hepatotoxicity:** LIVMARLI treatment is associated with a potential for drug-induced liver injury (DILI).

Please see Important Safety Information throughout and full [Prescribing Information](#).



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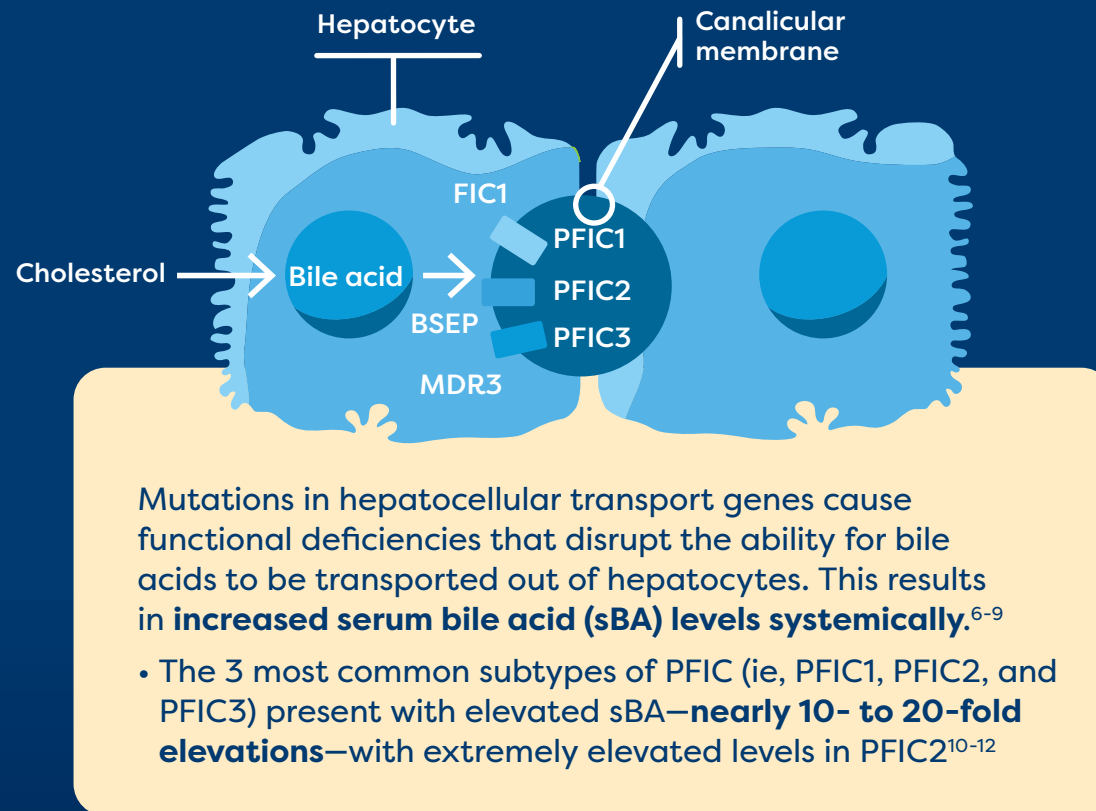
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# BILE ACID BUILDUP MAY FUEL CHOLESTATIC PRURITUS\* NOW AND IMPACT THE LIVER LATER<sup>2,3</sup>

Across all progressive familial intrahepatic cholestasis (PFIC) subtypes, there is an inhibition of bile flow between the liver and small intestine, resulting in a **persistent state of cholestasis**.<sup>4,5</sup>



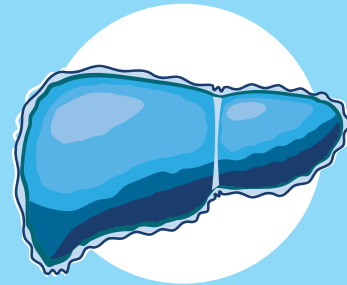
BSEP=bile salt export pump; FIC1=familial intrahepatic cholestasis associated protein 1; MDR3=multidrug resistance class III.

\*The pathophysiology of cholestatic pruritus in PFIC is not completely known.

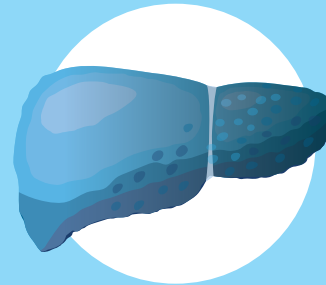


# CONSEQUENCES OF CHOLESTASIS

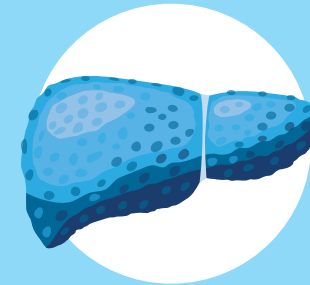
Cholestasis leads to bile acid buildup in the liver and is the main driver of<sup>2,4,13,14</sup>:



INFLAMMATION



PROGRESSIVE LIVER INJURY



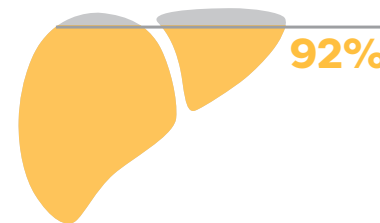
FIBROSIS

In PFIC1 and PFIC2, it has been reported that **approximately 50%** of patients are alive and have their native liver at 10 years old.<sup>15</sup>

- In PFIC2 specifically, **only 32% of patients** are alive and have their native liver by 18 years old<sup>16</sup>



Many patients with uncontrolled cholestatic pruritus continue to opt for surgical biliary diversion and/or liver transplant.<sup>4,16</sup>



Among 38 pediatric patients with PFIC who underwent surgical biliary diversion, **the most common indication was cholestatic pruritus (92%).**<sup>17</sup>

End-stage liver disease (**80%**) was the most common indication for liver transplant in pediatric patients with PFIC, followed by **refractory cholestatic pruritus (20%).**<sup>18</sup>

# CHOLESTATIC PRURITUS IS MORE THAN JUST SCRATCHING

Cholestatic pruritus, which has been correlated with elevated serum bile acids (sBA), is a consequence of ongoing cholestasis.<sup>4</sup>

- Other consequences may include jaundice or growth deficiencies<sup>4</sup>

Cholestatic pruritus affects **76% to 100%** of patients with progressive familial intrahepatic cholestasis (PFIC)<sup>19</sup>

It has been identified as the most debilitating symptom.<sup>4</sup>

When cholestatic pruritus remains uncontrolled, patients with PFIC can also struggle with<sup>7,20,21</sup>:



Skin damage



Irritability



Physical discomfort



Impaired school performance



Decreased physical function



Negative impact on social activities

## THE IMPACT ON SLEEP AND FATIGUE

~60%

of caregivers of patients with progressive familial intrahepatic cholestasis (PFIC) report that their child needed soothing or help falling asleep due to cholestatic pruritus.<sup>22</sup>

ZZZ

Sleep disruptions caused by cholestatic pruritus are associated with fatigue.<sup>23</sup>



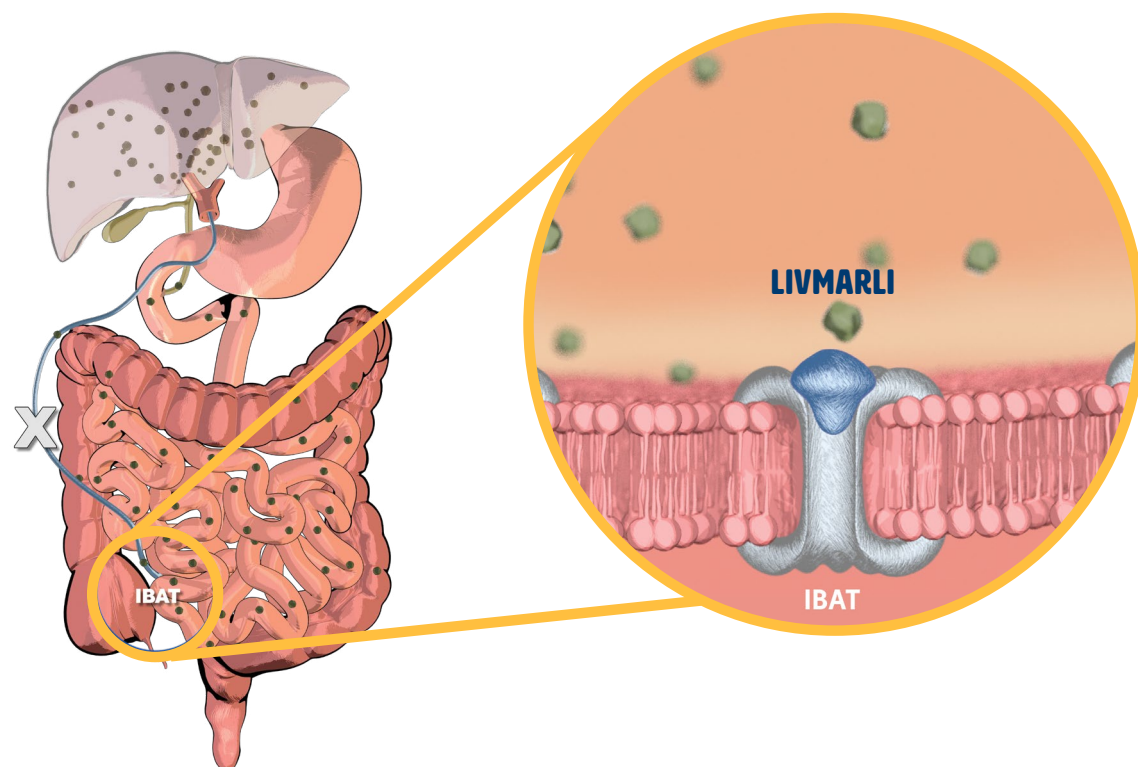
Consequently, cholestatic pruritus may contribute to reduced quality of life, impacting aspects of school or emotional, mental, or physical functioning.<sup>4,21</sup>

There is a need for effective treatment options that reduce bile acid buildup and promptly relieve cholestatic pruritus.<sup>4</sup>



# LIVMARLI BATTLES BILE ACID BUILDUP

LIVMARLI is an ileal bile acid transporter (IBAT) inhibitor designed to decrease the bile acid pool in the body.<sup>1,24,25</sup>



LIVMARLI interrupts recirculation of bile acids to the liver and increases their fecal excretion to **reduce bile acid levels in the body (as measured by serum bile acids [sBA])**, with minimal systemic absorption.<sup>1,24,25</sup>

Although the complete mechanism by which LIVMARLI improves cholestatic pruritus in patients with progressive familial intrahepatic cholestasis (PFIC) is unknown, it may involve inhibition of the IBAT, which results in decreased reuptake of bile salts, as observed by a decrease in sBA.<sup>1</sup>

## IMPORTANT SAFETY INFORMATION (cont'd)

### WARNINGS AND PRECAUTIONS

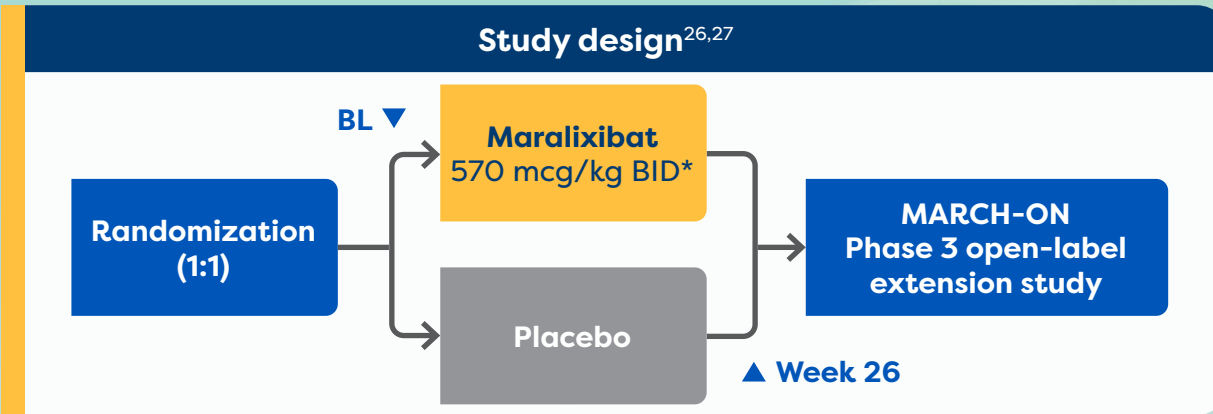
**Hepatotoxicity:** In the PFIC trial, treatment-emergent hepatic decompensation events and elevations of liver tests or worsening of liver tests occurred. Two patients experienced DILI attributable to LIVMARLI. Two additional patients experienced DILI in the open-label extension portion of the trial. Of these 4 patients, 1 patient required liver transplant and another patient died.

Please see Important Safety Information throughout and full [Prescribing Information](#).



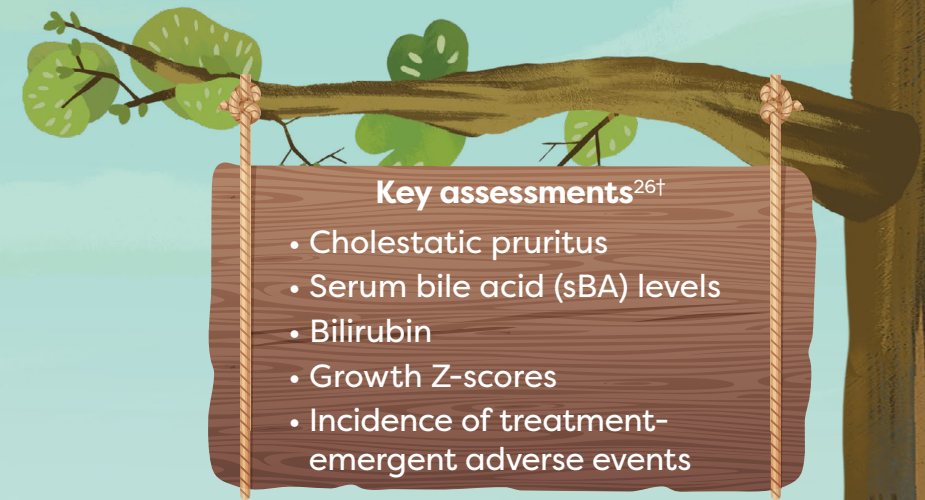
# THE BROADEST POPULATION OF PFIC SUBTYPES STUDIED

The MARCH-PFIC study was a 26-week, Phase 3, randomized, placebo-controlled study that assessed efficacy and safety of treatment with LIVMARLI in patients  $\geq 12$  months to  $< 18$  years old with cholestatic pruritus in progressive familial intrahepatic cholestasis (PFIC).<sup>1,26</sup>



**The study populations for MARCH-PFIC included<sup>26</sup>:**

BSEP cohort (n=31)	All-PFIC cohort (n=64)	Full cohort (N=93) <sup>‡§</sup>
Non-truncated BSEP (n=31)	Non-truncated BSEP (n=31) FIC1 (n=13), MDR3 (n=9), TJP2 (n=7), MYO5B (n=4)	Non-truncated BSEP (n=36), truncated BSEP (n=9), FIC1 (n=17), MDR3 (n=9), TJP2 (n=8), MYO5B (n=4), heterozygous variant (n=2), no pathogenic variant (n=8)



**MARCH-PFIC is the largest Phase 3 study conducted in children with PFIC. It included PFIC types that had not previously been studied.<sup>26,28</sup>**

BID=twice daily; BL=baseline; BSEP=bile salt export pump; FIC1=familial intrahepatic cholestasis associated protein 1; MDR3=multidrug resistance class III; MYO5B=myosin VB; TJP2=tight junction protein 2.

\*In the dose escalation period, the dose was increased weekly starting at 142.5 mcg/kg twice daily to a maximum dose of 570 mcg/kg twice daily.<sup>26</sup>  
 †Endpoints were analyzed using a mixed model for repeated measurements (MMRM) considering data from all study visits.<sup>1,26</sup>  
 ‡**Limitations of Use:** LIVMARLI is not recommended in a subgroup of PFIC type 2 patients with specific *ABCB11* variants resulting in nonfunctional or complete absence of bile salt export pump (BSEP) protein.<sup>1</sup>  
 §The full study cohort included 8 patients with prior surgery to treat PFIC. Surgery participants had the following PFIC types: non-truncated BSEP (LIVMARLI: 3, placebo: 0); FIC1 (LIVMARLI: 2, placebo: 2); and TJP2 (LIVMARLI: 0; placebo: 1).<sup>26</sup>

**IMPORTANT SAFETY INFORMATION (cont'd)**

**WARNINGS AND PRECAUTIONS**

**Hepatotoxicity:** Obtain baseline liver tests and monitor during treatment. Liver-related adverse reactions and physical signs of hepatic decompensation should also be monitored. Dose reduction or treatment interruption may be considered if abnormalities occur in the absence of other causes. Permanently discontinue LIVMARLI if a patient experiences the following: persistent or recurrent liver test abnormalities, clinical hepatitis upon rechallenge, or a hepatic decompensation event.

**Please see Important Safety Information throughout and full Prescribing Information.**





# THE BROADEST POPULATION OF PFIC SUBTYPES STUDIED



## Participants had the following baseline characteristics (full cohort)<sup>26</sup>:

Characteristics	LIVMARLI (n=47)	Placebo (n=46)
<b>Mean age at baseline visit, years</b>	4.8	4.7
<b>Sex (male), %</b>	43	48
<b>Treatment for cholestatic pruritus at baseline, %</b>		
Ursodeoxycholic acid	83	85
Rifampicin	55	50
<b>Trial parameter, mean</b>		
ItchRO(Obs) weekly morning average severity score	2.8	2.9
sBA, $\mu\text{mol/L}$	263	243
ALT, U/L	108	121
TB, mg/dL	4.1	3.8
DB, mg/dL	3.0	2.8

- Cholestatic pruritus was assessed each day in the morning and evening, using the Itch Reported Outcome Observer (ItchRO[Obs]) scale<sup>1,26</sup>
- Participants were included in the study if their average ItchRO(Obs) score was  $\geq 1.5$  in the 4 weeks prior to baseline<sup>1</sup>
- Changes in ItchRO(Obs) score of  $\geq 1.0$  are shown to be clinically meaningful<sup>26</sup>

ALT=alanine transaminase; DB=direct bilirubin; ItchRO(Obs)=Itch Reported Outcome (Observer); sBA=serum bile acid; TB=total bilirubin.

## IMPORTANT SAFETY INFORMATION (cont'd)

### WARNINGS AND PRECAUTIONS

**Gastrointestinal (GI) Adverse Reactions:** Diarrhea and abdominal pain were reported as the most common adverse reactions. Monitor for dehydration and treat promptly. Consider reducing the dosage or interrupting LIVMARLI dosing if a patient experiences persistent diarrhea or diarrhea with bloody stool, vomiting, dehydration requiring treatment, or fever.

**Please see Important Safety Information throughout and full [Prescribing Information](#).**



# TRACK THEIR SCORE, MEASURE TREATMENT SUCCESS

ItchRO scale—a helpful tool for identifying patients and tracking progress

## What is ItchRO?

The **ItchRO** scale is an assessment tool that can help measure itch-related symptoms in patients suffering from cholestatic pruritus. The scale determines symptom severity using a **0–4 scale**, where 0 is none and 4 is very severe. ItchRO takes itch-related symptoms into consideration, including patients' **skin damage, sleep, and irritability**.<sup>21,29</sup>

## How can ItchRO scores help you measure treatment success?

- Tracking changes in ItchRO scores over time can be an effective way to determine whether a patient's symptoms are getting better or worse. **The goal is to reduce ItchRO scores as much as possible**
- **A change in ItchRO score of 1.0 or more was considered to be clinically meaningful**<sup>26</sup>

## What could a $\geq 1$ -point ItchRO(Obs) reduction mean for patients?<sup>21,26,29</sup>

- Less rubbing or scratching when undistracted
- Fewer sleep problems
- Less moody and/or irritable

### IMPORTANT SAFETY INFORMATION (cont'd)

#### WARNINGS AND PRECAUTIONS

**Fat-Soluble Vitamin (FSV) Deficiency:** Patients can have FSV deficiency (vitamins A, D, E, and K) at baseline, and LIVMARLI may adversely affect absorption of FSVs. Treatment-emergent bone fracture events have been observed more frequently with patients treated with LIVMARLI compared with patients treated with placebo. If bone fractures or bleeding occur, consider interrupting LIVMARLI and supplement with FSVs. LIVMARLI can be restarted once FSV deficiency is corrected and maintained at corrected levels.

Please see Important Safety Information throughout and full [Prescribing Information](#).

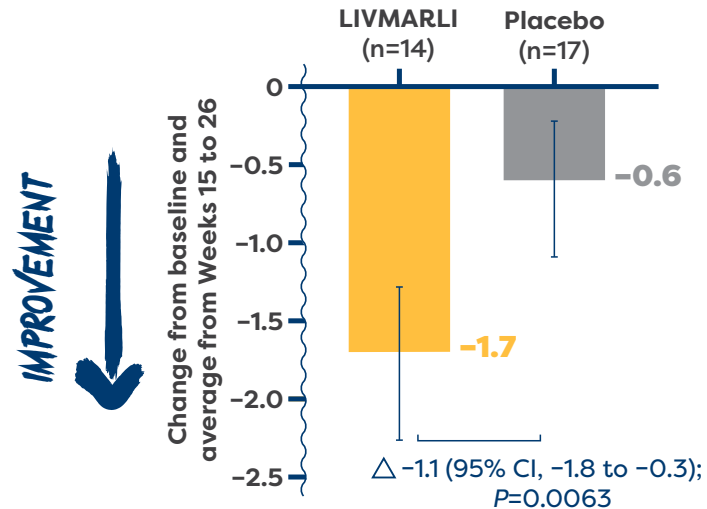


# IMPROVEMENTS IN CHOLESTATIC PRURITUS

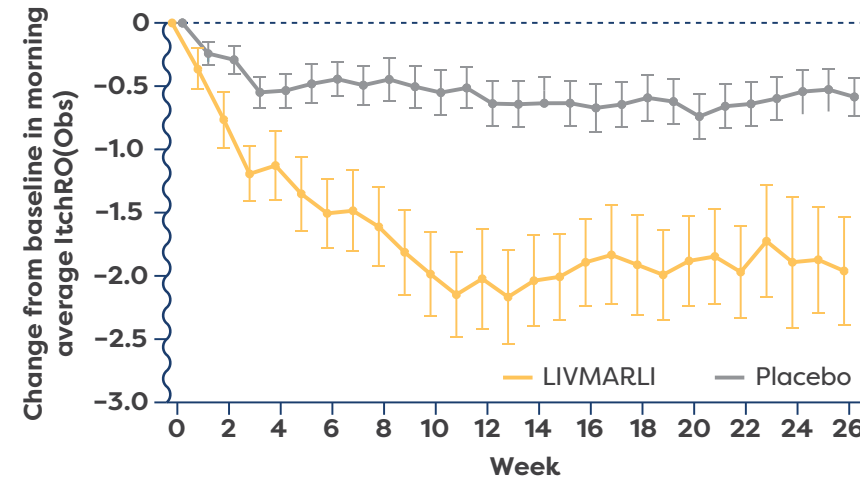
LIVMARLI was shown to provide statistically significant improvements in cholestatic pruritus versus placebo at 6 months. Improvements were seen as early as Week 2.<sup>1,26</sup>

## BSEP cohort (Primary endpoint)<sup>26</sup>

### Cholestatic pruritus score (ItchRO[Obs])



### Weekly average cholestatic pruritus score (ItchRO[Obs]) over time



BSEP=bile salt export pump; ItchRO(Obs)=Itch Reported Outcome (Observer).

## IMPORTANT SAFETY INFORMATION (cont'd)

### WARNINGS AND PRECAUTIONS

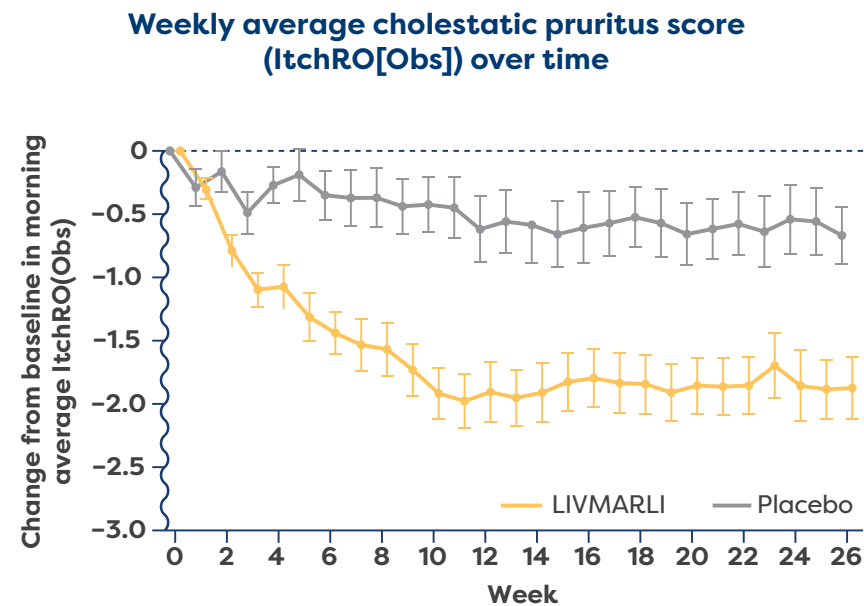
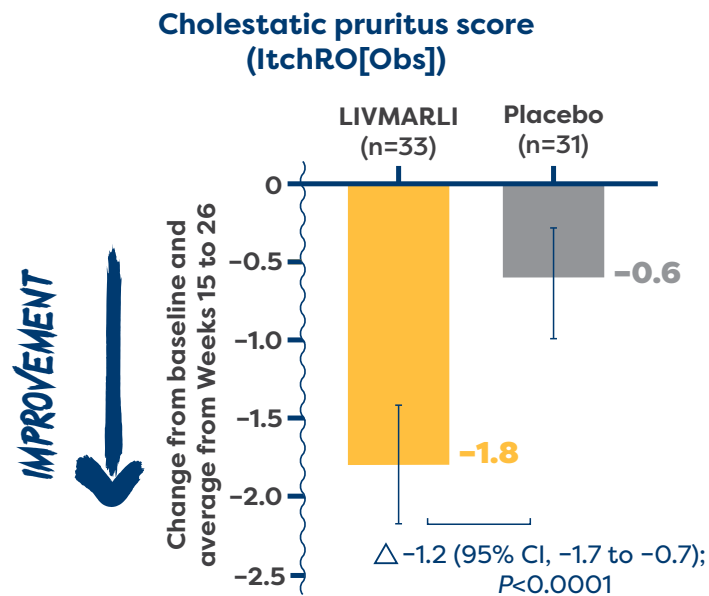
**Risk of Propylene Glycol Toxicity (Pediatric Patients Less Than 5 Years of Age):** Total daily intake of propylene glycol should be considered for managing the risk of propylene glycol toxicity. Monitor patients for signs of propylene glycol toxicity. Discontinue LIVMARLI if toxicity is suspected.

Please see Important Safety Information throughout and full [Prescribing Information](#).



# IMPROVEMENTS IN CHOLESTATIC PRURITUS

## All-PFIC cohort (Secondary endpoint)<sup>1,26</sup>



ItchRO(Obs)=Itch Reported Outcome (Observer); PFIC=progressive familial intrahepatic cholestasis.

### IMPORTANT SAFETY INFORMATION (cont'd)

#### ADVERSE REACTIONS

The most common adverse reactions are diarrhea, FSV deficiency, abdominal pain, liver test abnormalities, hematochezia, and bone fractures.

Please see Important Safety Information throughout and full [Prescribing Information](#).



# IMPROVEMENTS IN CHOLESTATIC PRURITUS

During the first  
6 months of  
treatment,

# 64%

of patients in the All-progressive familial intrahepatic cholestasis (PFIC) cohort were considered cholestatic pruritus responders and experienced **clinically meaningful improvements** in cholestatic pruritus vs 29% of patients treated with placebo ( $P=0.0064$ ).<sup>26</sup>

- Cholestatic pruritus responders had a  $\geq 1$ -point Itch Reported Outcome (Observer) (ItchRO[Obs]) improvement or a score of  $\leq 1.0$

**More days  
with little or  
no cholestatic  
pruritus**

Over the 6-month period, patients treated with LIVMARLI ( $n=33$ ) had **significantly more days with little to no cholestatic pruritus** than those who received placebo ( $n=31$ ) (62% vs 28%, least squares [LS] mean difference 0.34,  $P<0.0001$ )<sup>30</sup>

**Improvements  
sustained  
through 2 years**

In patients who remained on LIVMARLI ( $n=13$ ) during the open-label extension, **statistically significant improvements in cholestatic pruritus from baseline were sustained through 2 years** ( $P<0.001$ ).<sup>27</sup>



## IMPORTANT SAFETY INFORMATION (cont'd)

### DRUG INTERACTIONS

Administer bile acid binding resins at least 4 hours before or 4 hours after administration of LIVMARLI. A decrease in the absorption of OATP2B1 substrates (eg, statins) due to OATP2B1 inhibition by LIVMARLI in the GI tract cannot be ruled out. Consider monitoring the drug effects of OATP2B1 substrates as needed.

**Please see Important Safety Information throughout and full [Prescribing Information](#).**



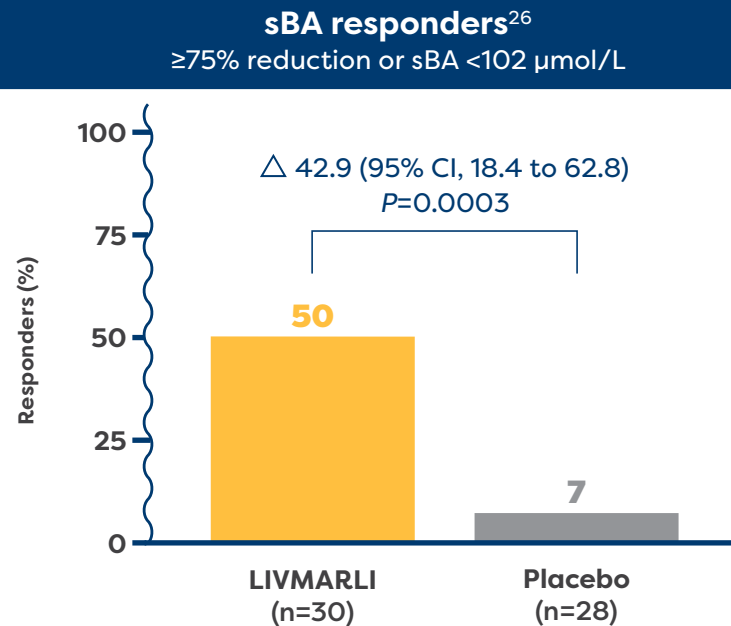
# IMPROVEMENTS IN SERUM BILE ACID LEVELS

In the All-progressive familial intrahepatic cholestasis (PFIC) cohort,

# 50%

of patients treated with LIVMARLI were **considered serum bile acid (sBA) responders** vs 7% of patients treated with placebo ( $P=0.0003$ ).<sup>26</sup>

- sBA responders were defined as patients who achieved a  $\geq 75\%$  reduction in sBA levels or sBA  $< 102 \mu\text{mol/L}$ <sup>26</sup>



In the All-PFIC cohort, patients taking LIVMARLI saw **statistically significant improvements in sBA levels** compared with placebo ( $-157 \mu\text{mol/L}$  vs  $3 \mu\text{mol/L}$ , least squares [LS] mean difference  $-160 \mu\text{mol/L}$ ,  $P<0.0001$ ).<sup>26</sup>

## IMPORTANT SAFETY INFORMATION (cont'd)

### DOSING INFORMATION

LIVMARLI should be taken twice daily 30 minutes before a meal. The provided oral dosing dispenser must be used to accurately measure the dose. Any remaining LIVMARLI should be discarded 100 days after first opening the bottle.

Please see Important Safety Information throughout and full [Prescribing Information](#).



# WELL-CHARACTERIZED SAFETY AND TOLERABILITY PROFILE

LIVMARLI has well-established safety and tolerability for patients with cholestatic pruritus in progressive familial intrahepatic cholestasis (PFIC).<sup>1,26</sup>

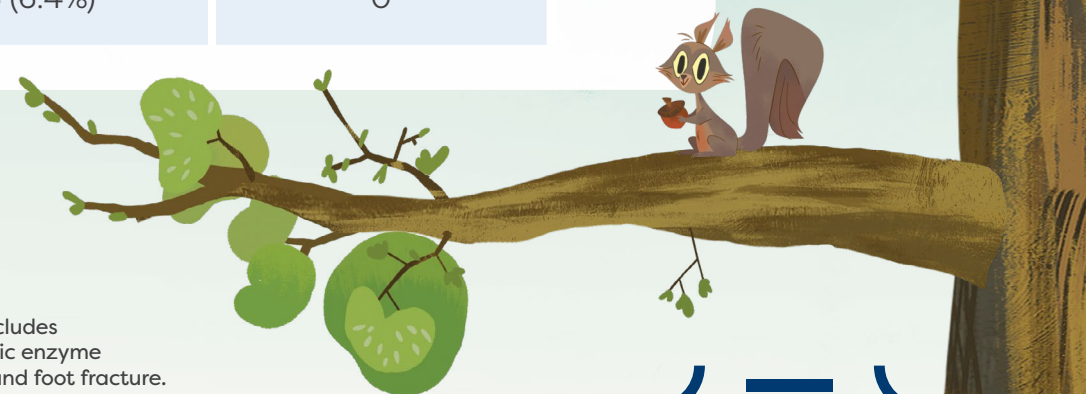
Adverse reactions occurring in  $\geq 5\%$  and at a rate greater than placebo in patients treated with LIVMARLI in the MARCH-PFIC clinical study<sup>1</sup>

Adverse reaction	LIVMARLI (n=47) n (%)	Placebo (n=46) n (%)
Diarrhea	27 (57.4%)	9 (19.6%)
Abdominal pain*	13 (27.7%)	7 (15.2%)
Transaminases increased (ALT or AST)*	8 (17%)	3 (6.5%)
Hematochezia or rectal hemorrhage	4 (8.5%)	1 (2.2%)
Bone fractures*	3 (6.4%)	0

ALT=alanine transaminase; AST=aspartate aminotransferase.

\*Abdominal pain includes abdominal pain, abdominal pain upper, and abdominal distension; transaminases increased includes hypertransaminasemia, ALT abnormal, ALT increased, AST abnormal, AST increased, transaminases increased, and hepatic enzyme increased; bone fracture includes upper limb fracture, lower limb fracture, radius fracture, ulna fracture, femur fracture, and foot fracture.

Please see Important Safety Information throughout and full [Prescribing Information](#).



# WELL-CHARACTERIZED SAFETY AND TOLERABILITY PROFILE

The most common adverse reaction seen with LIVMARLI in the MARCH-PFIC study was diarrhea.<sup>1</sup>

Diarrhea was the most frequent adverse reaction; the majority of episodes were mild and transient. Diarrhea resolved, on average, within 5.5 days.<sup>1,26</sup>

- One patient with an event of mild diarrhea discontinued treatment.<sup>1,26</sup>
- Treatment interruptions or dose reductions occurred in 3 patients due to diarrhea or abdominal pain<sup>1</sup>

Treatment with LIVMARLI is associated with a potential for drug-induced liver injury.<sup>1</sup>

- Treatment-emergent elevations of liver tests or worsening of liver tests, relative to baseline values, and hepatic decompensation events were observed<sup>1</sup>
- Two patients experienced drug-induced liver injury (DILI) attributable to LIVMARLI. One patient received 570 mcg/kg twice daily and the second patient required dose interruption and reduction<sup>1</sup>
- Two additional patients experienced DILI in the open-label extension portion of the trial<sup>1</sup>
- Of these 4 patients, 1 patient required liver transplant and another patient died. The contribution of LIVMARLI in these 2 cases is uncertain<sup>1</sup>

- In the placebo-controlled arm of the trial, 2 patients treated with LIVMARLI developed cholangitis or cholecystitis within 3 weeks of drug discontinuation. Four patients treated with LIVMARLI developed cholecystitis or cholangitis in the open-label extension<sup>1</sup>
- Treatment-emergent bone fracture events were observed. Three patients treated with LIVMARLI experienced bone fractures compared with none with placebo. Two patients treated with LIVMARLI developed bone fractures in the open-label extension<sup>1</sup>
- Patients receiving LIVMARLI reported more frequent treatment-emergent events of hematochezia (4 [8.5%] vs 1 [2.2%]), and a decrease in hemoglobin  $\geq 2$  grams/dL from baseline (8 [17%] vs 1 [2.2%]) compared with patients receiving placebo<sup>1</sup>

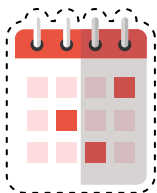
Patients with progressive familial intrahepatic cholestasis (PFIC) can have fat-soluble vitamin (FSV) deficiency (vitamins A, D, E, and/or K) at baseline.<sup>1</sup>

- LIVMARLI may affect absorption of FSV<sup>1</sup>
- In patients with PFIC, treatment-emergent FSV deficiency was reported in 13 (28%) patients treated with LIVMARLI vs 16 (35%) patients treated with placebo during 26 weeks of treatment<sup>1</sup>



# CONVENIENT DOSING

LIVMARLI is a grape-flavored, colorless to yellow liquid medicine with convenient dosing for patients with cholestatic pruritus due to progressive familial intrahepatic cholestasis (PFIC).<sup>1</sup>



**Taken twice daily,**  
30 minutes before  
a meal.<sup>1</sup>



**Recommended dosage**  
is 570 mcg/kg administered  
orally (PO) twice daily. Individual  
dose volume for LIVMARLI is  
based on a patient's weight.<sup>1</sup>



**Starting dose**  
is 285 mcg/kg once daily in the morning.  
This may be increased to 285 mcg/kg  
twice daily, 428 mcg/kg twice daily, and  
then 570 mcg/kg twice daily as tolerated.<sup>1</sup>

## Tips for taking liquid medicine:

- **Be mindful of placement.** Use the measuring device that comes with LIVMARLI to squirt the medicine into the inside of the cheek for minimal contact with taste buds
- **Add a flavorful twist.** Suggest patients suck on fruit, such as an orange or lemon, before or after taking LIVMARLI
- **Cool it.** Consider storing LIVMARLI in the refrigerator

## IMPORTANT SAFETY INFORMATION

### CONTRAINDICATIONS

LIVMARLI is contraindicated in patients with prior or active hepatic decompensation events (eg, variceal hemorrhage, ascites, or hepatic encephalopathy).

Please see Important Safety Information throughout and full [Prescribing Information](#).



# CONVENIENT DOSING

Monitor your patients' weight and adjust the dose accordingly.

## For patients with PFIC: 19 mg/mL solution volume per dose (mL) by weight<sup>1</sup>

Patient weight (kg)	285 mcg/kg (once daily titrated to twice daily)	428 mcg/kg (twice daily)	570 mcg/kg (twice daily as tolerated)
5	0.1	0.1	0.15
6 to 7	0.1	0.15	0.2
8	0.1	0.2	0.25
9	0.15	0.2	0.25
10 to 12	0.15	0.25	0.3
13 to 15	0.2	0.3	0.4
16 to 19	0.25	0.4	0.5
20 to 24	0.3	0.5	0.6
25 to 29	0.4	0.6	0.8
30 to 34	0.45	0.7	0.9
35 to 39	0.6	0.8	1
40 to 49	0.6	0.9	1
50 to 59	0.8	1	1
60 or higher	0.9	1	1



The maximum daily dose volume for patients is 38 mg (2 mL).<sup>1</sup>

### IMPORTANT SAFETY INFORMATION (cont'd)

#### WARNINGS AND PRECAUTIONS

**Hepatotoxicity:** LIVMARLI treatment is associated with a potential for drug-induced liver injury (DILI).

Please see Important Safety Information throughout and full [Prescribing Information](#).



# Helping you and your patients through every step

**Mirum Access Plus** is available with support and resources to help you and your office navigate insurance coverage, as well as assist your patients with progressive familial intrahepatic cholestasis (PFIC) with treatment costs and prescription fulfillment.

## Financial Support for Patients



- **Mirum Access Plus Savings Program:** Eligible patients with commercial or private insurance may pay as little as \$10 out of pocket per fill for LIVMARLI\*
- **Mirum Patient Assistance Program (PAP):** For eligible patients without insurance coverage, Mirum Access Plus Patient Assistance Program provides LIVMARLI to patients at no cost†



*"We begin our support the minute a new prescription for a patient has been received and verified. Our goal is to provide information about our program and the medication prior to the patient receiving it in hopes that they will feel knowledgeable and supported as they begin their journey with LIVMARLI."*

– Mirum Access Plus Navigator

**Prescribing is easy**—Visit [www.LIVMARLIhcp.com/mirum-access-plus/](http://www.LIVMARLIhcp.com/mirum-access-plus/) to download the Patient Enrollment Form (PEF). **Simply send the prescription, by fax using the PEF or by eRx, straight to EVERSANA pharmacy.**

**If you have any questions about Mirum Access Plus, contact us at 1-855-MRM-4YOU (1-855-676-4968) Monday through Friday, 8:00 AM through 8:00 PM ET.**

\*Eligibility restrictions: This program is not available to individuals who use any state or federal government-funded health care program to cover a portion of medication costs, such as Medicare, Medicaid, TRICARE, Department of Defense, or Veterans Administration, or any other state or federal government-funded health care program.

†Subject to program terms and conditions.



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## IMPORTANT SAFETY INFORMATION (cont'd)

### WARNINGS AND PRECAUTIONS

**Hepatotoxicity:** In the PFIC trial, treatment-emergent hepatic decompensation events and elevations of liver tests or worsening of liver tests occurred. Two patients experienced DILI attributable to LIVMARLI. Two additional patients experienced DILI in the open-label extension portion of the trial. Of these 4 patients, 1 patient required liver transplant and another patient died.

Please see Important Safety Information  
throughout and full [Prescribing Information](#).

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