SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ADRENALIN OSEL 1 mg/1 mL IM/IV/SC Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml ampoule contains;

Active substance: 1 mg adrenaline

Excipients:

Sodium chloride	8.0 mg
Sodium metabisulphite	1.5 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Ampoule (intramuscular, intravenous, intracardiac, intratracheal or subcutaneous).
Sterile, clear, colorless solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

ADRENALIN is indicated for:

- Cardiac arrest and cardiopulmonary reanimation

  If artificial respiration and open or closed heart compression do not benefit, ADRENALIN can be administered intravenously, intracardiac or endotracheally after intravenous sodium bicarbonate administration.
- Anaphylactic shock and acute allergic reactions

  Used as a physiological antagonist of histamine against angioedema, drug and serum reactions, insect bites and other allergens. If there is shock, it is not given subcutaneously.

  In addition, the patient in shock should be given an H1 receptor antagonist (chlorpheniramine) intravenously.
- In acute asthma attacks and bronchospasm

  It is administered subcutaneously.
- Stopping capillary (superficial) bleeding in the skin and mucous membranes.

  It is given locally as a solution.
- To extend the duration of action of local anesthetics.

  It is added by dentists as a vasoconstrictor

4.2. Posology and method of administration

Posology /administrationfrequency and duration

Dosage in cases of bronchospasm and hypersensitivity reactions: The usual starting dose for adults in acute anaphylaxis, severe asthma and allergic reactions is 0.1-0.5 mg (0.1-0.5 ml) of ADRENALIN, administered subcutaneously or intramuscularly. If the cause of the allergy is a drug administered subcutaneously or intramuscularly, ADRENALIN injection can be applied to the same places to delay and reduce absorption.

Initial doses of ADRENALIN should be small, these can be increased if necessary. However, the dose given at one time should not exceed 1 mg.

Subcutaneous doses can be repeated at 10-15-minute intervals in anaphylactic shock. In severe asthma attacks, subcutaneous doses can be repeated at intervals of 20 minutes to 4 hours, depending on the patient's response.

In chronic obstructive pulmonary disease, 0.3 mg (0.3 ml) of adrenaline is given 3 times with 20 minutes intervals and this scheme can be repeated every 2 hours.

In severe anaphylactic shock, the intravenous route should be used to get the drug into the circulation.

For this, 0.1-0.2 mg (0.1-0.2 ml) of ADRENALINE is diluted with 8-10 parts of water for injection and given slowly by intravenous injection. If necessary, this can be repeated every 5-15 minutes.

Dosage in case of cardiac arrest: For cardiac reanimation in adults, 0.5-1 mg (0.5-1 ml) of ADRENALIN is diluted and injected intravenously or intracardiac. Intravenous route is preferred in order not to prevent heart massage. 1-2 mg (1-2 ml) of ADRENALIN is added to 10 ml of sterile distilled water and instilled into the trachea through the endotracheal tube, or 0.3 mg (0.3 ml) of ADRENALIN is administered subcutaneously after the first intravenous injection or as an intravenous infusion at a rate of 1-4 μg / min. It is given.

Other application methods and dosages: Local hemostatic adrenaline solutions at a concentration of 1: 50.000 (0.002%) - 1: 1.000 (0.1%) are applied to the skin, mucosa and tissue surfaces as wet dressing or spray.

Adrenaline is added to local anesthetic solutions at a ratio of 1: 500.000-1: 50.000. The most commonly used concentration is 1: 200,000.

Method of administration:

ADRENALIN is preferably injected subcutaneously. It can also be performed intramuscularly,

but the gluteus muscles should not be used (Anaerobe microorganisms may colonize in the skin of this area and the vasoconstrictor effect of ADRENALIN can accelerate the formation of Clostridium welchii infection by causing hypoxia.).

In emergencies, ADRENALIN can be diluted and given as a very slow intravenous injection. In case of cardiac arrest, diluted adrenaline solution can be given by intracardiac injection or endotracheal instillation. Heart massage should also be applied when injected into the heart.

In this way, the drug is provided to participate in the coronary circulation. Adrenaline can be given to an aerosol, vaporizer, IPPB device as oral inhalation.

Adrenaline solutions used for this purpose are more concentrated and injecting them systemically should be avoided. ADRENALİN can be diluted and applied locally to the skin, mucosa and tissue surfaces. Wet dressing or spray forms are used for this.
Adrenaline dose is expressed by the amount of adrenaline in adrenaline salts.

Additional information on special populations:

Renal failure:

No data available.

Hepatic failure:

No data available.

Pediatric population:

Dosage in cases of bronchospasm and hypersensitivity reactions: In cases of severe asthma and anaphylaxis, ADRENALIN is given 0.01 mg / kg (0.01 ml / kg) or 0.3 mg / m^2 (0.3 ml / m^2) subcutaneously to children. One-time pediatric dose should not exceed 0.5 mg (0.5 ml). The doses can be repeated at intervals of 20 minutes to 4 hours, depending on the patient's condition and response.

Dosage in case of cardiac arrest: In children, ADRENALIN 0.005-0.01 mg / kg is injected intracardiac or 0.01 mg / kg ADRENALIN is given intravenously. For this purpose, ready-made ampoules with a concentration of 1: 10.000 should be used. In this way, dilution errors are avoided. It is not used in children under 2 years of age. It is not recommended for use in children under the age of 12 except in emergencies.

Geriatric population:

The recommended dosage for adults is administered with caution.

4.3. Contraindications

In hypertension, hyperthyroidism, coronary insufficiency, diabetes, pheochromocytoma, subaortic stenosis, hypovolemic shock (except anaphylactic shock), organic heart diseases,

arrhythmias, cardiac dilatation, organic brain injury, cerebrovascular diseases, narrow-angle hydrocarbon or halo-caulosis therapy in general anesthesia. Contraindicated in patients with hypersensitivity to adrenaline. In addition, when mixed with local anesthetics, it should not be used on the fingers, ear, nose and genital areas.

4.4. Special warnings and special precautions for use

These warnings and precautions are relative, as ADRENALIN is planned to be used in life threatening situations.

It should be administered slowly to the elderly, patients with ischemic heart disease, hypertension, diabetes mellitus, hyperthyroidism or psychoneurosis. Particular attention should be paid to those with chronic bronchial asthma and emphysema patients who develop degenerative heart disease. Coronary insufficiency can cause angina pain.

It can rarely cause severe hypersensitivity reactions and bronchospasm since it contains sodium metabisulfite as a preservative.

This medicinal product contains less than 1 mmol (23 mg) sodium per ampoule; that is, it can be considered essentially free of sodium.

4.5 Interaction with other medicinal products and other forms of interaction

Tricyclic antidepressants, maprotiline, levodopa, methyldopa, MAO inhibitors, bretyllium, clonidine, dopexamine, entacapone, doxapram, oxytocin, sodium levothyroxine, chlorpheniramine and diphenhydramine can potentiate the effect of adrenaline, causing arrhythmias and severe hypertension.

Digitalis glycosides and mercury diuretics may increase the arrhythmogenic effect of adrenaline.

Ergo alkaloids or oxytoxin may increase the vasoconstrictor effect.

If adrenaline or local anesthetics containing adrenaline were used during delivery, uterotonics such as vasopressin, ergonovine, methylergonovine may cause severe hypertensive crises and postpartum cerebral hemorrhage.

Beta-adrenergic blockers (propranolol) antagonize the bronchodilator effect of adrenaline.

Alpha-adrenergic blockers, prazosin, terazosin, haloperidol, loxapine, phenothiazine and thioxanthines may antagonize the vasoconstrictor effect of adrenaline.

In its halogenated hydrocarbon composition, general anesthetics and cyclopropane increase the arrhythmogenic effect of adrenaline by making the myocardium sensitive.

Sympathomimetic drugs and phosphodiesterase inhibitors increase the arrhythmogenic effect.

Beta-adrenergic antagonists reduce the inotropic effect of adrenaline.

Adrenaline is inactivated in alkaline solutions (sodium bicarbonate, furosemide). It should not be

used to treat hypotension caused by Droperidol. Blood pressure drops further.

Substances containing ephedra and caffeine from herbal medicines can aggravate the effect of adrenaline.

Adrenaline lowers vitamin C and intracellular potassium and magnesium concentrations in plasma.

When adrenaline is given to patients receiving digoxin, quinidine or fluorohydrocarbons, these patients are at a higher risk of developing cardiac arrhythmias. Hyperglycemia caused by adrenaline may impair blood sugar control in diabetic patients treated with hypoglycemic drugs.

Adrenaline specifically reverses the antihypertensive effects of adrenergic neuron blockers such as guanetidine and has a risk of severe hypertension.

Additional information on special populations:

No data available.

Pediatric population:

No data available.

4.6 Pregnancy and lactation

General advice

Pregnancy category: C

Women with childbearing potential / Contraception

There are insufficient data on the use of adrenaline in pregnant women.

Animal studies are insufficient for effects on pregnancy and / or embryonal / fetal development and / or parturition and / or postnatal development (see 5.3).

The potential risk for humans is unknown.

Pregnancy

Adrenaline crosses the placenta. There is evidence of a slight increase in the incidence of congenital anomalies. Injection of adrenaline can cause fetal tachycardia, cardiac irregularities, extrasystoles, and increased heart noise. Adrenaline should not be used during labor. Otherwise, it may prolong the second period of labor.

Adrenalin should be used during pregnancy, but only if the benefits to the mother outweigh the potential risks to the fetus.

Lactation

No research has been conducted on whether adrenaline can be used safely during breastfeeding. It should be used with caution in nursing mothers.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

Adrenaline is metabolized in the body in a short time and its pharmacodynamic effects can only be sustained by continuous administration of the drug. Patients who are given adrenaline are not recommended to drive and use machines unless their organ functions return to normal physiological levels.

4.8 Undesirable effects

Nervous system disorders

Nervousness, anxiety, restlessness, headache, dizziness, lightheadedness, insomnia.

Eye diseases

The appearance or worsening of narrow angle glaucoma, temporary stinging and burning sensations in the eye, eye pain, allergic eyelid reaction, eye irritation.

Cardiac diseases

Tachycardia (parenteral), strong heartbeat, flushing, pallor, chest pain, increased myocardial oxygen consumption, heart arrhythmias, sudden death, angina pectoris, vasoconstriction. Ventricular fibrillation may occur and cause cerebral hemorrhage and pulmonary edema in patients with severe hypertension.

Respiratory, thoracic and mediastinal disorders

Wheezing, dyspnoea.

Gastrointestinal diseases

Nausea, vomiting, dry mouth, dry throat.

Musculoskeletal, connective tissue and bone disorders

Weakness, tremors.

Kidney and urinary disorders

Acute urinary retention, decrease in renal and splanchnic blood flow in patients with obstruction at the bladder outlet.

Other

Some biochemical effects such as increased sweating, cold extremities, local ischemic necrosis, inhibition of insulin secretion and hyperglycemia, gluconeogenesis, glycolysis, lipolysis, ketogenesis, which can occur even with low doses.

Reporting of suspected adverse reactions

If you get any side effects not listed in this leaflet, talk to your doctor or pharmacist. You can also report side effects directly to your doctor or pharmacist. You can also report side effects directly to your country’s related health authority. By reporting side effects, you can help provide more information on the safety of this medicine.

4.9 Overdose

Symptoms: Ventricular fibrillation and cardiac arrhythmias that can result in death; pulmonary edema and cerebral hemorrhage caused by severe hypertension.

Treatment: The effects of adrenaline can be overcome with combined alpha- and beta-adrenergic blocker drugs such as labetalol or beta-blockers can be used to treat any supraventricular arrhythmia; Phentolamine can be used to control alpha-induced effects in the peripheral circulation.

Quick-acting nitrates and vasodilators such as sodium nitroprusside may help.
Emergency life support should be provided.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Adrenergic and dopaminergic drugs
ATC code: C01CA24
Adrenaline is a catecholamine that acts as an agonist on both alpha- and beta-adrenergic receptors and is synthesized endogenously in the adrenal medulla. Adrenaline has the following pharmacodynamic effects, depending on the physiological state and its concentration in the blood:

- Heart Stimulation: Increases the number of beats, cardiac output, cardiac contraction, oxygen requirement and conduction rate in the purkinje system, increases automaticity and ectopic stroke tendency (positive inotrope, chronotrope and dromotropic effect).
- Vascular System: The contraction of the arterial and precapillary sphincters increases blood pressure. It causes vasoconstriction in skin, mucosa and splanchnic vascular systems. It antagonizes the histamine effect. In acute allergic and anaphylactic reactions, it reduces increased capillary permeability by constructing enlarged capillaries under the effect of histamine. It stops the plasma from leaking out of the capillaries. It increases blood volume, increases blood pressure.
- Other effects: Relaxes gastrointestinal smooth muscles, bronchial smooth muscles, uterine smooth muscles (especially in pregnant women) and detrusor muscles in the bladder. It raises blood sugar, accelerates glucogenolysis, and inhibits insulin secretion.
- When given as an infusion, the following effects are seen depending on the dose and delivery rate;

At a dose of <0.01 μg / kg per minute: dilatation of blood vessels, decrease in blood pressure.

At a dose of 0.04-0.1 µg / kg per minute: Increase in heart rate, flow rate and stroke volume; decrease in peripheral vascular resistance.

At a dose> 0.2 µg / kg per minute: Vasoconstriction and increase in total peripheral resistance.

At a dose> 0.3 µg / kg per minute: Decrease in renal blood flow, gastrointestinal motility, pylorus tone and splanchnic blood flow.

5.2 Pharmacokinetic properties

General properties:

Absorption:

Adrenaline is rapidly absorbed after intramuscular and subcutaneous injection. To prevent local vasoconstriction, massage should be done instead of injection. The effect of adrenaline given intravenously is seen immediately and this effect lasts for 1-2 minutes. Its effect is seen in 5-10 minutes by the subcutaneous route and lasts for 5-10 minutes.

Distribution:

Adrenaline is rapidly distributed to the heart, spleen, various glandular tissues and adrenergic nerves.

Approximately 50% is bound to plasma proteins. Adrenaline enters the fetal circulation through the placenta.

Biotransformation:

Adrenaline entering the systemic circulation is metabolized by diffusion, enzymatic degradation in the liver (by catechol-O-methyltransferase (COMT) and monoamine oxidase (MAO)) and reuptake from adrenergic nerve endings.

Elimination:

The half-life of circulating adrenaline is 1 minute. It is excreted in the urine as a derivative of methanephrine and normetanephrine. In addition, adrenaline is also excreted in breast milk.

Linearity / nonlinear case:

No data available.

5.3 Preclinical safety data

Adrenaline has been used in the clinic since 1901. When given in high doses, adrenaline raises blood pressure, which can cause cerebrovascular bleeding and pulmonary edema.

In addition, cardiac arrhythmias, ventricular fibrillation and acute ischemia have been reported in coronary disease. These complications are especially seen when adrenaline is given to patients who have received halothane and halogenated hydrocarbon general anesthetics.

When the degraded (discolored) 1: 100 adrenaline solution was administered by inhalation or

applied to the mucous membranes, a picture similar to schizophrenia was observed with symptoms such as delusion, hallucination, and depersonalization. This is because adrenochrome, the oxidation product of adrenaline, is transformed into adrenolutine, an indole-oxidation product.

Injection of local anesthetic solutions containing adrenaline into the fingers may cause gangrene, and parenteral injection of adrenaline may cause tissue necrosis.

The carcinogenic and mutagenic potential of adrenaline and its effects on fertility have not been studied. A teratogenic effect has been reported in rats and hamsters when given at a dose 100 times the maximum human dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride

Sodium metabisulphite

Water for injection

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

48 months

6.4 Special precautions for storage

Store at room temperature between 15-25 ° C, protected from light. Do not keep it in the refrigerator.

6.5 Nature and contents of container

Type I, amber colored glass ampoule is presented in carton boxes containing 1 ml x 10 ampoules and 1 ml x 100 ampoules.

6.6 Special precautions for disposal

Unused products or waste materials must be disposed of in accordance with the "Medical Waste Control Regulation" and "Packaging and Packaging Waste Control Regulation".

7. MARKETING AUTHORISATION HOLDER

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