SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
DARROW

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Active ingredients:
- Sodium chloride - 4.0 g/l
- Sodium lactate - 5.9 g/l
- Potassium chloride - 2.6 g/l
- Na⁺ - 120 mmol/l
- K⁺ - 35 mmol/l
- Cl⁻ - 105 mmol/l
- Lactate - 50 mmol/l

3. PHARMACEUTICAL FORM
Isotonic solution for infusion

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
- Dehydration secondary to vomiting, diarrhea;
- Hypovolemia secondary to blood losses;
- Metabolic acidosis (with the exception of lactate acidosis).

4.2 Posology and method of administration

In adults
The solution is administered as an intravenous drip instilled at a rate of 20 gtt/min, and the 24-hour dose should not exceed 2,000 ml.
Due to the high potassium concentrations, the solution should be instilled without exceeding the maximal infusion rate in order to avoid plasma potassium elevation and thus cardiac rhythm disorders. If there are
indications for infusion at a higher rate, such infusion should be done under continuous ECG monitoring and plasma potassium monitoring. Solution for infusion quantity is estimated on the basis of the lost secretions and excretions (liter for liter) or according to the circadian demand of the individual.

In children
Darrow solution may be administered to children with diarrhea in a dose of 80 ml/kg diluted by 5% glucose – 100 ml/kg

4.3 Contraindications
Cardiovascular system
In arterial hypotension with oliguria, heart failure.

Kidneys. Urinary tract
In kidney failure

Blood electrolytes
In hyperkalemia, hyperlactatemia

General
In hyperkalemia, kidney failure, arterial hypotension with oliguria.

4.4 Special warnings and special precautions for use
N/A

4.5 Pregnancy and lactation
No restrictions apply for Darrow solution administration during pregnancy and nursing.

4.6 Effects on ability to drive and use machines
As Darrow solution is administered in patient settings, no activities such as driving and using machines are performed.

4.7 Undesirable effects
No adverse drug reactions are practically observed if Darrow solution for infusion is administered properly.

4.8 Overdose
Excessive Darrow solution body infusions may alter extracellular fluid composition and lead to potassium intoxication – rhythm disorders and even asystolia, paresthesia as an early sign.

_Treatment:_ Upon potassium intoxication signs, Calcium gluconate 10% 10-20 ml i.v. is administered as an antidote, with glucose 40% 40 ml with 12-16 IU insulin.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties (pharmacoterapeutic group, mechanism of action, pharmacodynamik effects)

Darrow solution for infusion belongs to the following group of medicines:

- Solutions for i.v. administration;
- Solutions affecting the electrolyte balance;
- 01 Electrolytes;

ATC code: B05B B

Darrow solution is isotonic, and it is a combination of sodium and potassium cations with lactate and chlorine anions at a ratio close to that in small intestine juice. Due to its relatively high content of potassium cations, Darrow solution is used predominantly for correction of hypokalemia conditions.

Lactate addition allows binding free H⁺ during lactate metabolism, and therefore Darrow solution acts as an alkalinizing agent.

Sodium plays an important role in tissue fluid osmotic balance maintenance. The sodium cation is the principal extracellular ion associated with the transmembrane action potential.
Sodium chloride is an important inorganic component of extracellular fluids, and its concentration (about 0.9 per cent) determines blood osmotic pressure. Following parenteral administration in the form of isotonic solution, it causes transient hydremia (passes rapidly to tissues by osmosis) and mild diuresis, and in dehydration it replenishes body fluid losses, however it produces no electrolyte balance. In intoxications, it facilitates dilution of toxic substances and their rapid elimination through the kidneys. Used as diluent of medicines, sodium chloride does not disturb the molecular balance in cells.

Sodium chloride removes purulent matter and promotes granulation tissue formation. Taken orally in appropriate quantities, it stimulates gastric secretion and appetite, and retains fluids in the body. In higher doses and extremely concentrated solutions, it causes vomiting. It may produce a hemostatic effect in hemorrhages from the lungs, stomach, etc., predominantly through reflexes.

Potassium is the principal intracellular ion (98% of potassium is intracellular), and it plays an important role in electrolyte balance. Potassium ions participate in nerve impulse conduction along nerve fibers, in synaptic transmission of nerve excitation and muscle contraction occurrence, in cardiac automation maintenance, etc. Myocardial contractile function, protein metabolism, glycogen synthesis, vegetative nervous system tone, all depend on the sodium-potassium ratio to a great extent.

Reduced potassium blood level increases the risk of arrhythmia development upon high digitalis dose intake. Potassium is antagonist of cardiac glycosides with respect to their effects on cardiac rhythm.

Chlorine anions enter the body in the form of sodium and potassium chloride. Their dynamics depends on sodium dynamics associated with the
function of kidneys and perspiration glands. Exceptions exist, as well – e.g. in acidosis, more chlorine anions are excreted with urine than sodium cations, as well as in abundant vomiting, more chlorine anions are eliminated, which participate in hydrochloric acid composition. Highest chlorine anion concentrations occur in extracellular fluids.

Upon i.v. sodium lactate administration, sodium cations are released, which bind and neutralize acid ions and radicals, while the lactate ion undergoes metabolism whereby part of it accumulates as glycogen, while another part decomposes to carbonic acid and hydrogen carbonate.

5.2 Pharmacokinetic properties (absorption, distribution, biotransformation, elimination)

The sodium and chlorine ions from sodium chloride have no specific pharmacological action. They are eliminated from the body through the kidneys by glomerular filtration with subsequent tubular reabsorption; through perspiration, gastric juice.

Potassium accumulates in cells by an energy-dependent pump, during which it is exchanged for sodium. High concentration gradient between tissues and extracellular fluid is maintained.

The volume of distribution of potassium is unstable. Extracellular potassium levels are easily elevated, however its total body quantity does not change significantly. Plasma potassium levels are leading for its application as a therapeutic agent.

Potassium is excreted predominantly through the kidneys. Unlike the extensively developed renal sodium sparing mechanisms, the kidneys respond weakly to reduced potassium intake. Even in severe hypokalemia, potassium in urine rarely drops under 5-10 mEq daily.
Conversely, higher potassium intake causes rapid renal response, and the excess is rapidly excreted by secretion in the distal tubules. With normal daily dietary potassium intake of about 100 mEq, about 85-90% are excreted with urine.
About 10-15 mEq potassium are eliminated daily with feces.
Potassium is easily eliminated from the body by dialysis. Dialysis may be used in hyperkalemia.

Lactate ion metabolism occurs along the pathway of accumulation of certain part of it as glycogen and along the pathway of decomposition of another part to carbonic acid and hydrocarbonates.

### 5.3 Preclinical safety data
Carcinogenicity, mutagenicity, and fertility impairment studies have indicated no evidence of such toxicity.

### 6. PHARMACEUTICAL PARTICULARS

#### 6.1 List of excipients

<table>
<thead>
<tr>
<th>Name of ingredient</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Water for injections</td>
<td>Ad 1,000 ml</td>
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#### 6.2 Incompatibilities

N/A

#### 6.3 Shelf life and storage conditions

3 years
Store not above 25°C.

**Shelf life after first opening**

Open containers are for single use!

#### 6.4 Special precautions for storage

N/A
6.5 Nature and contents of container
Glass bottles of 500 ml
Polypropylene bottles – 250 ml; 500 ml

6.6 Instructions for use and handling
Use solely absolutely clear solutions!
Use immediately after opening as a single use!

7. MARKETING AUTHORISATION HOLDER
BALKANPHARMA – TROYAPHARM AD
PO Box 82
5600 Troyan
Bulgaria
Phone: (0670) 22 607;
Fax: (0670) 24 139, 22 610

8. MARKETING AUTHORISATION IN OTHER COUNTRIES
None

9. DATE OF FIRST AUTHORISATION