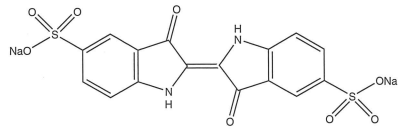
Indigo Carmine Injection

Name of the Drug
Indigo carmine

The chemical formula of indigo carmine is $C_{16}H_8N_2Na_2O_8S_2$. Its molecular weight is 466.35 and the CAS registry number is 860-22-0.

The chemical structure of indigo carmine is:



Description
Indigo carmine is a dye, which occurs as a dusky, purplish-blue powder or blue granules having a coppery lustre. It is slightly soluble in alcohol and has a solubility of approximately 10 mg/mL in water at 25°C. The dye forms blue or bluish-purple solutions. Indigo Carmine Injections have a pH of 3 to 6.5.

Indigo Carmine Injection is available in ampoules containing 20 mg/5 mL indigo carmine in Water for Injections. It is a clear indigo coloured sterile solution.

Pharmacology
The use of indigo carmine is based on its elimination from the body. Indigo carmine has a mild pressor effect secondary to alpha-receptor stimulation.

Pharmacokinetics
Indigo carmine has a relatively small particle size, and is easily and possibly exclusively filtered in the kidney, without appreciable tubular reabsorption. In patients with normal renal function, indigo carmine is cleared rapidly from the circulation after intravenous (IV) administration and has a plasma half-life of 4 to 5 minutes.

Indigo carmine is excreted largely by the kidneys, retaining its blue colour during passage through the body, appearing in the urine within 15 minutes after administration. Ten percent of a dose is eliminated during the first hour. There is no correlation between time to appearance of indigo carmine and creatinine clearance.

Excretion is delayed following intramuscular injection of indigo carmine.

Clinical Trials
Use of indigo carmine to localise ureteral orifices during cytoscopy and ureteral catheterisation, and as a marker to identify severed ureters and fistulous communications has been documented in a number of case series involving a total of 826 patients. Where it was reported, the dose of indigo carmine given was consistent with the recommended dose.

Indications
Indigo Carmine Injection is used to localise ureteral orifices during cytoscopy and ureteral catheterisation, and as a marker to identify severed ureters and fistulous communications.

Contraindications
Indigo Carmine Injection is contraindicated in patients who have known hypersensitivity to the drug or synthetic dyes.

Precautions
Mild pressor effects of indigo carmine have been reported in human experimental data. However, these effects have been transient and usually resolving within 30 minutes.

Severe allergic or cardiovascular reactions, including fatalities have occurred following administration of indigo carmine. Prior to administration of indigo carmine a planned course of action, including having appropriate and adequate facilities and personnel available must be in place and be capable of immediate implementation, in case a serious reaction occurs.

Carcinogenicity, mutagenicity, impairment of fertility
Long-term carcinogenicity studies have not been conducted with indigo carmine by the IV route. Indigo carmine was not carcinogenic in published long-term studies at dietary levels up to 5% in mice (maximum average intake 8259 and 9456 mg/kg/day in males and females, respectively) and 2% in rats (maximum average intake 1282 and 1592 mg/kg/day in males and females, respectively).

In published studies, indigo carmine was negative in a number of mutagenicity tests in *Salmonella typhimurium*, and did not induce DNA repair in rat hepatocytes *in vitro* or *in vivo*. However, indigo carmine induced chromosomal aberrations in several *in vitro* test systems, and in mice after a single intraperitoneal dose of 25 mg/kg or greater, or an oral dose of 2 mg/kg/day for 30 days.

No studies of the potential effects of indigo carmine on fertility have been conducted by the IV route. A published study reported no effects on male or female rat fertility at dietary levels up to 2% (approximately 1400 mg/kg/day).

Use in pregnancy
Pregnancy category B2
Embryofoetal development studies have not been conducted with indigo carmine by the IV route. Embryofoetal development studies with indigo carmine at oral gavage doses up to 250 mg/kg/day in rats (gestation days 6 to 15) and rabbits (gestation days 6 to 18) showed no evidence of teratogenicity.

An adverse effect of the foetus has been observed with the intra-amniotic injection of synthetic dyes. However, it is not known whether indigo carmine can cause foetal harm when intravenously administered to pregnant women. Therefore, indigo carmine should not be used during pregnancy.

Use in lactation
Since it is not known whether indigo carmine is distributed into human milk, it should not be administered to lactating women.

Use in Children
Experience in children is limited since there is no available information regarding the dosages of indigo carmine to be administered. It is recommended that smaller doses be given to paediatric patients. Since indigo carmine retains its blue colour during passage through the body, infants and children and underweight patients may experience skin discolouration following large doses.

Laboratory abnormalities
Indigo carmine may also interfere with colorimetric methods of urinalysis.

Adverse Reactions
Mild pressor effects of indigo carmine have been reported in human experimental data and case studies in the literature. Rarely, hypertension, bradycardia, nausea and vomiting, bronchoconstriction, rash, pruritus and skin discolouration have been observed.

Dosage and Administration
Indigo Carmine Injection should be administered by intravenous injection. The recommended amount of indigo carmine to be administered to adults is 20 to 40 mg. Indigo carmine should appear in the bladder within 10 to 15 minutes.

Overdosage
There is no data available describing the symptoms or treatment of an overdosage of indigo carmine. Since indigo carmine retains its blue colour during passage through the body, infants and children and underweight patients may experience skin discolouration following large doses. Treatment is symptomatic and supportive.

Presentation
Indigo Carmine Injection is supplied in single ampoules containing 20 mg/5 mL indigo carmine, in Water for Injections.

Poison Schedule of the Drug
Indigo carmine is unscheduled.

Name and Address of Sponsor
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