SUMMARY OF PRODUCT CHARACTERISTICS

1.NAME OF THE HUMAN MEDICINAL PRODUCT

POLİFLEKS 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

POLİFLEKS 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, POLİFLEKS 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 POLİFLEKS 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 POLİFLEKS 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 POLİFLEKS 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.

POLİFLEKS 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. POLİFLEKS 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 (≥1/10), common (≥1/100 to <1/10); uncommon (≥1/1000 to <1/100); rare (≥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)*, hyperammoniemia (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 POLİFLEKS 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

POLİFLEKS 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 (NH_2CH_2COOH) 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-phosphogliseratte.

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, POLİFLEKS 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, POLİFLEKS 1.5% GLYCINE is not absorbed into the body. However, it 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 + $NAD^+ \longrightarrow CO_2 + NH_4^+ + N^5, N^{10}$ – 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 POLİFLEKS 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

Name : POLİFARMA İLAÇ SAN. VE TİC. A.Ş.

Address : Vakıflar OSB Mahallesi, Sanayi Caddesi
No: 22/1 Ergene/Tekirdağ/TURKEY

Tel : +90 282 675 14 04

Fax : +90 282 675 14 05

8. MARKETING AUHTORISATION NUMBER

2017/316

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16.05.2017

10. DATE OF REVISION OF THE TEXT