

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Livmarli

Oral solution

Active ingredient:

Each 1 ml contains 10 mg maralixibat chloride (equivalent to 9.5 mg of maralixibat).

For the list of inactive ingredients, see section 6: 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. What is this medicine intended for?

Livmarli is indicated for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 1 year of age and older.

Therapeutic group: medicines for treatment of bile duct diseases.

2. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the other ingredients in this medicine (see section 6 'Additional information').

Special warnings regarding the use of this medicine

Before treatment with Livmarli, tell your doctor or pharmacist if:

- You have liver problems.
- You are pregnant, think you are pregnant or plan to become pregnant. It is not known whether Livmarli may harm the fetus.
- You are breastfeeding or plan to breastfeed. It is not known whether Livmarli passes into breast milk.

Children and adolescents:

Livmarli is intended for treating children one year of age and older. There is no information regarding the safety and efficacy of using Livmarli in children under 1 year of age.

Tests and follow-up:

- Your doctor may refer you for liver function tests before and during the treatment with Livmarli.
- Your doctor may refer you for a blood test for levels of fat soluble vitamins (vitamins A, D, E, and K) before and during the treatment with Livmarli.

Drug interactions:

If you are taking or have recently taken other medicines, including non-prescription medications and dietary supplements, tell your doctor or pharmacist, especially if you are taking:

- Cholesterol lowering medicines that bind bile acids (cholestyramine, colestipol, etc.) - these medicines might decrease the activity of Livmarli. You should take them at least 4 hours before or 4 hours after taking Livmarli.
- Cholesterol lowering medicines of the statins family, since the effect of Livmarli on the absorption level of these medicines/activity of these medicines cannot be excluded.

Using this medicine and food:

This medicine should be taken 30 minutes before a meal in the morning.

Pregnancy, breastfeeding and fertility:

Pregnancy

If you are pregnant or plan to become pregnant, consult your doctor or pharmacist since it is not known whether Livmarli may harm the unborn baby.

Breastfeeding

If you are breastfeeding or plan to breastfeed, consult your doctor since it is not known whether Livmarli passes into breast milk.

Fertility

There are no clinical data regarding the effect of Livmarli on fertility. No direct or indirect effects on fertility and reproduction were observed in animal studies.

Driving and using machines:

Livmarli has no or only negligible effect on the ability to drive and use machines.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

Only your doctor will determine your dose and how you should take this medicine.

- Before using Livmarli for the first time, talk to your doctor or pharmacist about how to measure the required dose.
- Your doctor may instruct you to start at a low dose, which will be increased afterwards, especially if you have not used Livmarli in the past.
- Do not change the dose of Livmarli without your doctor's instruction.
- Livmarli is taken by mouth, once a day, 30 minutes before a meal in the morning.
- If you take cholesterol lowering medicines that bind bile acids (such as cholestyramine, colestipol, etc.), you should take them at least 4 hours before or 4 hours after taking Livmarli.
- According to your liver function test results, your doctor may change the dose of Livmarli or even stop treatment with the medicine.

According to your blood test results for fat soluble vitamins (vitamins A, D, E, and K), your doctor may instruct you to change the dose of Livmarli or even to stop treatment with the medicine. In addition, according to these test results, your doctor may consider instructing you to take dietary supplements containing these vitamins.

Do not exceed the recommended dose.

If you have accidentally taken a higher dose:

If you have taken more Livmarli than needed, report immediately to your doctor, pharmacist or nurse.

If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you have forgotten to take Livmarli:

- If you have missed a dose and less than 12 hours have passed from the scheduled intake time, take the dose as soon as you remember. Take your next dose at the usual scheduled time.
- If you have missed a dose and more than 12 hours have passed from the scheduled intake time, skip this dose and take your next dose at the usual scheduled time.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop treatment with this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose every time you take a medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

Like with all medicines, using Livmarli may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Stop using Livmarli and contact your doctor immediately if you experience any of the serious side effects listed below - you might need urgent medical treatment:

- **A change in liver function test results:** Changes in liver function test results are common in patients with Alagille syndrome, but may worsen during treatment with the medicine. These changes may be severe and may indicate liver injury. Contact your doctor if you experience one or more of the following symptoms:
 - nausea or vomiting
 - yellowing of the skin or the white part of the eyes
 - dark or brown urine
 - pain on the right side of the abdomen
 - loss of appetite
- **Gastrointestinal problems:** diarrhea, abdominal pain and vomiting during treatment with the medicine. Contact your doctor immediately if any of these effects worsen or appear more often than usual.
- **Fat soluble vitamin deficiency (vitamins A, D, E, and K) stored in body fat.** This phenomenon is common in patients with Alagille syndrome, but may worsen due to treatment with Livmarli.

Additional side effects:

Very common side effects - affect more than 1 in 10 users:

- gastrointestinal bleeding

Common side effects - affect 1-10 in 100 users:

- bone fractures

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: <https://sideeffects.health.gov.il>

You may also report by email to the registration holder's patient safety unit at: drugsafety@neopharmgroup.com

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.

- Do not use the medicine after the expiry date (exp. date) which is stated on the package and the bottle. The expiry date refers to the last day of that month.

Storage conditions:

- Store below 25°C.
- Livmarli can be used for 100 days after first opening the package.
- After first opening of the package store below 30°C.
- The measuring syringe should be clean and stored in a dry place when not in use.
- Throw away any remaining Livmarli.

6. Additional information

- **In addition to the active ingredient, this medicine also contains:**
Purified water, propylene glycol, sucralose, grape flavor and disodium EDTA dihydrate
- **What the medicine looks like and contents of the pack**
Clear solution, colorless to yellow.

The medicine is supplied in a plastic bottle of 30 ml.

Manufacturer's name and address:

Mirum Pharmaceuticals, Inc., 950 Tower Lane, Foster City, CA 94404, USA

Registration holder's name and address:

Neopharm (Israel) 1996 Ltd., 6 Hashiloach Street, POB 7063, Petach Tikva, 4917001.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Livmarli: 170-65-37132-99

Revised in November 2023 according to MOH guidelines.

Livmarli SOL PIL vr 02A

Instructions for use

Livmarli (maralixibat)

Oral solution

This page contains instructions for using Livmarli. Read the page of instructions for use before taking Livmarli for the first time and each time you receive Livmarli. The information may be updated. This page does not replace consultation with your doctor regarding your medical condition and required treatment.

Follow your doctor's instructions regarding the required dose of Livmarli.

Consult your doctor or pharmacist about preparation or administration of the dose of Livmarli.

Important information about the manner of measuring the dose of Livmarli

- Before taking Livmarli for the first time, consult your doctor or pharmacist about correct measurement of the required dose.
- There are measuring syringes of different volumes, as listed in Table 1. Use the measuring syringe suitable for the required dose, which will be provided with the medicine.

Dose (ml)	Dosing syringe volume (ml)
0.1 to 0.5	0.5
0.6 to 1	1
1.25 to 3	3

- The required dose may change over time. Use the table above to choose the syringe volume suitable for your prescribed dose.
- If you do not have a syringe of the volume suitable for your prescribed dose, consult your doctor or pharmacist.
- The syringe can be used for up to 100 days if cleaned correctly (see section 3). After 100 days, replace it with a new syringe. A new replacement dosing dispenser-syringe may be used within the 100 days if necessary.
- **Do not** use a teaspoon or any other measuring device to measure the required volume.
- **Do not** open more than one bottle at a time.
- **Do not** administer more than the required dose.
- **Do not** use Livmarli after 100 days of first opening the bottle, or after the expiry date stated on the package (see section 4).
- When you start using a new bottle of Livmarli, use a new syringe.

What does the Livmarli package contain?

Each Livmarli package contains:

Livmarli (9.5 mg/ml):

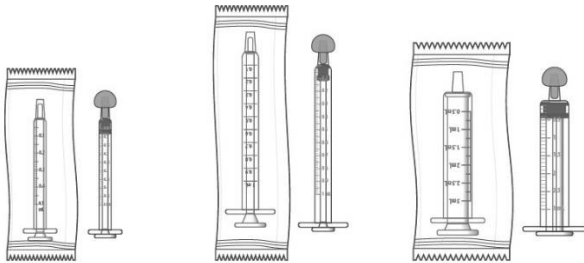


Cap (child-resistant)

Bottle opening adapter

Bottle

Dosing syringes for measurement and medicine administration, provided separately from the medicine:



0.5 ml
syringe

1 ml syringe

3 ml
syringe

Note: Dosing syringe sizes shown here are for example only.

Section A: Preparing the bottle

1. Remove the Livmarli bottle from the carton box (Figure 1).

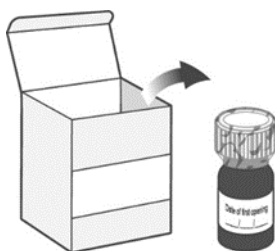


Figure 1

- Record the date of opening on the bottle (Figure 2).



Figure 2

- Remove the plastic seal from the bottle (Figure 3).



Figure 3

Section B: Preparing and administering Livmarli

Step 1: Drawing the dose

- 1.1 Open the bottle by pushing down firmly on the child-resistant cap and turning it to the left (counter-clockwise) (Figure 4).

Do not throw away the child-resistant cap.

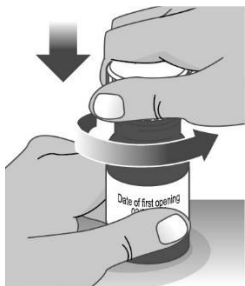


Figure 4

1.2 If you are using a new syringe, remove it from the wrapper (Figure 5). Throw away the syringe wrapper into household trash.

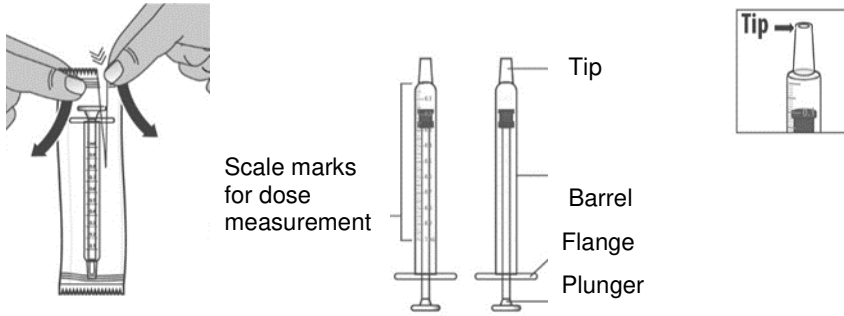


Figure 5

If you are re-using the measuring syringe, ensure that the syringe has been cleaned (see section C). If there is a cap on the measuring syringe, remove it and throw it away into household trash (Figure 6).

Important:

- Ensure that you use the correct syringe size for your prescribed dose (see Table 1).
- After 100 days, replace the syringe with a new measuring syringe. A new replacement dosing dispenser-syringe may be used within the 100 days if necessary.
- Check the measuring syringe for damage to its barrel, plunger or tip (Figure 7). If you cannot identify the scale marks, or if it becomes difficult to move the plunger, replace the syringe with a new measuring syringe.

Note: You can mark your prescribed dose on the measuring syringe with a thin permanent marker to make it easier for you to draw the required amount.

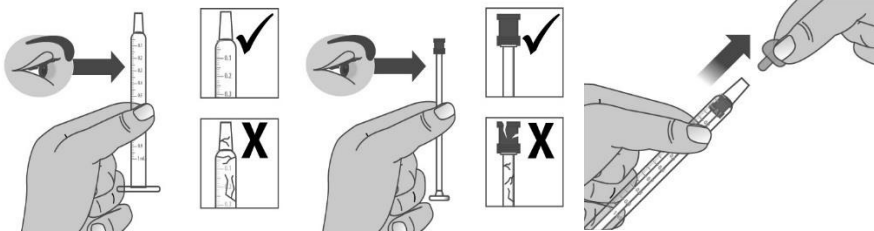


Figure 7

Figure 6

1.3 Push the plunger down completely to remove air from the measuring syringe (Figure 8).

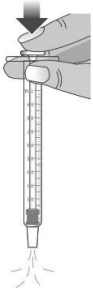


Figure 8

1.4 Ensure that the cap was removed from the bottle and insert the tip of the measuring syringe into the bottle. The syringe tip should fit precisely to the bottle opening (Figure 9).

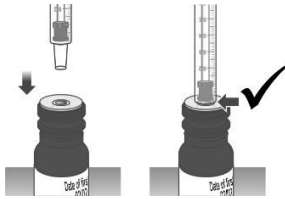


Figure 9

1.5 Hold the syringe in place and turn the bottle upside down (Figure 10).

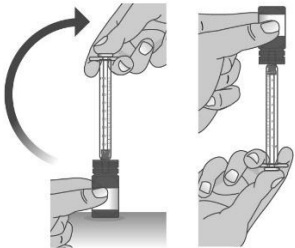


Figure 10

1.6 Pull the plunger slowly until the plunger tip is aligned with the mark on the syringe for your prescribed dose of Livmarli (Figure 11).

See Figure 12 demonstrating how to align the plunger tip with the mark on the syringe.

Note: The medicine should be clear, colorless to yellowish. If it is not, do not use the medicine and consult your pharmacist.

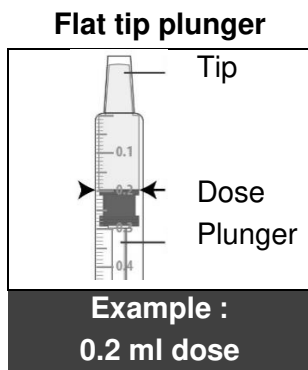


Figure 12

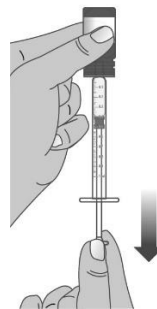
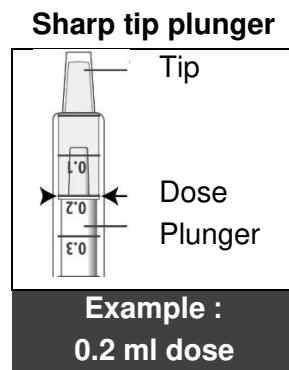


Figure 11

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

1.7 Check that the syringe is free of air bubbles. If you notice air bubbles, push the plunger back so that the medicine returns into the bottle, and then draw your prescribed dose (Figure 13).

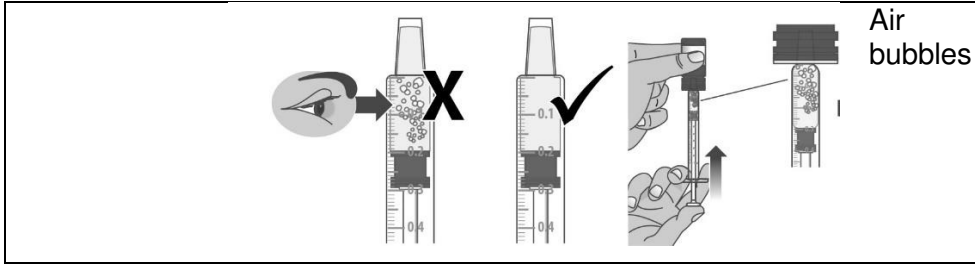


Figure 13

1.8 After you have measured the correct dose, leave the measuring syringe in the bottle, and turn the bottle upwards (Figure 14).

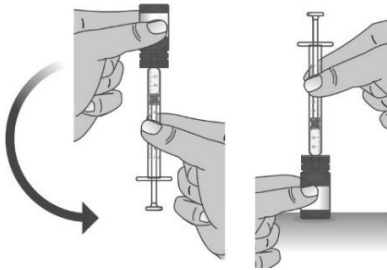


Figure 14

1.9 Carefully disconnect the syringe from the bottle by pulling the barrel upwards (Figure 15).

Do not push the syringe plunger at this step.

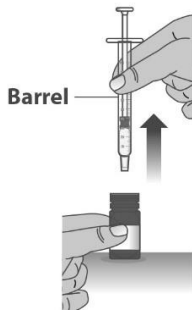


Figure 15

Step 2: Dose administration

Note: Livmarli should be taken while sitting or standing. After taking Livmarli, wait a few minutes before transition to lying position.

2.1 **Place** the syringe tip adjacent to the internal side of the cheek (Figure 16) and gently push the plunger completely to administer the entire dose of Livmarli (Figure 17).

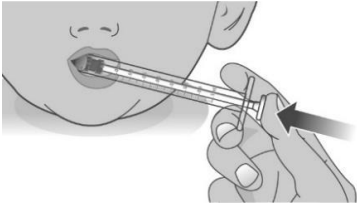


Figure 17

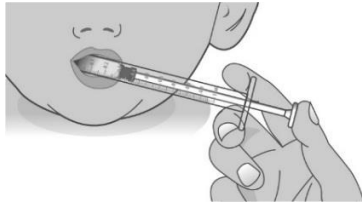


Figure 16

2.2 Swallow the medicine dose.

If you are not sure that the entire dose was swallowed, do not use another dose. Wait until the time of the next dose.

2.3 Place the child-resistant cap back on the bottle and turn it to the right (clockwise) (Figure 18).

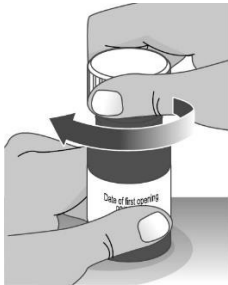


Figure 18

Section C: Instructions for cleaning the measuring syringe

Step 1: Rinsing the measuring syringe

1.1 Fill a glass with water (Figure 19).



Figure 19

1.2 Clean the syringe by pulling the plunger slowly and filling the syringe with water from the glass (Figure 20).

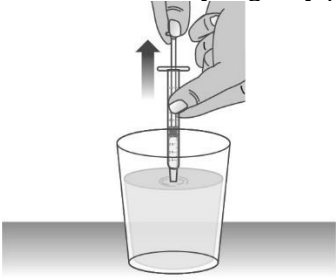


Figure 20

1.3 Over the sink, empty the water out of the syringe (Figure 21). Repeat the action several times to ensure that all the medicine residues have been washed away.

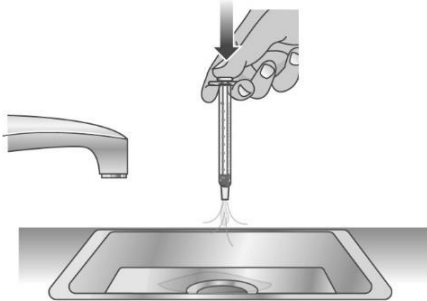


Figure 21

Step 2: Drying the measuring syringe

2.1 Separate the plunger from the syringe barrel by pulling them away from each other (Figure 22).

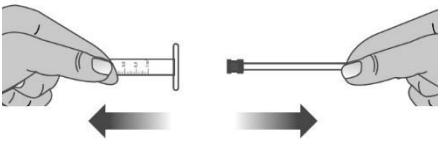


Figure 22

2.2 Shake off excess water (Figure 23).

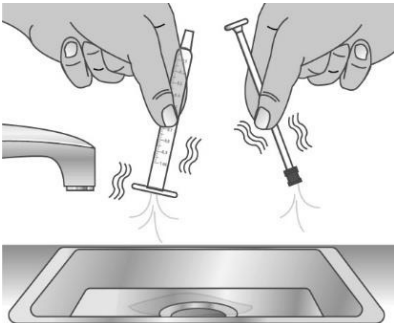


Figure 23

2.3 Place the barrel and plunger on a clean paper towel to air dry. Store the measuring syringe in a clean, dry place until the next dose administration (Figure 24).

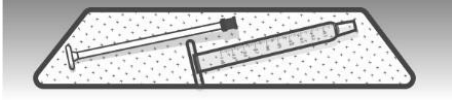


Figure 24

Before the next dose administration, reassemble the syringe parts by pushing the plunger into the barrel (Figure 25).

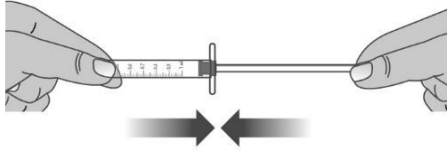


Figure 25