Package leaflet: Information for the patient

FOMEPIZOLE SERB 5 mg/ml concentrate for solution for infusion
Fomepizole (as sulphate)

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This include any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. WHAT FOMEPIZOLE SERB IS AND WHAT IT IS USED FOR

FOMEPIZOLE SERB is an antidote. It is used as an emergency treatment for oral ethylene glycol poisoning.

Your doctor has prescribed you this medicine because you have ingested a toxic substance called ethylene glycol (clear, colorless, odorless liquid with a sweet taste, widely used as an automotive antifreeze).

FOMEPIZOLE SERB halts the progression of ethylene glycol poisoning and allows removal of ethylene glycol from blood.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE FOMEPIZOLE SERB

Do not use FOMEPIZOLE SERB
- If you are allergic to fomepizole or any of the other ingredients of this medicine (listed in section 6).
- If you are allergic to other medicines belonging to the same family (pyrazoles). In such case, you may also be allergic to fomepizole.

Warnings and precautions
Take special care with FOMEPIZOLE SERB
- If you experience:
  - a sudden swelling of the throat, face, lips or mouth,
  - redness, skin rush or itching.

  It is an allergic reaction. In this case, your doctor will monitor the observed signs.
  If your allergic reaction becomes more important or gets worse, you should immediately stop your treatment in absence of any other obvious cause.
- If you have liver problems (impaired liver function). In this situation, your doctor will ask you to perform blood test in order to monitor your liver function.

Talk to your doctor before using FOMEPIZOLE SERB.

Other medicines and FOMEPIZOLE SERB.
You should not combine medicines containing alcohol and FOMEPIZOLE SERB. It may reduce their elimination.
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines.

Pregnancy, breast-feeding
You should not use FOMEPIZOLE SERB if you are pregnant or if you are breast-feeding unless absolutely necessary.
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines
You should not drive or use any tools or machines the first few days after treatment is discontinued.
Dizziness and vertigo may occur after treatment. If you experience any of these signs, you should not drive or use any tools or machines.

FOMEPIZOLE SERB contains sodium
This medicine contains 55 mg of sodium (main component of cooking/table salt) per ampoule. This is equivalent to 2.8% of the recommended maximum daily dietary intake of sodium for an adult.

3. HOW TO USE FOMEPIZOLE SERB

Dosage
This medicine will be given by your doctor. It will be given to you as a slow injection into one of your veins.

The dose of FOMEPIZOLE SERB varies from one patient to another. Your doctor will decide the correct dose.

It depends on :
- your age, your weight,
- how your liver and kidneys are working,
- if you need a medical procedure for removing ethylene glycol from your blood (also called hemodialysis).

If you have been given more FOMEPIZOLE SERB than you should, the following effects may occur:
- dizziness,
- drunkenness,
- feeling sick (nausea),
- vertigo
- headaches,
- blurred vision,
- slurred speech.

If you experience any of these signs, you should contact your doctor immediately.

In these circumstances your doctor may decide to undertake a medical procedure called hemodialysis which will remove excess drug from blood.

If you forget to use FOMEPIZOLE SERB
Take the next dose as usual. Do not take a double dose to make up for a forgotten dose.

If you have any further questions on the use of this medicine, ask your doctor.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The most commonly adverse effects are:
- Dizziness,
- Headaches.

The following side effects may commonly occur:
- **Allergic reactions:**
  - In administration area: injection site reaction, injection site inflammation.
  - Skin: a sudden swelling of the throat, face, lips or mouth, redness, skin rush or itching.

If you experience any of these signs, you should tell your doctor.
He/she will monitor the observed signs.
If your allergic reaction becomes more important or gets worse, you should immediately stop your treatment in absence of any other obvious cause.

Other side effects that may occur with FOMEPIZOLE SERB:
- **Heart and circulation:**
  - abnormal pulse rate,
  - strong heart beat.
- **Nervous system:**
  - vertigo,
  - anxiety, agitation,
  - blurred vision, vision disorders,
  - fits (convulsions),
  - slurred speech.
- **Stomach and gut :**
  - feeling sick (nausea), being sick (vomiting),
  - diarrhea, indigestion (dyspepsia),
  - hiccups.
- **Alteration in the blood :**
  - temporary increase of liver enzymes (test done to check liver function),
  - increased blood pressure
  - increased CPK (test done to check muscular function),
  - increase in some white blood cells count (eosinophils),
  - decrease in red cells (anemia).

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via :
HPRA Pharmacovigilance, Earlsfort Terrace , IRL - Dublin 2, Tel: +353 1 6764971,
Fax: +353 1 6762517 - Website: www.hpra.ie, e-mail: medsafety@hpra.ie
By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE FOMEPIZOLE SERB

Keep this medicine out of the sight and reach of children.
Do not freeze.
The product should be diluted immediately after opening and any unused product should be discarded.
After dilution, chemical and physical in-use stability has been demonstrated for 24 hours at 25°C.
From a microbiological point of view, the product should be used immediately. If not used immediately, in–use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic condition.

Do not use this medicine after the expiry date which is stated on the carton and the label after EXP. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What FOMEPIZOLE SERB contains

- **The active substance is:** fomepizole (5 mg per 1 ml of concentrate for solution for infusion).
- **The other ingredients are:** sodium chloride and water for injections.

An ampoule of 20 ml contains 160 mg fomepizole sulphate, equivalent to 100 mg fomepizole.

What FOMEPIZOLE SERB looks like and contents of the pack

FOMEPIZOLE SERB is a concentrate for solution for infusion. It is a clear and colourless solution. Each box contains 5 ampoules of 20 ml.

Marketing Authorisation Holder and Manufacturer
Marketing authorisation :
SERB S.A.
Avenue Louise, 480
1050 Brussels
Belgium

Manufacturer:
Etablissement Pharmaceutique de l'AP-HP
(Assistance Publique-Hôpitaux de Paris) AGEPS
7, rue du Fer à Moulin - BP 09
75221 PARIS Cedex 05 – FRANCE

or

CENEXI
52 rue Marcel et Jacques Gaucher
94120 Fontenay-sous-Bois
France

This medicine is authorised in the Member States of the European Economic Area under the following names:

Austria	Fomepizole SERB	Zul Nr: 1-24520
Belgium	FOMEPIZOLE SERB	BE233326
France	FOMEPIZOLE SERB	34009 562 842 4 5
Finland	FOMEPIZOLE SERB	16705
Germany	FOMEPIZOLE SERB	Zul.-Nr. 52 450.00.00
Iceland	FOMEPIZOLE SERB	IS/1/01/044/01
Ireland	FOMEPIZOLE SERB	PA20595/001/001
Luxembourg	FOMEPIZOLE SERB	2001120031
Norway	FOMEPIZOLE SERB	MTnr. 2001-06270
Sweden	FOMEPIZOLE SERB	17485
The Netherlands	FOMEPIZOLE SERB	RVG 26970

This leaflet was last revised in 02/2022

The following information is intended for healthcare professionals only:
The treatment should begin whenever ethylene glycol poisoning is suspected, as early as possible after its ingestion, even in absence of signs of toxicity.

Dosage
In the absence of ethylene glycol assay, ethylene glycol poisoning should be suspected on the following criteria:

- patient's history,
- osmolar gap > 20 mOsm/kg H20,
- metabolic acidosis with anion gap > 16 mmol/l (presence of high levels of glycolates),
- calcium oxalate crystals in the urine.

An assay for plasma ethylene glycol should be performed at admission, but this determination should not delay start of treatment with FOMEPIZOLE SERB. Plasma ethylene glycol levels should be monitored every 12 to 24 hours.
FOMEPIZOLE SERB must be diluted before use and administered by slow intravenous infusion.
The concentrate should be diluted with 0.9% sodium chloride solution or 5% glucose solution for intravenous use.
Dosage depends on plasma ethylene glycol concentration, renal function and on body weight.

Patients with normal renal or mild to moderate impaired renal function as assessed by serum creatinine (100 to 265 µmol/l) in whom hemodialysis is not required :
Administration should be performed by slow intravenous infusion, over 30 to 45 minutes, given as follows: infusion of a loading dose of 15 mg/kg followed by doses every 12 hours until ethylene glycol levels have been reduced (below 0.2 g/l (3.2 mmol/l)).

Fomepizole dose (mg/kg body weight)					
Loading dose	**2nd dose (12 hours)**	**3rd dose (24 hours)**	**4th dose (36 hours)**	**5th dose (48 hours)**	**6th dose (60 hours)**
15	**10**	**10**	**10**	**7.5 to 15**	**5 to 15**

The number of maintenance doses and the dose after 48 hours will depend on initial concentration and the time course of the ethylene glycol levels.

Generally 4 to 5 maintenance doses are recommended for initial ethylene glycol levels between 3 to 6 g/l (48 to 96 mmol/l) and 1 to 3 maintenance doses are recommended for initial ethylene glycol levels between 0.35 to 1.5 g/l (5.6 to 24 mmol/l).

Patients with severe impaired renal function as assessed by serum creatinine (> 265 µmol/l):
Hemodialysis is indicated in combination with FOMEPIZOLE SERB.
Hemodialysis and fomepizole sulphate administration should be discontinued when the metabolic acidosis is corrected and plasma ethylene glycol levels have been reduced below 0.2g/l (3.2 mmol/l).
A loading dose of 15 mg/kg is infused over 30 to 45 minutes, followed by 1 mg/kg/hour continuous infusion for the entire duration of the hemodialysis.
Hemodialysis should also be initiated under at least one of the following features in combination with fomepizole :

- arterial pH < 7.10,
- drop in arterial pH > 0.05 resulting in a pH outside the normal range despite bicarbonate infusion,
- inability to maintain arterial pH > 7.30 despite bicarbonate therapy,
- decrease in serum bicarbonate concentration of more than 5 mmol/l despite bicarbonate therapy,
- rise in serum creatinine by > 90 µmol/l (1 mg/dl).

Elderly patients

Clinical experience in elderly patients is limited. The regimen has to be adjusted to the renal function (see above).

Children

There is no available data regarding the pharmacokinetics of FOMEPIZOLE SERB in children. Clinical experience is limited and based on similar weight-adjusted doses.

Instruction for preparation for infusion

For single use only. Any unused product must be discarded.

Only clear and colourless solution without visible particles should be used.

FOMEPIZOLE SERB is to be diluted before use.

FOMEPIZOLE SERB, concentrate for solution for infusion should not be given undiluted; the diluted concentrate should not be given by bolus injection.

This medicinal product must not be mixed with other medicinal products.

Preparation of solution for infusion must take place in aseptic conditions.

The concentrate should be diluted with 0.9 % sodium chloride solution or 5 % glucose solution for intravenous use:

- in patient with normal renal function : each single dose will be diluted with 100 to 250 ml of the above solutions and infused over 30 to 45 minutes.
- in patient with impaired renal function: for continuous infusion in patient undergoing hemodialysis, the concentrate may exceptionally be diluted in a reduced volume of the above solutions, in order to avoid fluid overload.

FOMEPIZOLE SERB contains 55 mg (2.4 mmol) sodium per ampoule equivalent to 2.8% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

It is recommended that FOMEPIZOLE SERB is diluted in a glucose solution for patients on a controlled sodium diet.

After dilution, chemical and physical in-use stability has been demonstrated for 24 hours at 25 °C.

From a microbiological point of view, the product should be used immediately.

If not used immediately, in–use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless dilution has taken place in controlled and validated aseptic condition.

For any information about this medicine, please contact the Marketing Authorisation Holder: **SERB S.A.** Avenue Louise 480 1050 Brussels Belgium