דצמבר 2023

רופא/ה נכבד/ה
רוקח/ת נכבד/ה,

חברת טרדיס גת בע"מ מודיעה על עדכון בטיחות בעלון לרופא של התכשיר

Fluoresceine SERB

Solution for Injection 10G/100ML

ההתוויה הרשומה לתכשיר בישראל:
For examination of the retina by Fluorescent Angiography

בהודעה זו מצויינים השינויים המהותיים בלבד שבוצעו בעלון. כמו כן בוצעו שינויים נוספים.
מקרא: תוספת – באדום; הסרה – מחיקה

QUALITATIVE AND QUANTITATIVE COMPOSITION

Fluorescein sodium 10g/100 ml of solution for injection.

One 5 mL ampoule contains 0.5g of fluorescein sodium.

One 5 mL ampoule contains 65.5 mg of sodium.

Paediatric population
The safety and the efficacy of Fluorescein SERB in children and adolescents below 18 years have not been established. Therefore, Fluorescein SERB should not be used.

Method of administration

Intravenous use.
Fluorescein SERB should not be mixed with other medicinal products (see section 6.2 and section 6.6) and should preferably be injected into the antecubital vein after taking precautions to avoid extravasation (see section 4.4).

4.4. Special warnings and precautions for use

Cardiovascular complications

Severe cardiovascular complications such as chest pain, myocardial infarction and shock have occurred following administration of fluorescein sodium (see section 4.8).

Pre-existing conditions and concomitant treatments

The benefit to risk of the angiography procedure should also be considered in patients with pre-existing conditions such as cardiovascular disease, diabetes mellitus and multiple concomitant drug therapies.

Laboratory tests

The fluorescence may interfere with the analysis of blood and urinary parameters for a period of 3 to 4 days. Interference of fluorescein with serum concentration determination of digoxin and cortisol has been reported. Caution is advised when performing therapeutic drug monitoring for drugs with a narrow therapeutic window.

Excipient with known effect

This medicinal product contains 65.5 mg of sodium per ampoule, equivalent to 3.3% of the maximum daily amount recommended by the WHO which is 2 g of sodium per adult.

4.5 Interaction with other medicinal products and other forms of interaction

- ~~Solutions for injection with an acid pH (in particular antihistamines) may induce precipitation of fluorescein due of their alkaline pH. For this reason they are contraindication for use via the same intravenous line (see section 6.1). It is recommended that concomitant use of Fluorescein sodium with other solutions be avoided. Physico-chemical incompatibility cannot be ruled out.~~
- ~~Analytical interferences with blood parameters (particularly serum digoxin and serum cortisol levels) and urinary parameters are possible 3 to 4 days due to the fluorescence. Caution should be used when interpreting serum concentrations for drugs with narrow therapeutic range (e.g. quinidine, digoxin).~~

No interaction studies have been performed.

A few cases of potential interactions with organic anion transporters have been described. Compounds that inhibit or compete with active organic anion transport (e.g. probenecid) may affect the systemic profile of fluorescein.

4.6. Fertility, pregnancy and lactation

Breast-feeding

Fluorescein sodium is excreted in breast milk. The effect of fluorescein sodium on infants/newborns is unknown.

Breast-feeding should be discontinued for 7 days after treatment with fluorescein sodium. The milk should be pumped off and discarded during this period.

Fertility

No human data on the effect of fluorescein on fertility are available. No animal studies have been performed to evaluate the effects of intravenously-administered fluorescein on fertility.

Effects on ability to drive and use machines

If mydriasis is necessary for the examination with fluorescence angiography, visual acuity is influenced and thus affects the ability to react in traffic or use machinery. Therefore, it should be considered whether it is advisable to drive or operate machines in these circumstances.

~~Due to the mydriasis induced by the angiography examination, patients should not drive or use machines while still experiencing visual disorders (glare, blurred vision).~~

Summary of the safety profile

The most frequently reported adverse reactions are nausea and vomiting.

Less frequent, but more severe adverse reactions have been reported shortly after injection, in particular angioedema, respiratory disorders (bronchospasm, laryngeal oedema, respiratory disorders), anaphylactic shock, hypotension, loss of consciousness, respiratory arrest, and cardiac arrest.

Tabulated list of adverse reactions

The following adverse drug reactions have been described in connection with the use of fluorescein sodium. Frequencies are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000), or not known (cannot be estimated from the available data).

MedDRA System Organ Class	**MedDRA Preferred Term (PT)**	**Frequency**
Blood and lymphatic system disorders	Thrombocytopenia	Very rare
Immune system disorders[1]	Anaphylactic shock, Anaphylactic reaction, Hypersensitivity	Uncommon
	Anaphylactoid reaction	Rare
Nervous system disorders	Loss of consciousness	Uncommon
	Coma, syncope, seizure, headache, dizziness, paraesthesia, dysgeusia, tremor	Rare
	Hypoaesthesia	Very rare
	Cerebrovascular accident, aphasia	Not known
Cardiac disorders	Cardiac arrest, acute myocardial infarction, circulatory collapse, bradycardia, tachycardia	Rare
Vascular disorders	Hypotension	Uncommon
	Shock, pallor, hot flush	Rare
	Thrombophlebitis, hypertension	Not known
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema, asthma, dyspnoea, cough, throat irritation, sneezing, bronchospasm	Rare
	Respiratory arrest, pulmonary oedema	Very rare
	Respiratory disorder, throat tightness	Not known
Gastrointestinal disorders	Vomiting, nausea	Uncommon
	Abdominal pain	Rare
	Salivary hypersecretion	Very rare
	Retching	Not known
Skin and subcutaneous tissue disorders	Rash, erythema, urticaria, pruritus	Uncommon

MedDRA System Organ Class	MedDRA Preferred Term (PT)	Frequency
	Dermatitis, hyperhidrosis, skin discolouration[2]	Rare
	Cold sweat	Very rare
Renal and urinary ~~tract~~ disorders	Chromaturia[3]	Rare
General disorders and administration site conditions	Extravasation[4], malaise	Uncommon
	Chest pain, oedema, asthenia, feeling hot, chills	Rare
	Infusion site thrombosis, pain	Not known

[1] ***Hypersensitivity reactions, including rare cases of anaphylactic/anaphylactoid shock, which may have fatal outcome.***

[2] ***A yellowish discoloration of the skin may appear following administration, but usually disappears within 6 to 12 hours.***

[3] ***Urine, which may also exhibit a bright yellow colouration, returns to its normal colour after 24 to 36 hours.***

[4] ***Extravasation of the solution which causes intense pain and may be followed by tissue necrosis (see section 4.4 Special warnings and precautions for use).***

Pharmacokinetic properties

Distribution

After intravenous injection, fluorescein is quickly distributed and appears in the retinal tissue within ~~few~~ 15-20 seconds.

Approximately ~~50-84%~~ 80% of fluorescein is bound to plasmatic proteins (mainly to albumin) and 15 to 17% to erythrocytes.

Biotransformation

After intravenous administration, fluorescein is quickly transformed into fluorescein glucuronide which also has fluorescent properties.

After 4 to 5 hours, almost all plasma fluorescence is due to fluorescein glucuronide.

Plasma pharmacokinetics of fluorescein are the same in diabetic and non-diabetic patients.

Elimination

Fluorescein is excreted in the urine, as unchanged fluorescein glucuronide metabolite, within 24-36 hours after administration. The urine may attain a bright yellow colour during this period.

Plasma elimination half-lives of fluorescein and fluorescein glucuronide are about 23.5 and 264 minutes respectively.

~~After 4 to 5 hours, almost all plasma fluorescence is due to fluorescein glucuronide.~~

~~Plasma pharmacokinetics of fluorescein are the same in diabetic and non-diabetic patients.~~

~~Fluorescein and its metabolites are eliminated in bile and urine.~~

~~90% of elimination occurs within 48 hours.~~

~~Fluorescein is detectable in urine within 24 to 36 hours.~~

Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology.

Incompatibilities

In the absence of compatibility studies, this product must not be mixed with other medicinal products.

Solutions for injections with an acid pH (in particular antihistamines) can induce fluorescein precipitation because of its alkaline pH and should not be injected simultaneously in the same intravenous line. It is recommended to avoid mixing Fluorescein with other solutions or using it concomitantly with intravenous solutions. The physico- chemical incompatibility cannot be excluded.

Special precautions for disposal and other handling

Fluoresceine SERB is intended for single use only.

העלון לרופא נשלח למשרד הבריאות לצורך פרסום במאגר התרופות של משרד הבריאות וניתן לקבלו מודפס על ידי פניה ישירה לבעל הרישום.

בברכה,
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