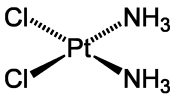
For the use only of a Registered Medicial Practitioner or a Hospital or a Laboratory Only
Cisplatin Injection BP
ZUVIPLAT

COMPOSITION:
ZUVIPLAT is sterile aqueous solution containing 1mg of Cisplatin I.P. in each ml.

DESCRIPTION
ZUVIPLAT is an anticancer drug of an entirely new category for antitumor activity and low toxicity from among a variety platinum compound developed according to the discovery by Barnett Rosenberg in the U.S.A that platinum compound inhibit the mitosis of Escherichia coli.
Structure:



CLINICAL PHARMACOLOGY
MODE OF ACTION: It is accepted that the antitumor activity of ZUVIPLAT derives from its binding to DNA.

PHARMACOKINETCS: following single: i.v dose ZUVIPLAT concentrates in the liver, kidney and large and small intestine in animals and human. ZUVIPLAT apparently has poor penetration into the central nervous system.
The half in the β phase is 58-73 hours. About 90% of the drugs bound to protein and this binding is only partly reversible. Urinary excretion of ZUVIPLAT range between 27-45% of the administered dose within the first 5 days the rest presumable is fixed in tissue and metabolized

INDICATION:
ZUVIPLAT can be used itself or in addition to other modalities or preferable in established combination therapy with other approved chemotherapeutic agent. It is indicated in metastic ovarian turnovers, squamous cell carcinoma of the head and neck and advance bladder carcinoma.

DOSAGE AND ADMINISTRATION:
ZUVIPLAT solution should be used intravenously only and should be administered by i.v dose every 3-4 week. An alternative regimen is 15-20 mg per sq. i.v daily for 5 days every 3-4 week
In clinical use of ZUVIPLAT injection, take the following measure for reducing the nephrotoxicity of the drug:
Administer 1000-2000 ml. of an adequate fluid deficit replacement over 4 hours or more prior to the administration of ZUVIPLAT injection.
Administer ZUVIPLAT injection as a mixture with 500-1000 ml of physiological saline or a dextrose – saline solution by intravenous drip over 2 hours or more. When it take the intravenous drip over 2 hours or more. When it take the intravenous drip of ZUVIPLAT injection a long time, keep the dripping bottle away from light.
After the administration of ZUVIPLAT injection, administer 1000-2000 ml of an adequate fluid deficit replacement over 4 hours or more.

During the administration of ZUVIPLAT injection, exercise care so as to maintain the urinary output and administer diuretic such as mannitol and furosemide.

PRECAUTIONS FOR ADMINISTRATION:

ZUVIPLAT solution should be drawn up out of the vial using a syringe and sterile technique and added to 2 liters of either a 5% dextrose in1/3 normal saline solution, or 5% dextrose in a normal saline solution. 37.5 gm of mannitol should also be added in the infusion solution.

As with other potentially toxic compounds. Caution in handling the solution of ZUVIPLAT should be exercised. Skin reactor associated with accidental exposure to ZUVIPLAT may occur. The use of the gloves is recommended. If ZUVIPLAT solution comes in the contract with skin or mucosa, immediately wash thoroughly with soap and water.

Do not mix ZUVIPLAT injection with 5% dextrose, amino acid solution or any solution containing sodium locate for administration for intravenous drip, because ZUVIPLAT may be degraded in such a mixture.

Because ZUVIPLAT react with aluminum to form precipitate, resulting in deteriorated activity

Because ZUVIPLAT is a chelate compound, ZUVIPLAT injection should not be mixed with any other anticancer drugs

ZUVIPLAT injection when mixed with physiological saline or a dextrose- saline solution, should be administered as early as possible

Because ZUVIPLAT is degraded by light keep ZUVIPLAT injection away from direct sunlight When it take the intravenous drip of PLATINEX injection a long time keep the dripping bottle away from light

WARNING:

Because gastrointestinal symptoms such as nausea, vomiting and anorexia are complained of the all treated patients, keep under close observation for change is condition and take adequate measure when such complaint have appeared.

Because the treatment with ZUVIPLAT injection may in some cases be associated with severe adverse reaction such as renal failure and myelosuppression, keep the patients under close observation for change in condition e. g by frequent Laboratory examination (such as renal function test, hematology and hepatic function test)

When an abnormality has been found take adequate measure such as reduction in the dose of ZUVIPLAT injection may in some cases be associated with severe, persistent adverse reaction, exercise particular care in such a case. Exercise care especially on the onset or aggravation of infection and hemorrhagic tendency under the treatment with ZUVIPLAT injection

PRECAUTIONS

When ZUVIPLAT injection is administered to children, exercise particular care on the onset of adverse reaction, and administer the drug with the utmost care. (There is a report from another country that ototoxicity is a frequent adverse reaction to ZUVIPLAT).

When it is necessary to administer ZUVIPLAT injection to children and patients at the reproductive age. Its effect on the genital organs need to be consider.

PRECAUTION SPECIAL:

Patients with renal disorder
Patients with hepatic disorder
Patients with myelosuppression
Patients with auditory disorder.

OTHER PRECAUTION:

It has been report that the administration of ZUVIPLAT injection may in some cases be associated with congestive heart failures and abnormal ECG, and also with hypomagnesaemia and hypocalcemia 3
ZUVIPLAT has proved mutagenic in bacteria
Its has been reported that the intra peritoneal administration of ZUVIPLAT to mice caused pulmonary adenoma and skin turnover

USE IN PREGNANCY:

ZUVIPLAT is carcinogenic and should be considered teratogenic. Termination of pregnancy (especially first trimester) should be considered in patients given ZUVIPLAT

ADVERSE REACTION:

Gastrointestinal tract: Nausea, vomiting, anorexia, may be complained of by almost al m patients: and other gastrointestinal symptoms such as diarrhea and abdominal pain also may occasionally be complained of.
Kidney: Because the treatment with ZUVIPLAT injection may in some cases be associated with renal failure keep the patients under close observation for such a change. When any abnormality has occurred in laboratory parameters such as BUN, serum creatinine and creatinine clearances value, withdraw the treatment and take adequate measure. And when any other abnormalities such as hematuria and urinary protein also have occurred withdraw the treatment and take adequate measure
Blood: Leucopenia, throbopenia and anemia may appear on rare occasions.
Auditory Organ: Hearing loss of the high frequency range and tinnitus may appear in some cases
Hypersensitivity: Symptoms and sign of hypersensitivity such as rashes may appear occasionally
Nervous System: Symptoms of the peripheral nervous system such as numbness and paresthesia of the finger and toes may appear on rate occasion
Liver: Abnormal hepatic function test such as elevation of S-GOT, S-GPT and A1- P may sometime be observed
Other changes: Generalized malaise dizziness, alopecia, fever, general edema, hypotension and hiccups may occur in some cases.

DRUG INTERACTIONS

Plasma levels of anticonvulsant agents may become sub therapeutic during cisplatin (cisplatin injection) therapy.
In a randomized trial in advanced ovarian cancer, response duration was adversely affected when pyridoxine was used in combination with altretamine (hexamethylmelamine) and cisplatin (cisplatin injection) .

OVERDASE

Caution should be exercised to prevent inadvertent overdosage with cisplatin (cisplatin injection)
Acute overdosage with this drug may result in kidney failure, liver failure, deafness, ocular toxicity (including detachment of the retina), significant myelosuppression, intractable nausea and vomiting and/or neuritis. In addition, death can occur following overdosage.
No proven antidotes have been established for cisplatin (cisplatin injection) overdosage. Hemodialysis, even when initiated four hours after the overdosage, appears to have little effect on removing platinum from the body because of cisplatin (cisplatin injection) 's rapid and high degree of proteinbinding.

Management of overdosage should include general supportive measures to sustain the patient through any period of toxicity that may occur.

CONTRAINDICATIONS:
Patients with severe renal disorder.
Patients with a previous history of severe hypersensitivity to ZUVIPLAT injection

STORAGE:
Store between 15ºC to 25ºC. Do not freeze. Protect from light
CAUTION TO BE TAKEN IN HANDLING:
Use ZUVIPLAT injection by the direction or according to the prescription of physician.
When ZUVIPLAT injection is mixed with a fluid deficit replacement, the mixture should be used as early as possible
Keep the vial in the vial carton even after its outer package has been opened.

EXPIRY:
The date of expiry is indicated on the outer package

PRESENTATION:
ZUVIPLAT is available in amber coloured vials containing 1mg/ml. in packs of 10 ml and 50ml vials.