Gemtor® for IV Injection

Gemcitabine Hydrochloride Ph. Eur. for Injection as lyophilized powder

DESCRIPTION

Gemtor® for IV Injection is a preparation of Gemcitabine Hydrochloride. Gemcitabine kills cells undergoing DNA synthesis and blocks the progression of cells through the G1/S-phase boundary. Gemcitabine is metabolized by nucleoside kinases to diphosphate (dFdCDP) and triphosphate (dFdCTP) nucleosides. Gemcitabine diphosphate inhibits ribonucleotide reductase, an enzyme responsible for catalyzing the reactions that generate deoxynucleoside triphosphates for DNA synthesis, resulting in reductions in deoxynucleotide concentrations, including dCTP. Gemcitabine triphosphate competes with dCTP for incorporation into DNA. The reduction in the intracellular concentration of dCTP by the action of the diphosphate enhances the incorporation of Gemcitabine triphosphate into DNA (self-potentiation). After the Gemcitabine nucleotide is incorporated into DNA, only one additional nucleotide is added to the growing DNA strands, which eventually results in the initiation of apoptotic cell death.

INDICATIONS

- In combination with carboplatin, for the treatment of advanced ovarian cancer that has relapsed at least 6 months after completion of platinum-based therapy.
- In combination with paclitaxel, for first-line treatment of metastatic breast cancer after failure of prior anthracycline-containing adjuvant chemotherapy, unless anthracyclines were clinically contraindicated.
- In combination with cisplatin, for the treatment of non-small cell lung cancer.
- As a single agent for the treatment of pancreatic cancer.

DOSAGE AND ADMINISTRATION

- **Ovarian Cancer:** 1000 mg/m^2 over 30 minutes on Days 1 and 8 of each 21-day cycle.
- **Breast Cancer:** 1250 mg/m^2 over 30 minutes on Days 1 and 8 of each 21-day cycle.
- **Non-Small Cell Lung Cancer:** 1000 mg/m^2 over 30 minutes on Days 1, 8, and 15 of each 28-day cycle or 1250 mg/m^2 over 30 minutes on Days 1 and 8 of each 21-day cycle.
- **Pancreatic Cancer:** 1000 mg/m^2 over 30 minutes once weekly for the first 7 weeks, then one week rest, then once weekly for 3 weeks of each 28-day cycle.

CONTRAINDICATIONS

Hypersensitivity

SIDE EFFECTS

- Nausea/vomiting
- Anemia, neutropenia, thrombocytopenia
- Hepatic transaminitis
- Increased alkaline phosphatase, proteinuria, hematuria
- Fever
- Rash
- Dyspnea
- Peripheral edema

WARNING AND PRECAUTION

Schedule-dependent toxicity: Increased toxicity with infusion time greater than 60 minutes or dosing more frequently than once weekly.

Myelosuppression: Monitor for myelosuppression prior to each cycle and reduce or withhold dose for severe myelosuppression.

Pulmonary Toxicity and Respiratory Failure: Discontinue Gemcitabine immediately for unexplained new or worsening dyspnea or evidence of severe pulmonary toxicity.

Hemolytic-Uremic Syndrome (HUS): Monitor renal function prior to initiation and during therapy. Discontinue Gemcitabine for HUS or severe renal impairment.

USE IN PREGNANCY AND LACTATION

Pregnancy Category D. Gemcitabine can cause fetal harm when administered to a pregnant woman. Based on its mechanism of action, Gemcitabine is expected to result in adverse reproductive effects. Gemcitabine was teratogenic, embryotoxic, and fetotoxic in mice and rabbits. If Gemcitabine is used during pregnancy, or if the patient becomes pregnant while taking Gemcitabine, the patient should be apprised of the potential hazard to a fetus.

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Gemcitabine, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

PHARMACEUTICAL PRECAUTION

Do not store above 30 °C temperature. Keep away from light and wet place. Keep out of reach of children.

Instructions for reconstitution (and further dilution, if performed)

The only approved diluent for reconstitution of Gemcitabine sterile powder is Sodium Chloride 9 mg/mL (0.9%) solution for injection (without preservative). Due to solubility considerations, the maximum concentration for Gemcitabine upon reconstitution is 40 mg/mL. Reconstitution at concentrations greater than 40 mg/mL may result in incomplete dissolution and should be avoided.

1. Use aseptic technique during the reconstitution and any further dilution of Gemcitabine for intravenous infusion administration.

2. To reconstitute, slowly add the appropriate volume of sterile Sodium Chloride 9 mg/mL (0.9%) solution for injection (as stated in the table below) and shake to dissolve.

Presentation	Volume of Sterile Sodium Chloride 9 mg/mL (0.9%) solution for injection to be added	Displacement Volume	Final Concentration
200 mg	5 mL	0.26 mL	38 mg/mL
1 g	25 mL	1.3 mL	38 mg/mL

Further dilution with sterile Sodium Chloride 9 mg/mL (0.9 %) solution for injection, without preservative, can be done. Reconstituted solution is a clear, colourless to light straw-coloured solution. Final concentrations may be as low as 0.1 mg/mL.

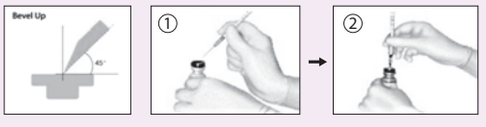
3. Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration. If particulate matter is observed, do not administer.

All items used for preparation, administration or otherwise coming into contact with Gemcitabine should undergo disposal according to hospital standard procedures applicable to cytotoxic agents.

To prevent coring

- Place the vial on a flat surface & position the needle point on center of the bullseye of the rubber stopper about a 45° angle keeping the needle tip facing as bevel up.

-Put downward pressure on the needle while gradually bringing the needle to an upright position (90° angle).



-To avoid fragments of the rubber closure, it is recommended not to insert needle repeatedly at the same location.

-To prevent vacuum formation, inject air into the vial equal to the volume to be withdrawn. When reconstituting a powdered drug, withdraw a volume of air equal to the amount of the diluent to be added.

Storage after reconstitution:

Chemical and physical in-use stability has been demonstrated for 24 hours at controlled room temperature of 20 °C to 25 °C (68°F to 77°F). From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at controlled room temperature, unless reconstitution (and further dilution, if applicable) has taken place in controlled and validated aseptic conditions.

Solutions of reconstituted Gemcitabine should not be refrigerated (2-8 °C), as crystallization may occur.

Handling

The normal safety precautions for cytostatic agents must be observed when preparing and disposing of the infusion solution. Handling of the solution for infusion should be done in a safety box and protective coats and gloves should be used. If no safety box is available, the equipment should be supplemented with a mask and protective glasses.

If the preparation comes into contact with the eyes, this may cause serious irritation. The eyes should be rinsed immediately and thoroughly with water. If there is lasting irritation, a doctor should be consulted. If the solution is spilled on the skin, rinse thoroughly with water.

PACKAGING

Gemtor® 200 for IV Injection : (as lyophilized powder) Each box contains 1 vial of Gemcitabine Hydrochloride Ph. Eur. equivalent to Gemcitabine 200 mg.

Gemtor® 1g for IV Injection : (as lyophilized powder) Each box contains 1 vial of Gemcitabine Hydrochloride Ph. Eur. equivalent to Gemcitabine 1 g.

SK+F ONCOLOGY

Manufactured by
ESKAYEF PHARMACEUTICALS LIMITED
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® REGD. TRADEMARK
R/PM0540 V05