

PATIENT INFORMATION LEAFLET

POLIFLEKS 1.5% GLYCINE solution for irrigation

Used for washing.

- **Active substance:** Glycine. Contains 15 grams of glycine per 1 liter of solution.
- **Excipients:** Sterile water for injection.

Before using this medicine, read all of this PATIENT INFORMATION LEAFLET carefully. Because, this leaflet includes important information for you.

- *Keep this PATIENT INFORMATION LEAFLET. You may need to read it again.*
- *If you have any further questions, ask your doctor or pharmacist.*
- *This medicine has been prescribed for you. Do not pass it on to others.*
- *During the use of this medicine, tell that you are using this medicine when you go to a doctor or hospital.*
- *Follow the written instructions exactly. Do not use **higher or lower** dose than the recommended dose.*

The following headlines are included:

- 1. What is POLIFLEKS 1.5% GLYCINE and what is it used for?***
- 2. Before you are given POLIFLEKS 1.5% GLYCINE***
- 3. How you will given POLIFLEKS 1.5% GLYCINE?***
- 4. Possible side effects?***
- 5. How to store POLIFLEKS 1.5% GLYCINE***

1. What is POLIFLEKS 1.5% GLYCINE and what it is used for?

- POLIFKELS 1.5% GLYCINE is a microbe free solution used to clear bladder and urinary tracts. The active substance of the drug, glycine, is an amino acid naturally produced in our bodies.
- It is presented in PVC bags of 3000 milliliters.
- POLIFLEKS 1.5% GLYCINE is the preferred washing solution over water to prevent the harmful effects of the fluids that are used in large amounts during operations performed through urinary tracts on a gland called prostate in men (transurethral prostate resection; TUR).

It may also be used to dilute some drugs that are present in the urinary tracts in concentrated form.

2. Before you are given POLIFLEKS 1.5% GLYCINE

DO NOT USE POLIFLEKS 1.5% GLYCINE if:

If you had an allergic reaction, namely shortness of breath, noisy breathing, skin rashes, itching or swelling on your body, after taking POLIFLEKS 1.5 GLYCINE or other drugs containing

any of its active substances or excipients, DO NOT USE this drug.

If you are not sure whether or not you are allergic to it, please consult your physician. Furthermore, if;

- You experience symptoms such as shortness of breath as a result of hydrothorax (lung edema);

Or after the administration of this drug begins,

- A progressive damage or dysfunction occurs in your kidneys,
- You progressively experience cardiac failure,
- You experience hydrothorax

DO NOT USE this drug.

USE POLIFLEKS 1.5% GLYCINE with CAUTION:

If:

- The packaging of the drug is not intact,
- The solution within is not transparent,
- The drug will be used in an operation that will be performed through your urinary tracts (as the fluids used for the operation may cross over to your blood stream).

Using POLIFLEKS 1.5% GLYCINE with food and beverages

In terms of application method of the drug, it does not have any interaction with food and beverages.

Pregnancy

Please consult your physician or pharmacist before taking the drug.

This drug will not be administered during pregnancy unless it is absolutely necessary.

If you realize that you are pregnant during your treatment, immediately consult your physician or pharmacist.

Lactation

Please consult your physician or pharmacist before taking the drug.

POLIFLEKS 1.5% GLYCINE may be used during lactation.

Ability to drive and use machines

POLIFLEKS 1.5% GLYCINE does not have any effects on driving, or operating machines.

Vital information regarding the some of the excipients contained in POLIFLEKS 1.5% GLYCINE

Unless you have hypersensitivity against any of the excipients contained in POLIFLEKS 1.5% GLYCINE, an adverse reaction is not expected to these substances.

Use in combination with other drugs

If you are planning to take, are taking, recently took, or will take this medicine with other medicine included over-the-counter medicine, vaccine and herbal medicine, please notify your physician.

POLIFLEKS 1.5% GLYCINE may not be compatible with some of the drugs diluted, and administered to your bladder through your urinary tracts. The physician or the healthcare professional that will perform the procedure, will exclude the known-incompatible drugs from the solution, and prefer other solutions to dilute these drugs.

In order to minimize the risk of incompatibility with a drug added to the solution, the healthcare professional will check for blurriness or residues in the final mixture immediately after mixing, and before and during the procedure periodically.

If you are currently taking or recently took any prescribed or over-the-counter drugs, please inform your physician or pharmacist.

3.How you will be given POLIFLEKS 1.5% GLYCINE?

Instructions regarding correct use and dosage/application frequency:

Your physician will determine how much of this drug you need, when it will be administered, and how long your treatment will take.

Method of administration:

It may be administered through a special tube (catheter) to the area that needs to be cleaned or washed.

If necessary, it may be heated in a water bath.

- The solution should be administered in microbe-free environments.
- The instructions for the irrigation set must be referred to for the preparation of the set.
- Remove the bags from their protective covers. Once the protective covers are removed, squeeze the bag to determine the tiny holes. If there are any leaks, the bag should not be used as it might be punctured and not sterile.
- Close the control clamp of the irrigation set.
- Remove the protective cover at the exit hole.
- Insert the connection part of the irrigation set, into the exit hole.
- Adhere to the user instructions of the irrigation set for administration.

Warning: This product is not for intravenous administration.

Various age groups:

Use in children:

The physician determines the dosage and frequency for children.

Special usage cases

Renal/Hepatic failure:

The product should not be used in cases of severe renal failure, where no urine is discharged. As there is a high risk of crossing over to the blood stream in cases such as transurethral prostatectomy where it is used in large amounts, the build of ammonia that results from the break-down of glycine in the body, requires attention.

If you are under the impression that POLIFLEKS 1.5% GLYCINE has a too weak or too strong effect, please contact your physician or pharmacist.

If you have taken more POLIFLEKS 1.5% GLYCINE than you should have:

If you have taken more POLIFLEKS 1.5% GLYCINE than you should have, contact a physician or a pharmacist.

When you take more POLIFLEKS 1.5% GLYCINE than you should have, excessive amounts of fluids or solid matter may build up in your body. In such cases, the physician who performed the operation, will re-assess your situation and implement the due corrective interventions.

If you forget to take POLIFLEKS 1.5% GLYCINE:

Do not double-dose to make up for forgotten doses.

Possible effects once POLIFLEKS 1.5% GLYCINE treatment is concluded:

No possible effects.

4. Possible side effects

As is the case with all drugs, individuals that are sensitive to the substances contained in POLIFLEKS 1.5% GLYCINE, may develop side-effects.

Side effects are categorized into the following categories:

Very common	: It can be seen in at least 1 of 10 patients
Common	: It can be seen in less than one in 10 patients but in more than one in 100 patients
Uncommon	: May be seen in less than 1 in 100 but more than 1 in 1000 patients.
Rare	: It can be seen in less than one in 1000 patients but in more than one in 10000 patients
Very rare	: It can be seen in less than 1 in 10000 patients
Unknown	: It can be seen in a number of patients that is too low to determine with the available data.

If any of the following occurs, stop using POLIFLEKS 1.5% GLYCINE and IMMEDIATELY inform your physician or to the ER unit of the nearest hospital:

- Hypersensitivity (allergy) symptoms:

- Rash, redness/swelling, inflammation in any section of the body;
- Difficulty to breathe, noisy breathing, chest pain;
- Feeling of extreme heat or cold in the body;
- Swelling on the hands, feet, lips, face or entire body,
- Vertigo, light-headedness,
- Heart throb.

These are all serious side-effects.

If you experience any one of these, it means that you are severely allergic to POLIFLEKS 1.5 GLYCINE. Immediate medical intervention or hospital admission might be required.

All of these severe side effects occur very rarely.

POLIFLEKS 1.5% GLYCINE may induce other, non-allergic side-effects. Most of the below listed side-effects are connected with the disruption the solution causes to liquid and solid matters after crossing over to the blood stream.

Unknown incidence:

- Urticaria
- Acidosis of bodily fluids
- Loss of salt
- Dehydration
- Decreased amount of salt (sodium) in bodily fluids (hyponatremia)
- Hyponatremia induced coma
- An increase in the levels of ammonia in the blood, with a possible outcome of coma and/or brain dysfunctions (hyperammonemia)
- Confusion
- Convulsions
- Vertigo
- Blurred vision
- Temporary blindness
- Decreased blood pressure (hypotension)
- Increased heart rate (tachycardia)
- Pains similar to pre-heart attack pains (angina)
- Hydrothorax
- Runny nose
- Increased secretion of saliva
- Nausea
- Vomiting

- Dry mouth
- Thirst
- Back pain
- Increased urinary discharge
- Urinary retention
- Shivering

These are all severe side effects. They may require immediate medical intervention.

If you notice any side effect not mentioned in this leaflet, please inform your doctor or pharmacist.

5. How to store POLİFLEKS 1.5% GLYCINE

Keep POLİFLEKS 1.5% GLYCINE out of the sight and reach of children, and in its original packaging.

Store it at temperatures under 25°C.

Each bag is labeled with its expiration date. The drug will not be provided to you after this date. **Use complying with expiration date.**

Do not use POLİFLEKS 1.5% GLYCINE after the expiration date printed on its packaging.

Marketing authorization holder and manufacturer:

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This patient information leaflet was approved on 16/05/2017.

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE HUMAN MEDICINAL PRODUCT

POLIFLEKS 1.5% GLYCINE SOLUTION FOR IRRIGATION

2. QUALITATIVE AND QUANTITATIVE COMPOUND

Active substance:

Each 100 ml solution contains 1.5 g glycine.

Excipient(s):

See 6.1 for excipients.

3. PHARMACEUTICAL FORM

Sterile, apyrogen solution for irrigation.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

POLIFLEKS 1.5% GLYCINE is indicated for irrigation procedures carried out with endoscopic tools in transurethral interventions where bladder distention, irrigation and lavage are required. It is used as a washing solution that separate blood and tissue particles during transurethral operations. It can also be used to unclog clogged catheters through lavage.

4.2 Posology and method of administration

Posology/frequency and duration of administration:

The dosage and administration frequency should be determined by the physician for each patient depending on the size of the irrigation is to be administered and the intervention to be carried out.

Technical rules of aseptic should be adhered to during irrigation. Bags must be used as soon as possible once opened and the remaining product in the bag should be disposed of, in order to prevent the risk of bacterial contamination.

Method of administration:

Urological irrigations are used through an administration set connected with urethral catheter. If necessary, it may be heated in a water bath.

See section 6.6 for details regarding administration.

Additional information on special populations:

Renal/Hepatic failure:

It is counter-indicated for severe renal failure with anuria.

As there are no studies on this population, there is no specific dosage recommendation for this patient group. As there is a high risk of glycine crossing over to the blood stream in cases such as transurethral prostatectomy where it is used in large amounts, the build of ammonia that results from the metabolism of glycine in the body, requires attention.

Pediatric population:

As there are no studies on this population, there is no specific dosage recommendation for this patient group.

Geriatric population:

As there are no studies on this population, there is no specific dosage recommendation for this patient group.

4.3 Contraindications

It should not be used in patients with anuria.

4.4 Special warnings and precautions for use**WARNINGS**

It should not be used as a parenteral injection.

Urological irrigation solutions should be used care in patients with severe heart-lung or renal dysfunction.

When irrigation fluids are used in transurethral prostatectomy, they may cross over to the systemic circulation in rather large volumes; therefore, POLIFLEKS 1.5% GLYCINE should be considered to be a systemic drug. Absorption of glycine containing irrigation solutions may significantly alter cardiopulmonary and renal dynamics.

A careful cardiovascular monitoring is necessary to avoid fluid overloads. In case of a fluid overload, an intense fluid and electrolyte treatment is required. Due to the possibility of liquid absorption in the following periods, liquid and electrolyte level monitoring could be considered outside the acute period. (See. Adverse reactions observed after marketing).

The solution should not be used if it is not clear, it contains particles, or the integrity of its packaging is not intact.

Bags must be used as soon as possible once opened, in order to prevent to procreation of bacteria and formation of pyrogens. As the solution does not contain any anti-microbial substances, unused irrigation solution should be discarded.

PRECAUTIONS

The amount of glycine containing fluids that can be absorbed into the systemic circulation through the prostatic veins opened during the surgical operation, is high, which may cause significant expansion of the intravascular fluids and fulminant congestive heart failure. Therefore, when POLIFLEKS 1.5% GLYCINE is used before and during transurethral prostatectomy, the cardiovascular state of patients, especially those with hearth diseases, should be carefully assessed. As a result of the transition of the intracellular fluids not containing sodium ions, into the extra-cellular space due to the crossover of glycine into systemic circulation, serum sodium levels may decrease and a current case of hyponatremia may become more prominent.

In case of hepatic dysfunction or the possibility thereof, caution is necessary. In such cases, the ammonia resulting from the metabolism of glycine may build up in the blood.

4.5 Interaction with other medicinal products and other forms of interaction

The drug has no known interactions.

4.6 Pregnancy and lactation

General recommendations

Pregnancy category: C

Women with childbearing potential/Contraception

There is no data available regarding the use of POLIFLEKS 1.5% GLYCINE in women with the potential to bear children, and its effects on birth control. No study has been carried out to determine whether birth control is necessary when using POLIFLEKS 1.5% GLYCINE.

Pregnancy

Studies on animals are insufficient in terms of effects on pregnancy and/or embryonal/fetal development and/or birth and/or after-birth development (see. Section 5.3). Potential risk towards humans is unknown.

POLIFLEKS 1.5% GLYCINE should not be used in pregnant women unless absolutely necessary.

Lactation

In case of systemic exposure of a breastfeeding women to glycine used for irrigation, no effect is foreseen for the breastfed child due to negligibly low levels. POLIFLEKS 1.5% GLYCINE may be used while breastfeeding.

4.7 Effects on ability to drive and operate machines

It has no known effects on driving and using machine.

4.8 Undesirable effects

Undesirable effects are caused when glycine which is used for irrigation, is absorbed into intravascular area.

Undesirable effects are categorized into the following categories:

Very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1000$ to $< 1/100$); rare ($\geq 1/10000$ to $< 1/1000$); very rare ($< 1/10000$), unknown (unpredictable based on the available data).

Immune system disorders

Unknown: Urticaria*, hypersensitivity (allergic reactions)*

Metabolism and nutrition disorders:

Unknown: Acidosis*, electrolyte loss*, dehydration*, hyponatremia (secondary as a result of fluid overloading)*, hyperammonemia (which may result in coma and/or encephalopathy)*,

Psychiatric disorders:

Unknown: Coma (connected with hypernatremia)*

Nervous system disorders:

Unknown: Confusion, convulsions*, light-headedness*

Vision disorders

Unknown: Blurred vision*, temporary blindness*

Cardiac disorders:

Unknown: Hypotension*, tachycardia*, pain resembling angina*

Respiration, chest disorders and mediastinal diseases:

Unknown: Pulmonary congestion*, rhinitis*

Gastrointestinal disorders:

Unknown: Increased saliva secretion, nausea, vomiting*, dry mouth*, thirst*

Musculoskeletal disorders, ligament and skeletal disorders:

Unknown: Back pain*

Renal and urinary disorders

Unknown: Prominent diuresis*, urinary retention*,

General disorders and administration site diseases:

Unknown: Shivering*

*Depends on fluid and electrolyte disorders

As soon as a side-effect is observed, irrigation should be stopped and the clinical status of the patient should be assessed.

Post-marketing experience

In cases where POLIFLEKS 1.5% GLYCINE was administered in procedures involving women not included in the indications, life threatening adverse events was reported in connection with fluid overloading.

4.9. Overdose and therapy

In case of excess fluid or solid overloading, the patient's status should be re-assessed and corrective intervention should be implemented. (See. Warnings, Measures and Undesirable effects).

5. PHARMACOLOGICAL PROPERTIES**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Surgical irrigation solutions

ATC code: B05CX03

POLIFLEKS 1.5% GLYCINE is a solution that is prepared for urological use, is sterile, apyrogen and non-hemolytic, does not contain electrolytes, or is mildly ionized. pH value of the solution is approximately 6.0. Its osmolarity is approximately 200 milliosmole/liter (normal physiological value range is 280-310 milliosmole/liter).

Glycine (NH₂CH₂COOH) is the amino-acid with the simplest structure, and is not one of the essential amino-acids. It is synthesized from “serine” which is another amino-acid that consists of 3-phosphoglycerate.

Used in treatment for various purposes, glycine is sometimes used in the treatment of hyperacidity in combination with anti-acidic medications, in addition to being used as a leading food supplement as an amino-acid. It is also added to the compound of certain aspirin preparations to decrease gastric irritation.

As a 1.5% sterile solution in water, POLIFLEKS 1.5% GLYCINE is hypotonic and is not conductive. Therefore, it is used as urogenital irrigation solution in certain surgical interventions (transurethral prostate resection and transurethral surgical interventions). In addition to being non-hemolytic and non-electrolytic, the solution is transparent and does not cloud the vision clarity during endoscopy.

Systemic absorption of glycine in irrigation administrations is minimal. Blood ammonia levels of patients with regular hepatic functions, do not rise.

5.2 Pharmacokinetic properties

General properties:

When used for its intended purpose, POLIFLEKS 1.5% GLYCINE is not absorbed into the body. However, it is known that the irrigation solutions may cross over to the systemic circulation in irrigation procedures carried out with large volumes during transurethral prostatectomy.

Absorption:

The amount of absorption into the intravascular area depends on the duration and size of the transurethral prostatectomy intervention.

Distribution:

Glycine that enters the systemic circulation, is distributed the same way as natural glycine already available in the circulation.

Biotransformation:

Glycine is bio-transformed in three ways. In animals, the most important way takes place by catalyzing the enzyme that breaks down glycine.

(Glycine + tetrahydrofolate + NAD⁺ → CO₂ + NH₄⁺ + N⁵, N¹⁰ – methylene tetrahydrofolate + NADH + H⁺).

In the second way, glycine undergoes a two-stage degradation. In the first stage, the biosynthesis of glycine occurring via serine hydroxymethyl transferase enzyme from serine is reversed. In the second stage, the resulting serine is converted into pyruvate through serine dehydratase enzyme.

In the third way, glycine is converted into glyoxylate through the D-amino acid oxidase enzyme. Glyoxylate is converted into oxalate through hepatic lactate dehydrogenizes enzyme with a NAD⁺ dependent reaction.

Elimination:

The half-life of glycine and its elimination from the body varies significantly based on its amount in the blood. A study demonstrated its half-life to be from 0.5 to 4.0 hours.

Linearity/Non-linearity:

No data available.

Patient characteristics

No data available.

5.3 Preclinical safety data

As glycine, which is a component of the solution, is an amino acid naturally synthesized in the body, no preclinical studies were carried out regarding the carcinogen, mutagen potential effects of POLIFLEKS 1.5% GLYCINE on fertility.

The safety of the other irrigation drugs diluted and added into the solution should be considered separately.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injection

6.2 Incompatibilities

Compatibility of the drugs to be added to the solution should be assessed beforehand. If the compatibility data is not available, the solution should not be mixed with any drugs. The drugs that are known to be incompatible should not be added to the solution.

6.3 Shelf Life

36 months

6.4 Special precautions for storage

It should be stored at room temperature under 25°C.

6.5 Nature and contents of container

Offered in PVC (Polifleks®) bags in LHDPE protective bags of 3000 ml.

6.6 Special precautions for disposal and other handling

The solution must be checked before use. **Only the clear products that are free from particles, and whose packaging is intact, should be used.**

It is used through an administration set connected with urethral catheter. Administration:

- The solution should be administered in aseptic environments.
- The instructions for the irrigation set must be referred to for the preparation of the set.
- Remove the bags from their protective covers. Once the protective covers are removed, squeeze the bag to determine the tiny holes. If there are any leaks, the bag should not be used as it might be punctured and not sterile.
- Close the control clamp of the irrigation set.
- Remove the protective cover at the exit hole.
- Insert the connection part of the irrigation set, into the exit hole.
- Adhere to the user instructions of the irrigation set for administration.

Warning: The product is not for intravenous administration.

Unused products or waste material must be disposed of in line with local regulations.

7. MARKETING AUHTORISATION HOLDER

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8. MARKETING AUHTORISATION NUMBER

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9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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