HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LIVMARLI safely and effectively. See full prescribing information for LIVMARLI.

LIVMARLI® (maralixibat) oral solution
Initial U.S. Approval: 2021

----------RECENT MAJOR CHANGES----------

Indications and Usage (1)	3/2024
Dosage and Administration (2)	3/2024
Contraindications (4)	3/2024
Warnings and Precautions (5.1)	3/2024
Warnings and Precautions (5.2)	3/2024
Warnings and Precautions (5.3)	3/2024

----------INDICATIONS AND USAGE----------

LIVMARLI is an ileal bile acid transporter (IBAT) inhibitor indicated for:

- the treatment of cholestatic pruritus in patients 3 months of age and older with Alagille syndrome (ALGS). (1.1)
- the treatment of cholestatic pruritus in patients 5 years of age and older with progressive familial intrahepatic cholestasis (PFIC). (1.2)
  - Limitations of Use:
    LIVMARLI is not recommended in a subgroup of PFIC type 2 patients with specific ABCB11 variants resulting in non-functional or complete absence of bile salt export pump (BSEP) protein. (14.2)

----------DOSAGE AND ADMINISTRATION----------

- ALGS: The recommended dosage is 380 mcg/kg once daily, taken 30 minutes before a meal in the morning. (2.1)
  - Starting dose is 190 mcg/kg orally once daily, and should be increased to 380 mcg/kg once daily after one week, as tolerated and not to exceed a maximum daily dose of 28.5 mg. (2.1)
- PFIC: The recommended dosage is 570 mcg/kg twice daily. (2.2)
  - Starting dose is 285 mcg/kg orally once daily in the morning and should be increased to 285 mcg/kg twice daily, 428 mcg/kg twice daily, and then to 570 mcg/kg twice daily, as tolerated and not to exceed a maximum daily dose of 38 mg. (2.2)

----------DOSAGE FORMS AND STRENGTHS----------

Oral solution: 9.5 mg of maralixibat per mL. (3)

----------CONTRAINDICATIONS----------

Patients with prior or active hepatic decompensation events (e.g., variceal hemorrhage, ascites, hepatic encephalopathy). (4)

----------WARNINGS AND PRECAUTIONS----------

- Hepatotoxicity: Obtain baseline liver tests and monitor patients frequently for the first 6 to 8 months after starting therapy, and as clinically indicated thereafter during treatment. If liver test abnormalities or signs of clinical hepatitis occur, consider dose reduction or treatment interruption. For persistent or recurrent liver test abnormalities relative to baseline, discontinue LIVMARLI. Monitor patients with compensated cirrhosis frequently. Permanently discontinue LIVMARLI if hepatic decompensation event occurs. (5.1)
- Gastrointestinal Adverse Reactions: Consider reducing the dosage or interrupting LIVMARLI treatment if a patient experiences persistent diarrhea or abdominal pain, or has diarrhea with bloody stool, vomiting, dehydration requiring treatment, or fever. Consider stopping LIVMARLI treatment if diarrhea or abdominal pain persists and no alternate etiology is identified. (5.2)
- Fat-Soluble Vitamin (FSV) Deficiency: Obtain baseline levels and monitor during treatment. Supplement if deficiency is observed. If FSV deficiency persists or worsens despite FSV supplementation, consider discontinuing LIVMARLI treatment. (5.3)
  - Fracture: Consider interrupting LIVMARLI treatment and supplement with FSV. LIVMARLI can be restarted once FSV deficiency is corrected and maintained at corrected levels.
  - Bleeding: Interrupt treatment with LIVMARLI. Treatment can be restarted if the FSV deficiency is corrected and bleeding has resolved.

----------ADVERSE REACTIONS----------

Most common adverse reactions (≥5%) are:

- ALGS: diarrhea, abdominal pain, vomiting, fat-soluble vitamin deficiency, liver test abnormalities, and bone fractures. (6.1)
- PFIC: diarrhea, fat soluble vitamin deficiency, abdominal pain, liver test abnormalities, hematochezia, and bone fractures. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Mirum Pharmaceuticals at 1-855-MRM-4YOU or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- Bile Acid Sequestrants: Modify LIVMARLI administration schedule. (7.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 03/2024

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

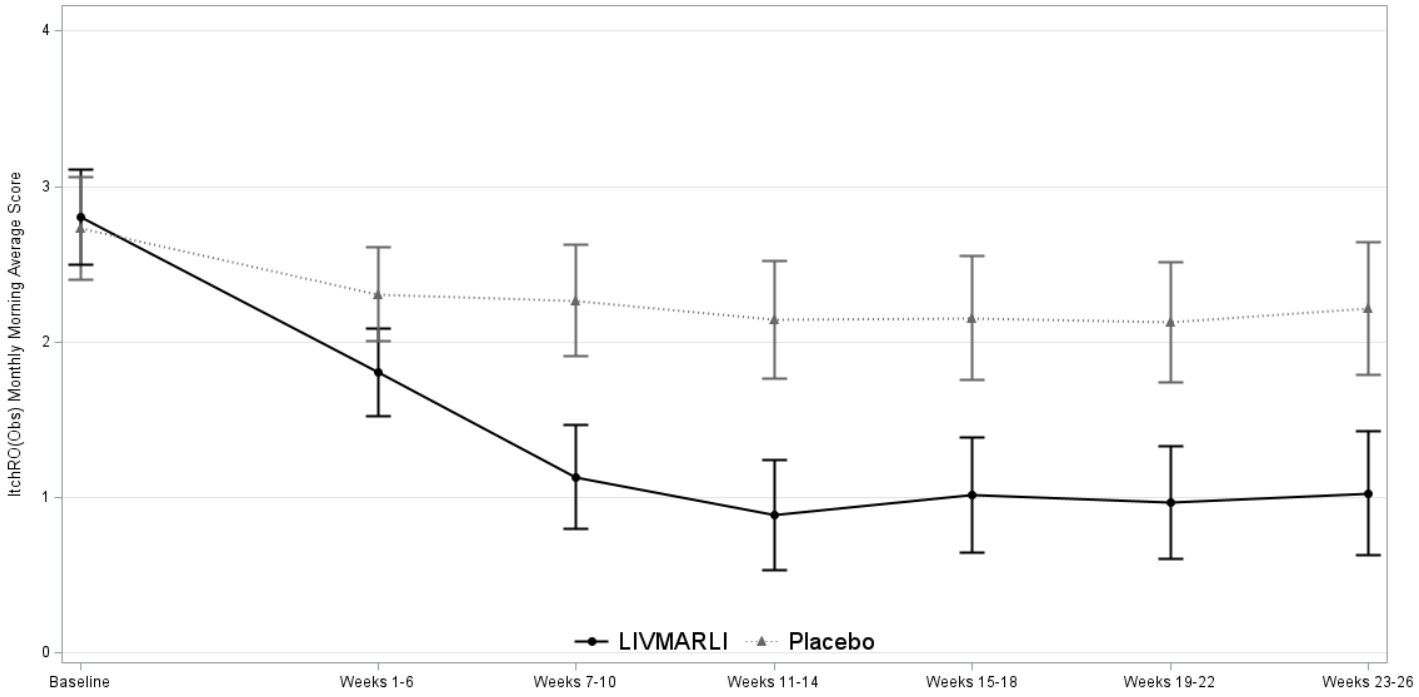
Table 6: Average Morning ItchRO(Obs) Pruritus Severity Scores in Trial 2

	Maralixibat (N=33)	**Placebo (N=31)**
Baseline Mean	2.9	2.7
Change from baseline to Weeks 15-26[a]		
Mean (95% CI)	-1.8 (-2.2, -1.4)	-0.6 (-1.0, -0.2)
Mean difference from Placebo (95% CI) p-value	-1.2 (-1.7, -0.7) <0.0001	

[a]Results based on least squares means from an analysis of a mixed-effect model for repeated measures (MMRM). Model adjusts for treatment group, visit, treatment group-by-visit interaction, baseline 4-week average morning ItchRO(Obs) severity score, baseline score-by-visit interaction, and PFIC type.

Figure 1 displays the means (95% confidence intervals) of patients' average morning ItchRO(Obs) severity scores in each treatment group for each 4-6 week time period.

Figure 1. **Mean of the Average Morning ItchRO(Obs) Pruritus Severity Scores Over Time in PFIC 1, 2, 3, 4, and 6**



Note: Figure 1 presents least squares mean (95% CI) estimates from a mixed model for repeated measures (MMRM) with observed value as the dependent variable and fixed categorical effects of treatment group, time period, treatment-by-time period interaction, and PFIC type.

Although the number of patients with BSEP3 in Trial 2 were limited, improvement in pruritus was not observed in 5 patients with BSEP3 who received LIVMARLI compared to 4 patients with BSEP3 who received placebo for 26 weeks.

16 HOW SUPPLIED/STORAGE AND HANDLING

Oral Solution

LIVMARLI is a clear, colorless to yellow oral solution.

Each amber plastic bottle contains LIVMARLI oral solution at a concentration of 9.5 mg per mL.

One 30 mL amber plastic bottle: NDC 79378-110-01

Storage and Handling

Store unopened LIVMARLI between 20°C and 25°C (68°F and 77°F), excursion permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature]. After opening the LIVMARLI bottle, store below 30°C (86°F) *[see Dosage and Administration (2.4)]*.

17 PATIENT COUNSELING INFORMATION

Advise the patient or their caregiver(s) to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Administration Instructions

Advise patients or their caregivers(s) to:

- Take LIVMARLI 30 minutes prior to a meal once or twice daily as prescribed using a calibrated measuring device (0.5 mL, 1 mL or 3 mL oral dispenser) provided by the pharmacist to measure and deliver the prescribed dose accurately *[see Dosage and Administration (2.1, 2.2 2.4)]*.
- Take LIVMARLI at least 4 hours before or 4 hours after taking a bile acid binding resin (e.g., cholestyramine, colesevelam, or colestipol) *[see Drug Interactions (7.1)]*.
- Store the opened bottle below 30ºC (86ºF). Discard any unused LIVMARLI 100 days after opening the bottle *[see How Supplied/Storage and Handling (16)]*.

Hepatotoxicity

Advise patients or their caregiver(s) that liver tests should be obtained before starting LIVMARLI and periodically during LIVMARLI therapy. Inform patients or their caregiver(s) of the risk of hepatotoxicity that could be fatal and that they will need to undergo monitoring for liver injury. Instruct patients or their caregiver(s) to immediately report any signs or symptoms of severe liver injury to their healthcare provider *[see Warnings and Precautions (5.1)]*.

Gastrointestinal Adverse Reactions

Advise patients or their caregiver(s) to notify their healthcare provider if they experience a new onset or worsening of gastrointestinal symptoms (abdominal pain, vomiting, bloody stool, and diarrhea) *[see Warnings and Precautions (5.2)]*.

Fat Soluble Vitamin (FSV) Deficiency

Advise patients or their caregiver(s) that INR (for vitamin K) and serum levels of vitamins A, D, E will be obtained before starting treatment and periodically during treatment to assess for FSV deficiency *[see Warnings and Precautions (5.3)]*. Inform patients or their caregiver(s) that they may bleed more easily, may bleed longer, or have a bone fracture. Advise patients or their caregiver(s) to call their healthcare provider for any signs or symptoms of bleeding or report any fractures.

Rx only

Manufactured for:
Mirum Pharmaceuticals, Inc.
950 Tower Lane, Suite 1050
Foster City, CA 94404

LB00004v6

PATIENT INFORMATION
LIVMARLI® (liv-MAR-lee)
(maralixibat)
oral solution

What is LIVMARLI?

- LIVMARLI is a prescription medicine used to treat:
  - cholestatic pruritus (itch) in patients 3 months of age and older with Alagille syndrome (ALGS).
  - cholestatic pruritus (itch) in patients 5 years of age and older with progressive familial intrahepatic cholestasis (PFIC).
- LIVMARLI is not for use in PFIC type 2 patients who have a severe defect in the bile salt export pump (BSEP) protein.
- It is not known if LIVMARLI is safe and effective in children with ALGS who are under 3 months of age.
- It is not known if LIVMARLI is safe and effective in children with PFIC who are under 5 years of age.
- It is not known if LIVMARLI is safe and effective in adults 65 years of age and older.

Before taking LIVMARLI, tell your healthcare provider about all of your medical conditions, including if you:

- are pregnant or plan to become pregnant. It is not known if LIVMARLI will harm your unborn baby. Tell your healthcare provider right away if you think that you are pregnant.
- are breastfeeding or plan to breastfeed. It is not known if LIVMARLI passes into your breast milk. Talk with your healthcare provider about the best way to feed your baby if you take LIVMARLI.

Tell your healthcare provider about all medicines that you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine. LIVMARLI may affect the way some other medicines work, and some other medicines may affect the way LIVMARLI works.

How should you take LIVMARLI?

Read the Instructions for Use that comes with LIVMARLI for information about the right way to prepare and take LIVMARLI.

- Before you take LIVMARLI for the first time, talk to your healthcare provider or pharmacist about how to measure the prescribed dose.
- Take LIVMARLI exactly as your healthcare provider tells you to.
- Your healthcare provider may start you on a low dose of LIVMARLI and then increase the dose, especially if you have not taken LIVMARLI.
- Do not change your dose of LIVMARLI unless your healthcare provider tells you to.
- LIVMARLI is taken by mouth, 1 or 2 times each day (if 2 times per day, take in the morning and evening), 30 minutes before a meal.
- If you miss a dose of LIVMARLI and you take LIVMARLI 1-time a day:
  - If it is 12 hours or less from the time you usually take LIVMARLI, **take the missed dose as soon as possible**. Then take your next dose at the usual time.
  - If it is more than 12 hours from the time you usually take LIVMARLI, **do not take the missed dose**. Take your next dose at the usual time.
- If you miss a dose of LIVMARLI and you take LIVMARLI 2-times a day:
  - If it is 6 hours or less from the time you usually take LIVMARLI, **take the missed dose as soon as possible**. Then take your next dose at the usual time.
  - If it is more than 6 hours from the time you usually take LIVMARLI, **do not take the missed dose**. Take your next dose at the usual time.
- If you take a medicine that lowers cholesterol by binding bile acids, such as cholestyramine, colesevelam, or colestipol, take it at least 4 hours before or 4 hours after you take LIVMARLI. Ask your healthcare provider if you are not sure if you take these medicines.
- If you take too much LIVMARLI, call your healthcare provider or go to the nearest emergency room right away.
- Throw away any remaining LIVMARLI 100 days after first opening the bottle.

What are the possible side effects of LIVMARLI?

LIVMARLI can cause serious side effects, including:

- **Liver injury.** Changes in certain liver tests are common in patients with ALGS and in patients with PFIC but may worsen during treatment with LIVMARLI. These changes may be a sign of liver injury and can be serious or may lead to liver transplant or death. Your healthcare provider should do blood tests and physical exams before starting and during treatment with LIVMARLI to check your liver function. Tell your healthcare provider right away if you get any signs or symptoms of liver problems, including:
  - nausea or vomiting
  - your skin or the white part of your eye turns yellow
  - dark or brown urine
  - pain on the right side of your stomach (abdomen)
  - fullness, bloating, or fluid in your stomach area (ascites)
  - loss of appetite
  - bleeding or bruising more easily than normal, including vomiting blood
- **Stomach and intestinal (gastrointestinal) problems.** LIVMARLI can cause stomach and intestinal problems, including diarrhea and stomach pain during treatment. Diarrhea can also cause the loss of too much body fluid (severe dehydration). Your healthcare provider should check your stool for blood and monitor you for too much body fluid loss.

  Tell your healthcare provider right away if you have any new or worsening signs or symptoms of stomach and intestinal problems including:
  - diarrhea
  - more frequent bowel movements than usual
  - stools that are black, tarry, sticky, or have blood or mucous
  - severe stomach-area pain or tenderness

  Tell your healthcare provider if you have any signs and symptoms of a loss of too much body fluid including:
  - vomiting
  - urinating less often than usual
  - dizziness
  - diarrhea
  - headache
- **A condition called Fat Soluble Vitamin (FSV) Deficiency caused by low levels of certain vitamins (vitamin A, D, E, and K) stored in body fat.** FSV deficiency is common in patients with ALGS and in patients with PFIC but may worsen during treatment with LIVMARLI. Your healthcare provider should do blood tests before starting and during treatment with LIVMARLI.

  Other common side effects of FSV deficiency reported during treatment with LIVMARLI were bone fractures and bleeding.

Your healthcare provider may change your dose, or temporarily or permanently stop treatment with LIVMARLI if you have certain side effects.

These are not all of the possible side effects of LIVMARLI. For more information, ask your healthcare provider or pharmacist. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store LIVMARLI?

- Store unopened LIVMARLI at room temperature between 68ºF and 77ºF (20ºC and 25ºC).
- After opening the LIVMARLI bottle, store below 30ºC (86ºF).

Keep LIVMARLI and all medicines out of the reach of children.

General information about the safe and effective use of LIVMARLI.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use LIVMARLI for a condition for which it was not prescribed. Do not give LIVMARLI to other people, even if they have the same symptoms that you have. It may harm them. You can ask your healthcare provider or pharmacist for information about LIVMARLI that is written for health professionals.

What are the ingredients in LIVMARLI?

Active ingredients: maralixibat chloride.

Inactive ingredients: edetate disodium, grape flavor, propylene glycol, purified water, and sucralose.

Manufactured for: Mirum Pharmaceuticals, Inc., 950 Tower Lane, Suite 1050, Foster City, CA 94404
For more information, go to www.LIVMARLI.com or call 1-855-MRM-4YOU
This Patient Information has been approved by the U.S. Food and Drug Administration Revised: 03/2024

INSTRUCTIONS FOR USE
LIVMARLI® [liv-MAR-lee]
(maralixibat)
oral solution

This Instructions for Use contains information on how to take LIVMARLI. Read this Instructions for Use before you start taking LIVMARLI for the first time and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment.

Follow your healthcare provider's instructions for the dose of LIVMARLI to give.

Ask your healthcare provider or pharmacist if you have questions about how to prepare or give the prescribed dose of LIVMARLI.

Important information about measuring LIVMARLI

- Before you give LIVMARLI for the first time, talk to your healthcare provider or pharmacist about how to correctly measure your prescribed dose.
- You may be given 1 or more dosing dispensers of different sizes as shown in Table 1 below. Always use the correct dosing dispenser size provided with LIVMARLI based on your current prescribed dose.

Table 1

Dose (mL)	Dosing dispenser size (mL)
0.1 to 0.5	0.5
0.6 to 1	1
1.25 to 3	3

- Your prescribed dose may change over time. Use the table above to choose the correct dosing dispenser size for your prescribed dose.
- If you do not have the correct dosing dispenser size for your prescribed dose, contact your healthcare provider or pharmacist.
- The dosing dispenser may be used for 100 days if cleaned correctly (see Section C). After 100 days, replace the dosing dispenser with a new one. A new replacement dosing dispenser may be used within the 100 days if necessary.
- **Do not** use a household teaspoon or any other dosing device to measure the dose.
- **Do not** open more than 1 bottle at a time.
- **Do not** give more than the prescribed dose.
- **Do not** use LIVMARLI after 100 days of first opening the bottle or after the throw away (discard) date listed on the pharmacy label (see Section D).
- When you start a new bottle of LIVMARLI, use a new dosing dispenser.

Storage information

- Store unopened LIVMARLI at room temperature, between 68°F and 77°F (20°C and 25°C).
- After opening the LIVMARLI bottle, store below 86°F (30°C).
- Store the dosing dispenser in a clean, dry place when not in use.

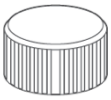
Keep LIVMARLI and all medicines out of the reach of children.

You will receive

LIVMARLI oral solution

Each package of LIVMARLI contains:

LIVMARLI (9.5 mg/mL):

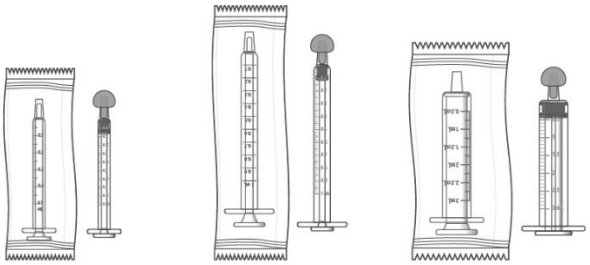


Child-resistant cap

Bottle adapter

Bottle

Dosing dispensers, provided separately by your pharmacist:



Note: Dosing dispenser sizes shown are for example only.

Section A: Prepare the bottle

1. Remove the LIVMARLI bottle from the box (See Figure A).

Note: The LIVMARLI bottle may not be in a box.

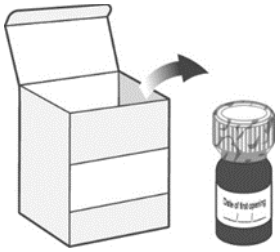


Figure A

2. Write the date (bottle open date) on the LIVMARLI bottle (See Figure B).

Note: The date of first opening or a throw away (discard) date may already be written on the bottle label by your pharmacist.

Figure B

3. Remove the plastic seal from the bottle (See Figure C).

Note: Your pharmacist may have already removed the plastic seal from the bottle.

Figure C

Section B: Prepare and give LIVMARLI

Step 1: Draw the dose

1.1: Open the bottle by pushing down firmly on the child-resistant cap and turning the cap to the left (counter-clockwise) (See Figure D).

Do not throw away the child-resistant cap.

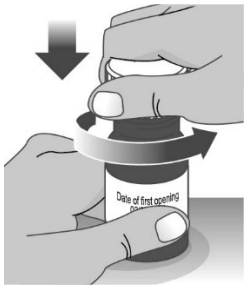


Figure D

1.2: If using a new dosing dispenser, remove the dosing dispenser from the wrapper (See Figure E). Throw away (dispose of) the wrapper in household trash.

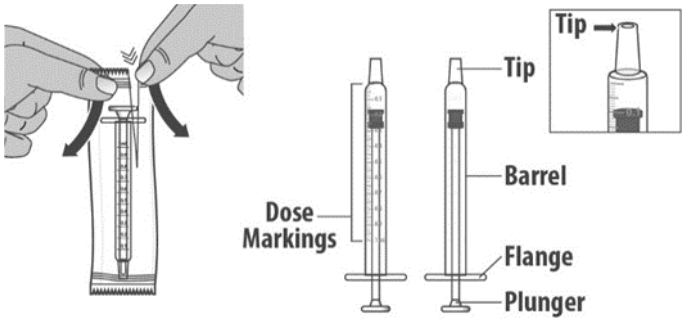


Figure E

If using a used dosing dispenser, make sure the dosing dispenser has been cleaned (See Section C).

If there is a cap on the dosing dispenser, remove it and throw away (dispose of) the cap into the household trash (See Figure F).

Important:

- Make sure you use the correct dosing dispenser size for your prescribed dose (See Table 1).
- After 100 days, replace with a new dosing dispenser provided. A new replacement dosing dispenser may be used within the 100 days if necessary.
- Check the dosing dispenser for any damage to the barrel, plunger or tip (See Figure G). If you cannot see the dosage marking or if it becomes hard to move the plunger, replace with a new dosing dispenser.

Note: You can mark the prescribed dose on the dosing dispenser with a thin permanent marker to draw up the prescribed dose more easily.

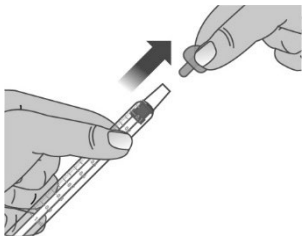


Figure F

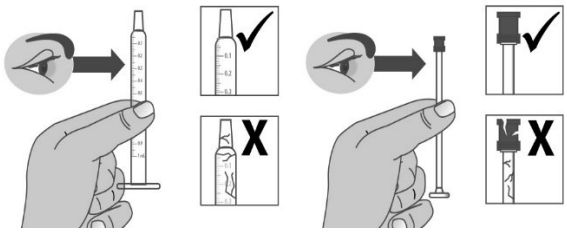


Figure G

1.3: Push the plunger down fully to remove air from the dosing dispenser (See Figure H).

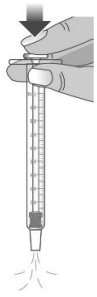


Figure H

1.4: Make sure the cap is removed from bottle and insert the tip of the dosing dispenser into the bottle. The tip of the dosing dispenser should fit securely into the hole of the bottle (See Figure I).

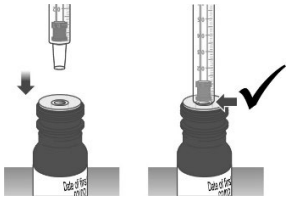


Figure I

1.5: Keep the dosing dispenser in place and turn the bottle upside down (See Figure J).

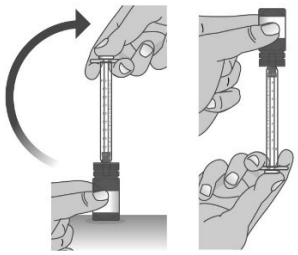


Figure J

1.6: Pull back the plunger slowly until the top of the plunger is even with the marking on the barrel of the dosing dispenser for your prescribed dose of LIVMARLI (See Figure K).

See Figure L on how to align the plunger with your prescribed dose.

Note: The medicine should appear colorless to light yellow and clear. If it is not, do not use the medicine and contact your pharmacist.

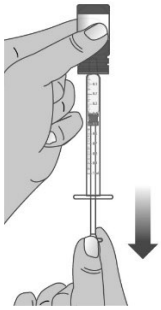


Figure K

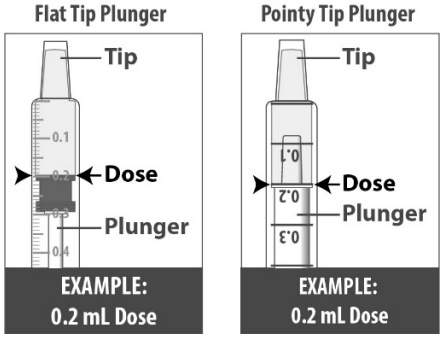


Figure L

Note: Your dose may be different than the dose shown in the figures.

1.7: Check the dosing dispenser for air bubbles. If you see any air bubbles, fully push the plunger so that the medicine flows back into the bottle and withdraw the prescribed dose (See Figure M).

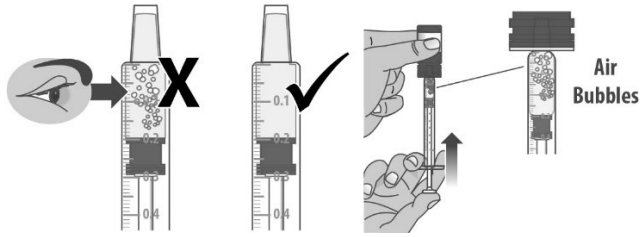


Figure M

1.8: When you have measured the correct dose, leave the dosing dispenser in the bottle, and turn the bottle right side up (See Figure N).

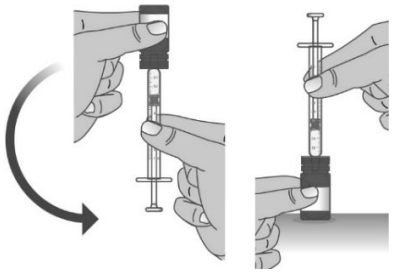


Figure N

1.9: Carefully remove the dosing dispenser from the bottle by pulling straight up on the barrel of the dosing dispenser (See Figure O).

Do not push the dosing dispenser plunger during this step.

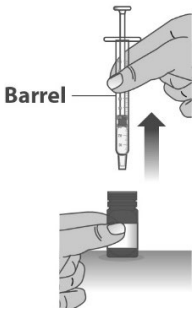


Figure O

Step 2: Give the dose

Note: LIVMARLI should be taken while sitting up or standing. After taking LIVMARLI wait a few minutes before lying down.

2.1: **Place** the tip of the dosing dispenser against the inside of the cheek (See Figure P) and slowly push the plunger all the way in to give the entire dose of LIVMARLI (See Figure Q).

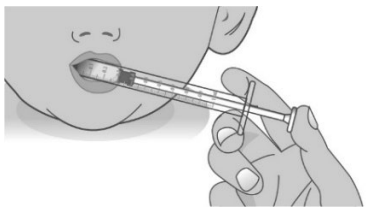


Figure P

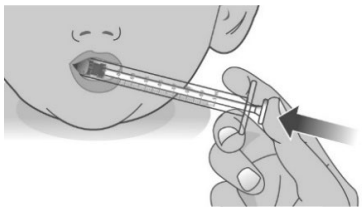


Figure Q

2.2: Swallow the dose.

If you are not sure the entire dose was swallowed, do not give another dose. Wait until the next scheduled dose.

2.3: **Place** the child-resistant cap back on the bottle and turn the cap to the right (clockwise) (See Figure R).

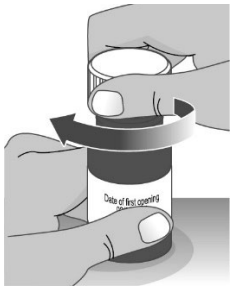


Figure R

Section C: Cleaning instructions for the dosing dispenser

Step 1: Rinse dosing dispenser

1.1: Fill a cup with water (See Figure S).

Figure S

1.2: Clean the dosing dispenser by pulling back on the plunger slowly to fill the dosing dispenser with water from the cup (See Figure T).

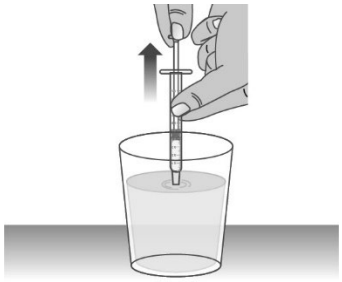


Figure T

1.3: Over a sink, push the water out of the dosing dispenser (See Figure U). Repeat several times to make sure that all of the LIVMARLI has been removed.

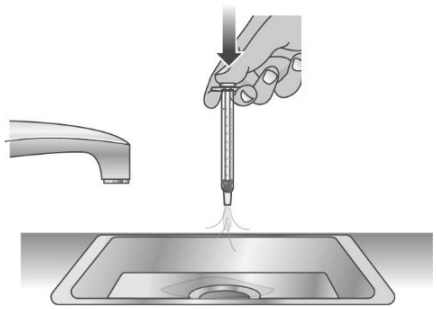


Figure U

Step 2: Dry the dosing dispenser

2.1: Remove the plunger from the barrel of the dosing dispenser by pulling the plunger and barrel away from each other (See Figure V).

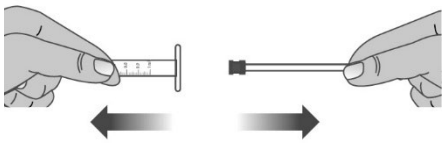


Figure V

2.2: Shake off excess water (See Figure W).

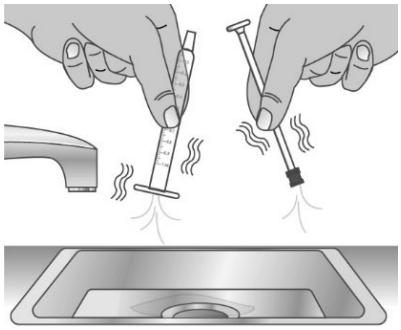


Figure W

2.3: Place the plunger and barrel on a clean, dry paper towel to air dry. Store the dosing dispenser in a clean, dry place until your next dose (See Figure X).

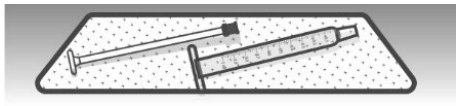


Figure X

Before you give the next dose, put the dosing dispenser back together by pushing the plunger into the barrel (See Figure Y).

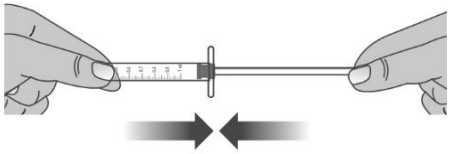


Figure Y

Section D: Disposal

- Throw away (dispose of) the bottle of LIVMARLI following the steps below 100 days after first opened or after the throw away (discard) date listed on the pharmacy label, even if there is still medicine in it.
  1. Mix medicine with a substance such as dirt, cat litter, or used coffee grounds.
  2. Place the mixture in a container such as a sealed plastic bag.

3. Delete all personal information on the prescription label of the empty medicine bottle, then throw away (dispose of) in the household trash or recycle the empty bottle.

- Throw away (dispose of) used dosing dispensers in the household trash.

This Instructions for Use has been approved by the U.S. Food and Drug Administration. Revised:03/2023

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