GEMZAR
Gemcitabine Hydrochloride

1. Trade Name of the Medicinal Product
Gemzar

2. Qualitative and Quantitative Composition
Gemcitabine hydrochloride equivalent to 200 mg gemcitabine.
Gemcitabine hydrochloride equivalent to 1 g gemcitabine.
Gemcitabine (INN) is a pyrimidine analogue

3. Pharmaceutical Form
Vials containing powder for solution for infusion.

4. Clinical Particulars
4.1 Therapeutic Indications
Non-Small Cell Lung Cancer:
Gemcitabine in combination with cisplatin is indicated as a first line treatment of patients with locally advanced (inoperable Stage IIIA or IIIB) or metastatic (Stage IV) non-small cell lung cancer.
Gemcitabine is indicated for the palliative treatment of adult patients with locally advanced or metastatic non-small cell lung cancer.
Pancreatic Cancer:
Gemcitabine is indicated as first-line treatment of patients with locally advanced (non-resectable Stage II or Stage III) or metastatic (Stage IV) adenocarcinoma of the pancreas. Gemcitabine is indicated for patients previously treated with 5-FU.
Bladder Cancer:
Gemcitabine is indicated for treatment of advanced bladder cancer (muscle invasive Stage IV tumours with or without metastases) in combination with cisplatin therapy.
Breast Cancer:
GEMZAR, **in combination with paclitaxel,** is indicated for the treatment of patients with unresectable, locally recurrent or metastatic breast cancer who have relapsed following adjuvant/neoadjuvant chemotherapy. Prior chemotherapy should have included an anthracycline unless clinically contraindicated.
Ovarian Cancer:
Gemcitabine, alone or in combination, is indicated for the treatment of patients with recurrent epithelial ovarian carcinoma who have relapsed following platinum-based therapy.
Other Therapeutic Activity:
Gemcitabine alone or in combination has shown activity in advanced breast and ovarian cancer.

4.2 Posology and Method of Administration

Non-Small Cell Lung Cancer:
Combination use: Adults: Gemcitabine in combination with cisplatin has been investigated using two dosing regimen. One regimen used a three week schedule and the other used a four week schedule.
The three week schedule used gemcitabine 1250 mg/m^2, given by 30 minute intravenous infusion, on days 1 and 8 of each 21 day cycle. Dosage reduction with each cycle or within a cycle may be applied based upon the amount of toxicity experienced by the patient. The four week schedule used gemcitabine 1,000 mg/m^2, given by 30 minute intravenous infusion, on days 1, 8, 15 of each 28 day cycle.
Dosage reduction with each cycle or within a cycle may be applied based upon the amount of toxicity experienced by the patient. Cisplatin has been used at doses between 75-100 mg/m^2 after administration of gemcitabine on day 1 of each 21-day or 28-day cycle.

Single-agent use: Adults: The recommended dose of gemcitabine is 1,000 mg/m^2, given by 30 minute intravenous infusion. This should be repeated once weekly for three weeks, followed by a one week rest period. This four week cycle is then repeated. Dosage reduction is applied based upon the amount of toxicity experienced by the patient.

Pancreatic Cancer:
Adults: The recommended dose of gemcitabine is 1,000 mg/m^2, given by 30 minute intravenous infusion. This should be repeated once weekly for up to 7 weeks, followed by a week of rest. Subsequent cycles should consist of injections once weekly for 3 consecutive weeks out of every 4 weeks. Dosage reduction is applied based upon the amount of toxicity experienced by the patient.

Bladder Cancer:
Combination use: Adults: The recommended dose for gemcitabine is 1,000 mg/ m^2, given by 30 minute infusion. The dose should be given on days 1, 8, and 15 of each 28 day cycle in combination with cisplatin. Cisplatin is given at a recommended dose of 70 mg/m^2 on day 1 following gemcitabine or day 2 of each 28 day cycle. This four week cycle is then repeated. Dosage reduction with each cycle or within a cycle may be applied based upon the amount of toxicity experienced by the patient. A clinical trial showed more myelosuppression when cisplatin was used in doses of 100 mg/m^2.

Breast cancer:
Combination use: Adults: Gemcitabine in combination with paclitaxel is recommended using paclitaxel (175 mg/m^2) administered on Day 1 over approximately 3 hours as an intravenous infusion, followed by gemcitabine (1250 mg/m^2) as a 30-minute intravenous infusion on Days 1 and 8 of each 21-day cycle. Dose reduction with each cycle or within a cycle may be applied based upon the amount of toxicity experienced by the patient. Patients should have an absolute granulocyte count of at least 1,500 (x10^6/L) prior to initiation of gemcitabine + paclitaxel combination.

Ovarian Cancer:
Single-agent use: Adults: The recommended dose of gemcitabine is 800-1250 mg/m^2, given by a 30-minute intravenous infusion. The dose should be given on Days 1, 8 and 15 of each 28 cycle. This four week cycle is then repeated. Dosage reduction with each cycle or within a cycle may be applied based upon the amount of toxicity experienced by the patient.

Combination use: Adults: Gemcitabine in combination with carboplatin is recommended using gemcitabine 1000 mg/m^2 administered on Days 1 and 8 of each 21-day cycle as a 30-minute intravenous infusion. After gemcitabine, carboplatin will be given on Day 1 consistent with a target AUC of 4.0 mg/ml.min. Dosage reduction with each cycle or within a cycle may be applied based upon the amount of toxicity. Patients receiving gemcitabine should be monitored prior to each dose for platelet, leucocyte and granulocyte counts and, if necessary, the dose of gemcitabine may be either reduced or withheld in the presence of haematological toxicity, according to the following scale:

Absolute granulocyte count (x10^6/l)	**Platelet count (x10^6/l)**	**% of full dose**
>1,000 and	>100,000	100
500-1,000 or	50,000-100,000	75
<500 or	<50,000	hold

For cisplatin dosage adjustment in combination therapy, see the manufacturers' prescribing information.

Periodic checks of liver and kidney functions, including transaminases and serum creatinine, should also be performed in patients receiving gemcitabine.
Gemcitabine is well tolerated during the infusion, with only a few cases of injection site reaction reported.
Gemcitabine can be easily administered on an outpatient basis.

Elderly patients: Gemcitabine has been well tolerated in patients over the age of 65. There is no evidence to suggest that dose adjustments are necessary in the elderly, although gemcitabine clearance and half-life are affected by age.

Children: Gemcitabine has been studied in limited Phase I and II trials in children in a variety of tumor types. These studies did not provide sufficient data to establish the efficacy and safety of gemcitabine in children.

Hepatic and renal impairment: Gemcitabine should be used with caution in patients with hepatic insufficiency or with impaired renal function as there is insufficient information from clinical studies to allow clear dose recommendation for this patient population.

4.3 Contra-indications
Gemcitabine is contraindicated in those patients with a known hypersensitivity to the drug.

4.4 Special warnings and precautions for use

Warnings
Prolongation of the infusion time and increased dosing frequency have been shown to increase toxicity.
Gemcitabine can suppress bone marrow function as manifested by leucopenia, thrombocytopenia and anaemia. However, myelosuppression is short lived and usually does not result in dose reductions and rarely in discontinuation (see sections 4.2 and 4.8). Gemcitabine should be discontinued at the first signs of any evidence of microangiopathic haemolytic anaemia such as rapidly falling haemoglobin with concomitant thrombocytopenia, elevation of serum bilirubin, serum creatinine, blood urea nitrogen, or LDH, which may indicate development of haemolytic uraemic syndrome (see section 4.8). Renal failure may not be reversible, even with discontinuation of therapy, and dialysis may be required.

Serious spontaneous reports of hemolytic uremic syndrome (HUS), capillary leak syndrome (CLS), adult respiratory distress syndrome (ARDS), and posterior reversible encephalopathy syndrome (PRES) with potentially severe consequences have been reported in patients receiving gemcitabine as single agent or in combination with other chemotherapeutic agents. These events can be related to vascular endothelial injury possibly induced by gemcitabine. Gemcitabine should be discontinued and supportive measures implemented if any of these develop during therapy. (see section 4.8)

In addition to ARDS, other severe pulmonary effects such as interstitial pneumonitis and pulmonary edema have been reported in patients receiving gemcitabine as single agent or in combination with other chemotherapeutic agents. Gemcitabine should be discontinued and supportive measures provided if these effects develop during therapy (see section 4.8)

Precautions
General: Patients receiving therapy with gemcitabine must be monitored closely. Laboratory facilities should be available to monitor patient status. Treatment for a patient compromised by drug toxicity may be required.

Laboratory tests: Therapy should be started cautiously in patients with compromised bone marrow function. As with other oncolytics, the possibility of cumulative bone marrow suppression when using combination or sequential chemotherapy should be considered.

Patients receiving gemcitabine should be monitored prior to each dose for platelet, leucocyte and granulocyte counts. Suspension or modification of therapy should be considered when drug-induced marrow depression is detected. Guidelines regarding dose modifications are provided in section 4.2 above. Peripheral blood counts may continue to fall after the drug is stopped.

Laboratory evaluation of renal and hepatic function should be performed periodically. Administration of gemcitabine in patients with concurrent liver metastases or a pre-existing medical history of hepatitis, alcoholism or liver cirrhosis may lead to exacerbation of the underlying hepatic insufficiency (see section 4.2).

4.5 Interactions with other Medicaments and other forms of interaction

Radiotherapy:
Concurrent (given together or ≤7 days apart):
Toxicity associated with this multimodality therapy is dependent on many different factors, including dose of gemcitabine, frequency of gemcitabine administration, dose of radiation, radiotherapy planning technique, the target tissue and target volume. Preclinical and clinical studies have shown that gemcitabine has radiosensitizing activity. In a single trial, where gemcitabine at a dose of 1,000 mg/m^2 was administered concurrently for up to 6 consecutive weeks with therapeutic thoracic radiation to patients with non-small cell lung cancer, significant toxicity in the form of severe, and potentially life threatening mucositis, especially oesophagitis, and pneumonitis was observed, particularly in patients receiving large volumes of radiotherapy [median treatment volumes 4,795 cm^3]. Studies done subsequently have suggested that it is feasible to administer gemcitabine at lower doses with concurrent radiotherapy with predictable toxicity, such as a phase II study in non-small cell lung cancer. Thoracic radiation doses of 66 Gy were administered with gemcitabine (600 mg/m^2, four times) and cisplatin (80 mg/m^2, twice) during 6 weeks. The optimum regimen for safe administration of gemcitabine with therapeutic doses of radiation has not yet been determined.

Non-concurrent (given > 7 days apart):
Analysis of the data does not indicate any enhanced toxicity when gemcitabine is administered more than 7 days before or after radiation other than radiation recall. Data suggest that gemcitabine can be started after the acute effects of radiation have resolved or at least one week after radiation.
Radiation injury has been reported on targeted tissues (e.g. esophagitis, colitis and pneumonitis) in association with both concurrent and non-concurrent use of gemcitabine.

4.6 Pregnancy and Lactation
The safety of this medicinal product for use in human pregnancy has not been established. Evaluation of experimental animal studies has shown reproductive toxicity, e.g. birth defects or other effects on the development of the embryo or fetus, the course of gestation or peri- and postnatal development. The use of gemcitabine should be avoided in pregnant or nursing women because of the potential hazard to the fetus or infant.

4.7 Effects on ability to drive and use machines
Gemcitabine has been reported to cause mild to moderate somnolence. Patients should be cautioned against driving or operating machinery until it is established that they do not become somnolent.

4.8 Undesirable effects
Haematological:
Because gemcitabine is a bone marrow suppressant, anaemia, leucopenia and thrombocytopenia can occur as a result of administration of gemcitabine. Myelosuppression is

usually mild to moderate, and is more pronounced for the granulocyte count. Thrombocythaemia is also very rarely reported. Febrile neutropenia is also commonly reported.

Gastro-intestinal:
Nausea and nausea accompanied by vomiting are each reported in one-third of patients, respectively. This adverse event requires therapy in about 20% of patients, is rarely dose-limiting, and is easily manageable with standard anti-emetics.

Renal:
Mild proteinuria and haematuria are reported in approximately half the patients, but are rarely clinically significant, and are not usually associated with any change in serum creatinine or blood urea nitrogen. However, a few cases of renal failure of uncertain aetiology have been reported, including, in very rare instances, cases of Haemolytic uraemic syndrome (HUS) in patients receiving gemcitabine. Hence, gemcitabine should be used with caution in patients with impaired renal function. (see section 4.4)

Allergic:
Anaphylaxis has been reported rarely.

Respiratory system:
Bronchospasm after gemcitabine infusion has been reported in less than 1% of patients. Bronchospasm is usually mild and transient, but parenteral therapy may be required. Gemcitabine should not be administered to patients with a known hypersensitivity to this drug (see section 4.3). Dyspnoea occurring within hours following gemcitabine injection is reported by approximately 8% of patients. This dyspnoea is usually mild, short-lived, rarely dose-limiting, and usually abates without any specific therapy. The mechanism of this event is unknown and the relationship to gemcitabine is not clear. Pulmonary effects, sometimes severe (such as pulmonary oedema, interstitial pneumonitis, or adult respiratory distress syndrome [ARDS]), have been reported rarely in association with gemcitabine therapy. (see section 4.4)

Infections and infestations:
Infections and Sepsis have been reported rarely.

Blood and lymphatic system disorders:
Thrombotic microangiopathy (TMA) has been reported very rarely in patients receiving gemcitabine. Hemolytic uremic syndrome (HUS) has been rarely reported. In these patients, renal failure may not be reversible even with discontinuation of therapy, and dialysis may be required (see section C.4 Special Warnings and Precautions for Use).

Hepatobiliary system:
Abnormalities of liver transaminase enzymes (AST and ALT) and alkaline phosphatase occur in about two-thirds of patients, but they are usually mild, non-progressive and rarely necessitate stopping treatment. However, gemcitabine should be used with caution in patients with impaired liver function (see section 4.2). Elevations in gamma-glutamyl transferase (GGT) and bilirubin levels have been reported rarely.

Injury, Poisoning and Procedural Complications:
Radiation toxicity and radiation recall reactions have been reported (see section 4.5).

Cardiovascular:
A few cases of hypotension were reported. Cases of myocardial infarction, congestive heart failure and arrhythmia have been reported, but there is no clear evidence that gemcitabine causes cardiac toxicity.

Vascular system:

Peripheral vasculitis and gangrene, and capillary leak syndrome have been reported very rarely. (see section 4.4)

Skin and Subcutaneous Tissue:
A rash is seen in approximately 25% of patients and is associated with pruritus in about 10% of patients. The rash is usually mild, not dose-limiting, and responds to local therapy. Desquamation, vesiculation and ulceration have been reported rarely. Severe skin reactions, including desquamation and bullous skin eruptions have been reported very rarely.

Nervous system:
Posterior reversible encephalopathy syndrome has been reported very rarely (see section 4.4)

Other Effects:
An entity resembling influenza is reported by approximately 20% of patients. This is usually mild, short-lived, and rarely dose-limiting. Fever, headache, back pain, chills, myalgia, asthenia and anorexia are the most commonly reported symptoms. Cough, rhinitis, malaise, sweating and insomnia are also commonly reported. Fever and asthenia are also reported frequently as isolated symptoms. The mechanism of this toxicity is unknown. Reports received indicate that paracetamol may produce symptomatic relief.
Oedema/peripheral oedema is reported by approximately 30% of patients. Some cases of facial oedema have also been reported.

Oedema/peripheral oedema is usually mild to moderate, rarely dose-limiting, is sometimes reported as painful and is usually reversible after stopping gemcitabine treatment. The mechanism of this toxicity is unknown. It is not associated with any evidence of cardiac, hepatic or renal failure. The following adverse effects are also commonly reported: alopecia (usually minimal hair loss), 13% of patients; somnolence, 10%; diarrhoea, 8%; oral toxicity (mainly soreness and erythema), 7%; and constipation, 6%.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medical product is important. It allows continued monitoring of the benefit/risk balance of the medical product. Health care professionals are asked to report any suspected adverse reactions via the following:
National reporting system: https://e-meso.pom.go.id and/or to pv-center@pom.go.id
Pharmaceutical industry reporting system:
Telephone: +62 21 21684084
or
Email: IDsafety@zuelligpharma.com

4.9 Overdose
There is no antidote for overdosage of gemcitabine. Single doses as high as 5.7 g/m^2 have been administered by IV infusion over 30 minutes every two weeks with clinically acceptable toxicity. In the event of suspected overdose, the patient should be monitored with appropriate blood counts and should receive supportive therapy, as necessary.

5. Pharmacological Properties
5.1 Pharmacodynamic properties

Cytotoxic Activity in Cell Culture Models:
Gemcitabine exhibits significant cytotoxicity activity against a variety of cultured murine and human tumour cells. It exhibits cell phase specificity, primarily killing cells undergoing DNA synthesis (S-phase) and under certain conditions blocking the progression of cells through the G1/S-phase boundary. *In vitro* the cytotoxic action of gemcitabine is both concentration and time dependent.

Antitumour Activity in Preclinical Models:

In animal tumour models, the antitumour activity of gemcitabine is schedule dependent. When administered daily gemcitabine causes death in animals with minimal antitumour activity. However, when an every third or fourth day dosing schedule is used, gemcitabine can be given at non-lethal doses that have excellent antitumour activity against a broad range of mouse tumours.

Cellular Metabolism and Mechanisms of Action:
Gemcitabine (dFdC) is metabolised intracellularly by nucleoside kinases to the active diphosphate (dFdCDP) and triphosphate (dFdCTP) nucleosides. The cytotoxic action of gemcitabine appears to be due to inhibition of DNA synthesis by two actions of dFdCDP and dFdCTP. First, dFdCDP inhibits ribonucleotide reductase which is uniquely responsible for catalysing the reactions that generate the deoxynucleoside triphosphates for DNA synthesis. Inhibition of this enzyme by dFdCDP causes a reduction in the concentrations of deoxynucleosides in general, and especially in that of dCTP. Second, dFdCTP competes with dCTP for incorporation into DNA (self-potentiation). Likewise, a small amount of gemcitabine may also be incorporated into RNA. Thus, the reduction in the intracellular concentration of dCTP potentiates the incorporation of dFdCTP into DNA. DNA polymerase epsilon is essentially unable to remove gemcitabine and repair the growing DNA strands. After gemcitabine is incorporated into DNA, one additional nucleotide is added to the growing DNA strands. After this addition there is essentially a complete inhibition in further DNA synthesis (masked chain termination). After incorporation into DNA, gemcitabine then appears to induce the programmed cellular death process known as apoptosis.

5.2 Pharmacokinetic Properties

Gemcitabine Pharmacokinetics
The pharmacokinetics of gemcitabine have been examined in 353 patients in seven studies. The 121 women and 232 men ranged in age from 29 to 79 years. Of these patients, approximately 45% had non-small cell lung cancer and 35% were diagnosed with pancreatic cancer. The following pharmacokinetic parameters were obtained for doses ranging from 500 to 2592 mg/m^2 that were infused from 0.4 to 1.2 hours. Peak plasma concentrations (obtained within 5 minutes of the end of the infusion): 3.2 to 45.5 μg/ml. Volume of distribution of the central compartment: 12.4 l/m^2 for women and 17.5 l/m^2 for men (inter-individual variability was 91.9%). Volume of distribution of the peripheral compartment: 47.4 l/m^2. The volume of the peripheral compartment was not sensitive to gender.

Plasma protein binding: Negligible.

Systemic clearance: Ranged from 29.2 $l/hr/m^2$ to 92.2 $l/hr/m^2$ depending on gender and age (inter-individual variability was 52.2%). Clearance for women is approximately 25% lower than the values for men. Although rapid, clearance for both men and women appears to decrease with age. For the recommended gemcitabine dose of 1,000mg/m^2 given as a 30 minute infusion, lower clearance values for women and men should not necessitate a decrease in the gemcitabine dose.

Urinary excretion: Less than 10% is excreted as unchanged drug.

Renal clearance: 2 to 7 $l/hr/m^2$.

Half-life: Ranged from 42 to 94 minutes depending on age and gender. For the recommended dosing schedule, gemcitabine elimination should be virtually complete within 5 to 11 hours of the start of the infusion. Gemcitabine does not accumulate when administered once weekly.

Metabolism:
Gemcitabine is rapidly metabolised by cytidine deaminase in the liver, kidney, blood and other tissues.

Intracellular metabolism of gemcitabine produces the gemcitabine mono, di and triphosphates (dFdCMP, dFdCDP and dFdCTP) of which dFdCDP and dFdCTP are considered active. These intracellular metabolites have not been detected in plasma or urine. The primary metabolite, 2'-deoxy-2',2'-difluorouridine (dFdU), is not active and is found in plasma and urine.

dFdCTP Kinetics:
This metabolite can be found in peripheral blood mononuclear cells and the information below refers to these cells.

Half-life of terminal elimination: 0.7-12 hours.
Intracellular concentrations increase in proportion to gemcitabine doses of 35-350 mg/m^2/30 min, which give steady state concentrations of 0.4-5 μg/ml. At gemcitabine plasma concentrations above 5 μg/ml, dFdCTP levels do not increase, suggesting that the formation is saturable in these cells. Parent plasma concentrations following a dose of 1,000 mg/m^2/30 min are greater than 5 μg/ml for approximately 30 minutes after the end of the infusion, and greater than 0.4 μg/ml for an additional hour.

dFdU Kinetics:
Peak plasma concentrations (3-15 minutes after end of 30 minute infusion, 1,000 mg/m^2): 28-52 μg/ml.
Trough concentration following once weekly dosing: 0.07-1.12 μg/ml, with no apparent accumulation.
Triphasic plasma concentration versus time curve, mean half-life of terminal phase - 65 hours (range 33-84 hr). Formation of dFdU from parent compound: 91%-98%.
Mean volume of distribution of central compartment: 18 l/m^2 (range 11-22 l/m^2).

Mean steady state volume of distribution (Vss): 150 l/m^2 (range 96-228 l/m^2).

Tissue distribution: Extensive.

Mean apparent clearance: 2.5 l/hr/m^2 (range 1-4 l/hr/m^2).
Urinary excretion: All.

Overall Elimination:
Amount recovered in one week: 92%-98%, of which 99% is dFdU, 1% of the dose is excreted in faeces.

5.3 Preclinical Safety Data
In repeat dose studies of up to 6 months in duration in mice and dogs, the principal finding was haematopoietic suppression. These effects were related to the cytotoxic properties of the drug and were reversible when treatment was withdrawn. The degree of the effect was schedule and dose-dependent.

Carcinogenesis, Mutagenesis, Fertility:
Cytogenetic damage has been produced by gemcitabine in an *in vivo* assay. Gemcitabine induced forward mutation *in vitro* in a mouse lymphoma (L5178Y) assay. Gemcitabine caused a reversible, dose and schedule dependent hypospermatogenesis in male mice. Although animal studies have shown an effect of gemcitabine on male fertility, no effect has been seen on female fertility.

Long-term animal studies have not been conducted to evaluate the carcinogenic potential of gemcitabine.

6. Pharmaceutical Particulars
6.1 List excipients
Mannitol

Sodium Acetate
Hydrochloric Acid
Sodium Hydroxide

6.2 Incompatibilities
Compatibility with other drugs has not been studied.

6.3 Shelf life
Three years

6.4 Special precautions for storage
Store below 30°C.
Solutions of reconstituted gemcitabine, in sterile 0.9% Sodium Chloride Injection, should be kept below 30°C.
Reconstituted solutions should be used immediately or may be stored for **24** hours if prepared in an appropriately controlled aseptic environment. Solutions should not be refrigerated, as crystallisation may occur.

6.5 Nature and Contents of container
The product is contained in either 10 ml or 50 ml sterile Type I flint glass vials, which meet the requirements of the Ph.Eur., and are closed with halobutyl rubber stoppers and sealed with aluminium seals with polypropylene caps. 1 vial per pack.

6.6 Instruction for use/Handling
Reconstitution:
Gemzar has only been shown to be compatible with 0.9% Sodium Chloride Injection. Accordingly, only this diluent should be used for reconstitution. Compatibility with other drugs has not been studied, therefore, it is not recommended to mix Gemzar with other drugs when reconstituted. 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. To reconstitute, add at least 5 ml of 0.9% Sodium Chloride Injection to the 200 mg vial or at least 25 ml of 0.9% Sodium Chloride Injection to the 1 g vial. Shake to dissolve. The appropriate amount of drug may be administered as prepared or further diluted with 0.9% Sodium Chloride Injection. Reconstituted solutions should be used immediately or may be stored for 24 hours if prepared in an appropriately controlled aseptic environment. Parenteral drugs should be inspected visually for particulate matter and discolouration, prior to administration, whenever solution and container permit.

Guidelines for the Safe Handling of Antineoplastic Agents:
Cytotoxic preparations should not be handled by pregnant staff. Trained personnel should reconstitute the drug. This should be performed in a designated area. The work surface should be covered with disposable plastic-backed absorbent paper. Adequate protective gloves, masks and clothing should be worn. Precautions should be taken to avoid the drug accidentally coming into contact with the eyes. If accidental contamination occurs, the eye should be washed with water thoroughly and immediately. Use luer-lock fittings on all syringes and sets. Large bore needles are recommended to minimise pressure and the possible formation of aerosols. The latter may also be reduced by the use of a venting needle.

Adequate care and precaution should be taken in the disposal of items used to reconstitute Gemzar. Any unused dry product or contaminated materials should be placed in a high risk waste bag. Sharp objects (needles, syringes, vials, etc) should be placed in a suitable rigid container. Personnel concerned with the collection and disposal of this waste should be aware of the hazard involved. Waste material should be destroyed by incineration. Any excess drug solution should be flushed directly into a drain with copious amounts of water.

6.7 Presentation

GEMZAR® 200 mg, box of 1 vial. Reg. No.
GEMZAR® 1 g, box of 1 vial. Reg. No.

HARUS DENGAN RESEP DOKTER

Manufactured by:
Vianex S.A.
Pallini Attiki, 15351, Greece.
for CHEPLAPHARM Arzneimittel GmbH, Greifswald, Germany

Released by:
Prestige Promotion
Verkaufsförderung &
Werbeservice GmbH,
Alzenau, Germany

Registered by:
PT. Wigo Health Indonesia
Kabupaten Semarang - Indonesia