141.0 mm

206.0 mm

100mg / 5ml Injection

IRINOSOL

Irinotecan

آئرینوسول

۱۰۰ ملی گرام/۵ ملی لیٹر انجکشن

(آئرونوٹیکن)

COMPOSITION

Each 5ml contains:

Irinotecan Hydrochloride Trihydrate.....100mg

(USP specifications)

DESCRIPTION

Irinotecan hydrochloride is an antineoplastic agent of the topoisomerase I inhibitor class. Irinotecan hydrochloride is a semisynthetic derivative of camptothecin, an alkaloid extract from plants such as Camptotheca acuminata or is chemically synthesized.

MECHANISM OF ACTION

Irinotecan is a derivative of camptothecin. Camptothecins interact specifically with the enzyme topoisomerase I, which relieves torsional strain in DNA by inducing reversible single-strand breaks. Irinotecan and its active metabolite SN-38 bind to the topoisomerase I-DNA complex and prevent religation of these single-strand breaks. Current research suggests that the cytotoxicity of irinotecan is due to double-strand DNA damage produced during DNA synthesis when replication enzymes interact with the ternary complex formed by topoisomerase I, DNA, and either irinotecan or SN-38. Mammalian cells cannot efficiently repair these double-strand breaks.

INDICATIONS

Irinotecan Injection is indicated as a component of first-line therapy in combination with 5-fluorouracil (5-FU) and Leucovorin (LV) for patients with metastatic carcinoma of the colon or rectum.

Irinotecan is indicated for patients with metastatic carcinoma of the colon or rectum whose disease has recurred or progressed following initial fluorouracil-based therapy.

DOSAGE & ADMINISTRATION

For adults only. Diluted Irinotecan solution for infusion should be infused into a peripheral or central vein.

Recommended dosage:

In monotherapy (for previously treated patient)

The recommended dosage of Irinotecan is 350 mg/m^2 administered as an intravenous infusion over a 30 to 90 minute period every three weeks.

In combination therapy (for previously untreated patient)

The safety and efficacy of Irinotecan in combination with 5-fluorouracil (5FU) and folinic acid (FA) have been assessed in the following schedule.

• Irinotecan plus 5FU/FA in every 2 weeks schedule

The recommended dose of irinotecan is 180 mg/m2 administered once every 2 weeks as an intravenous infusion over a 30- to 90-minute period, followed by an infusion of folinic acid and 5-fluorouracil.

• Normally, the same dose of irinotecan is used as administered in the last cycles of the prior irinotecan-containing regimen. Irinotecan must not be administered earlier than 1 hour after the end of the cetuximab infusion.

Dosage adjustments:

Irinotecan should be administered after appropriate recovery of all adverse events to Grade 0 or 1 NCI-CTC (National Cancer Institute Common Toxicity Criteria) grading and when treatment-related diarrhea is fully resolved.

At the start of a subsequent infusion of therapy, the dose of irinotecan, and 5FU when applicable, should be decreased according to the worst grade of adverse events observed in the prior infusion. Treatment should be delayed by 1 to 2 weeks to allow recovery from treatment-related adverse events.

With the following adverse events a dose reduction of 15 to 20% should be applied for irinotecan and/or 5FU when applicable:

• Haematological toxicity [neutropenia Grade 4, febrile neutropenia (neutropenia Grade 3-4 and fever Grade 2-4), thrombocytopenia and leukopenia (Grade 4)],

• Non-haematological toxicity (Grade 3-4).

Recommendations for dose modifications of cetuximab when administered in combination with irinotecan must be followed according to the product information for this medicinal product.

In combination with capecitabine for patients 65 years of age or more, a reduction of the starting dose of capecitabine to 800 mg/m^2 twice daily is recommended.

Treatment duration:

Treatment with irinotecan should be continued until there is an objective progression of the disease or an unacceptable toxicity.

Special populations:

Patients with impaired hepatic function

In monotherapy:

Blood bilirubin levels [up to 3 times the upper limit of the normal range (ULN)] in patients with performance status ≤ 2, should determine the starting dose of irinotecan. In these patients with hyperbilirubinaemia and prothrombin time greater than 50%, the clearance of irinotecan is decreased, and therefore the risk of hepatotoxicity is increased. Thus, weekly monitoring of complete blood counts should be conducted in this patient population.

• In patients with bilirubin levels up to 1.5 times the ULN, the recommended dosage of irinotecan is 350 mg/m^2.

• In patients with bilirubin levels between 1.5 to 3 times the ULN, the recommended dosage of irinotecan is 200 mg/m^2.

• Patients with bilirubin levels beyond 3 times the ULN, should not be treated with irinotecan.

• No data are available in patients with hepatic impairment treated with irinotecan in combination.

Patients with impaired renal function

Irinotecan is not recommended for use in patients with impaired renal function, as studies in this population have not been conducted.

Elderly

No specific pharmacokinetic studies have been performed in the elderly. However, the dose should be chosen carefully in this population due to their greater frequency of decreased biological functions. This population should require more intense surveillance.

Pediatric population

The safety and efficacy of irinotecan in children have not yet been established. No data are available.

Premedication

It is recommended that patients receive premedication with antiemetic agents. In clinical studies of the weekly dosage schedule, the majority of patients received 10 mg of dexamethasone given in conjunction with another type of antiemetic agent, such as a 5-HT3 blocker (e.g., ondansetron or granisetron). Antiemetic agents should be given on the day of treatment, starting at least 30 minutes before administration of Irinotecan. Physicians should also consider providing patients with an antiemetic regimen (e.g., prochlorperazine) for subsequent use as needed. A similar antiemetic regimen should be used with Irinotecan in combination therapy. Prophylactic or therapeutic administration of atropine should be considered in patients experiencing cholinergic symptoms.

Preparation of Infusion Solution

Inspect vial contents for particulate matter and discoloration and repeat inspection when drug product is withdrawn from vial into syringe.

Irinotecan Injection 20 mg/mL is intended for single use only and any unused portion should be discarded.

Irinotecan Injection must be diluted prior to infusion. Irinotecan should be diluted in 5% Dextrose Injection, USP, (preferred) or 0.9% Sodium Chloride Injection, USP, to a final concentration range of 0.12 mg/mL to 2.8 mg/mL.

Other drugs should not be added to the infusion solution.
The solution is physically and chemically stable for up to 24 hours at room temperature and in ambient fluorescent lighting. Solutions diluted in 5% Dextrose Injection, USP, and stored at refrigerated temperatures (approximately 2° to 8°C, 36° to 46°F), and protected from light are physically and chemically stable for 48 hours. Refrigeration of admixtures using 0.9% Sodium Chloride Injection, USP, is not recommended due to a low and sporadic incidence of visible particulates. Freezing Irinotecan and admixtures of Irinotecan may result in precipitation of the drug and should be avoided.
The Irinotecan Injection solution should be used immediately after reconstitution as it contains no antibacterial preservative. Because of possible microbial contamination during dilution, it is advisable to use the admixture prepared with 5% Dextrose Injection, USP, within 24 hours if refrigerated (2° to 8°C, 36° to 46°F). In the case of admixtures prepared with 5% Dextrose Injection, USP, or Sodium Chloride Injection, USP, the solutions should be used within 4 hours if kept at room temperature. If reconstitution and dilution are performed under strict aseptic conditions (e.g., on Laminar Air Flow bench), Irinotecan Injection solution should be used (infusion completed) within 12 hours at room temperature or 24 hours if refrigerated (2° to 8°C, 36° to 46°F).

Safe Handling

Care should be exercised in the handling and preparation of infusion solutions prepared from Irinotecan Injection. The use of gloves is recommended. If a solution of irinotecan contacts the skin, wash the skin immediately and thoroughly with soap and water. If Irinotecan contacts the mucous membranes, flush thoroughly with water. Several published guidelines for handling and disposal of anticancer agents are available.

Extravasation

Care should be taken to avoid extravasation, and the infusion site should be monitored for signs of inflammation. Should extravasation occur, flushing the site with sterile water and applications of ice are recommended.

PHARMACOKINETICS

After intravenous infusion of irinotecan in humans, irinotecan plasma concentrations decline in a multiexponential manner, with a mean terminal elimination half-life of about 6 to 12 hours. The mean terminal elimination half-life of the active metabolite SN-38 is about 10 to 20 hours. The half-lives of the lactone (active) forms of irinotecan and SN-38 are similar to those of total irinotecan and SN-38, as the lactone and hydroxy acid forms are in equilibrium. Over the recommended dose range of 50 to 350 mg/m2, the AUC of irinotecan increases linearly with dose; the AUC of SN-38 increases less than proportionally with dose. Maximum concentrations of the active metabolite SN-38 are generally seen within 1 hour following the end of a 90-minute infusion of irinotecan.

Distribution

Irinotecan exhibits moderate plasma protein binding (30% to 68% bound). SN-38 is highly bound to human plasma proteins (approximately 95% bound). The plasma protein to which irinotecan and SN-38 predominantly binds is albumin.

Metabolism

Irinotecan is subject to extensive metabolic conversion by various enzyme systems, including esterases to form the active metabolite SN-38, and UGT1A1 mediating glucuronidation of SN-38 to form the inactive glucuronide metabolite SN-38G. Irinotecan can also undergo CYP3A4-mediated oxidative metabolism to several inactive oxidation products, one of which can be hydrolyzed by carboxylesterase to release SN-38. In vitro studies indicate that irinotecan, SN-38 and another metabolite aminopentane carboxylic acid (APC), do not inhibit cytochrome P-450 isozymes. UGT1A1 activity is reduced in individuals with genetic polymorphisms that lead to reduced enzyme activity such as the UGT1A1*28 polymorphism. Approximately 10% of the North American population is homozygous for the UGT1A1*28 allele (also referred to as UGT1A1 7/7 genotype). In a prospective study, in which irinotecan was administered as a single-agent (350 mg/m2) on a once-every-3-week schedule, patients with the UGT1A1 7/7 genotype had a higher exposure to SN-38 than patients with the wild-type UGT1A1 allele (UGT1A1 6/6 genotype). SN-38 glucuronide had 1/50 to 1/100 the activity of SN-38 in cytotoxicity assays using two cell lines in vitro.

Excretion

The disposition of irinotecan has not been fully elucidated in humans. The urinary excretion of irinotecan is 11% to 20%; SN-38, glucuronide, 3%. The cumulative biliary and urinary excretion of irinotecan and its metabolites (SN-38 and SN-38 glucuronide) over a period of 48 hours following administration of irinotecan in two patients ranged from approximately 25% (100 mg/m2) to 50% (300 mg/m2)

WARNINGS AND PRECAUTIONS

The use of irinotecan should be confined to units specialized in the administration of cytotoxic chemotherapy and it should only be administered under the supervision of a physician qualified in the use of anticancer chemotherapy.

Given the nature and incidence of adverse events, irinotecan will only be prescribed in the following cases after the expected benefits have been weighed against the possible therapeutic risks:

- In patients with a risk factor, particularly those with a WHO performance status = 2.
- In the few rare instances where patients are deemed unlikely to observe recommendations regarding management of adverse events (need for immediate and prolonged anti-diarrhoeal treatment combined with high fluid intake at onset of delayed diarrhea). Strict hospital supervision is recommended for such patients.

When irinotecan is used in monotherapy, it is usually prescribed using the every-3-week dosage schedule. However, the weekly-dosage schedule may be considered in patients who need a closer follow-up or who are at particular risk of severe neutropenia.

Delayed diarrhea

Patients should be made aware of the risk of delayed diarrhoea occurring more than 24 hours after the administration of irinotecan and at any time before the next cycle. In monotherapy, the median time of onset of the first liquid stool was on day 5 after the infusion of irinotecan. Patients should quickly inform their physician of its occurrence and start appropriate therapy immediately.
Patients with an increased risk of diarrhoea are those who have had previous abdominal/pelvic radiotherapy, those with baseline hyperleucocytosis, those with performance status ≥ 2 and women. If not properly treated, diarrhoea can be life-threatening, especially if the patient is concomitantly neutropenic.
As soon as the first liquid stool occurs, the patient should start drinking large volumes of beverages containing electrolytes, and an appropriate anti-diarrhoeal therapy must be initiated immediately. The anti-diarrhoeal treatment will be prescribed by the department where irinotecan has been administered. After discharge from the hospital, the patients should obtain the prescribed medicinal products so they can treat the diarrhoea as soon as it occurs. In addition, they must inform their physician or the department administering irinotecan when/if diarrhoea is occurring.
The currently recommended anti-diarrhoeal treatment consists of high doses of loperamide (4 mg at the first intake and then 2 mg every 2 hours). This therapy should continue for 12 hours after the last liquid stool and should not be modified. In no instance should loperamide be administered for more than 48 consecutive hours at these doses, because of the risk of paralytic ileus, nor for less than 12 hours.
In addition to the anti-diarrhoeal treatment, a prophylactic broad-spectrum antibiotic should be given when diarrhoea is associated with severe neutropenia (neutrophil count < 500 cells/mm^3).
In addition to the antibiotic treatment, hospitalisation is recommended for management of the diarrhoea in the following cases:

- Diarrhoea associated with fever,
- Severe diarrhoea (requiring intravenous hydration),
- Diarrhoea persisting beyond 48 hours following the initiation of high-dose loperamide therapy.

Loperamide should not be given prophylactically, even in patients who experienced delayed diarrhoea at previous cycles.
In patients who experienced severe diarrhoea, a reduction in dose is recommended for subsequent cycles.

Haematology

In clinical studies, the frequency of NCI CTC Grade 3 and 4 neutropenia has been significantly higher in patients who received previous pelvic/abdominal irradiation than in those who had not received such irradiation. Patients with baseline serum total bilirubin levels of 1.0 mg/dL or more have also had a significantly greater likelihood of experiencing first-cycle Grade 3 or 4 neutropenia than those with bilirubin levels that

were less than 1.0 mg/dL.
Weekly monitoring of complete blood cell counts is recommended during irinotecan treatment. Patients should be aware of the risk of neutropenia and the significance of fever. Febrile neutropenia (temperature > 38°C and neutrophil count ≤ 1,000 cells/mm^3) should be urgently treated in the hospital with broad-spectrum intravenous antibiotics.
In patients who experienced severe haematological events, a dose reduction is recommended for subsequent administration.
There is an increased risk of infections and haematological toxicity in patients with severe diarrhoea. In patients with severe diarrhoea, complete blood cell counts should be performed.

Patients with reduced UGT1A1 activity

Patients that are UGT1A1 poor metabolisers, such as patients with Gilbert's syndrome (e.g. homozygous for UGT1A1*28 or *6 variants) are at increased risk for severe neutropenia and diarrhoea following irinotecan treatment. This risk increases with the irinotecan dose level.
Although a precise dose reduction in starting dose has not been established, a reduced irinotecan starting dose should be considered for patients that are UGT1A1 poor metabolisers, especially patients who are administered doses > 180 mg/m2 or frail patients. Consideration should be given to applicable clinical guidelines for dose recommendations in this patient population. Subsequent doses may be increased based on individual patient tolerance to treatment.
UGT1A1 genotyping can be used to identify patients at increased risk of severe neutropenia and diarrhoea, however the clinical utility of pre-treatment genotyping is uncertain, since UGT1A1 polymorphism does not account for all the toxicity seen from irinotecan therapy.

Liver impairment

Liver function tests should be performed at baseline and before each cycle. Weekly monitoring of complete blood counts should be conducted in patients with bilirubin ranging from 1.5 to 3 times the ULN, due to decrease of the clearance of irinotecan (see section 5.2) and thus increasing the risk of hepatotoxicity in this population. For patients with a bilirubin > 3 times the ULN.

Nausea and vomiting

A prophylactic treatment with antiemetics is recommended before each treatment with irinotecan. Nausea and vomiting have been frequently reported. Patients with vomiting associated with delayed diarrhoea should be hospitalised as soon as possible for treatment.

Acute cholinergic syndrome

If acute cholinergic syndrome appears (defined as early diarrhoea and various other signs and symptoms such as sweating, abdominal cramping, myosis and salivation), atropine sulphate (0.25 mg subcutaneously) should be administered unless clinically contraindicated.
These symptoms may be observed during or shortly after infusion of irinotecan, are thought to be related to the anticholinesterase activity of the irinotecan parent compound, and are expected to occur more frequently with higher irinotecan doses.
Caution should be exercised in patients with asthma. If the patient experiences an acute and severe cholinergic syndrome, the use of prophylactic atropine sulphate is recommended with subsequent doses of irinotecan.

Respiratory disorders

Interstitial lung disease presenting as lung infiltration is uncommon during irinotecan therapy. Interstitial lung disease can be fatal. Risk factors possibly associated with the development of interstitial lung disease include the use of pneumotoxic medicinal products, radiation therapy and colony stimulating factors. Patients with risk factors should be closely monitored for respiratory symptoms before and during irinotecan therapy.

Extravasation

While irinotecan is not a known vesicant, care should be taken to avoid extravasation and the infusion site should be monitored for signs of inflammation. Should extravasation occur, flushing the site and application of ice is recommended.

Elderly

Due to the greater frequency of decreased biological functions, in particular hepatic function, in elderly patients, dose selection with irinotecan should be cautious in this population.

Chronic inflammatory bowel disease and/or bowel obstruction

Patients must not be treated with irinotecan until resolution of the bowel obstruction.

Renal function

Increases in serum creatinine or blood urea nitrogen have been observed. There have been cases of acute renal failure. These events have generally been attributed to complications of infection or to dehydration related to nausea, vomiting, or diarrhoea. Rare instances of renal dysfunction due to tumour lysis syndrome have also been reported.

Irradiation therapy

Patients who have previously received pelvic/abdominal irradiation are at increased risk of myelosuppression following the administration of irinotecan. Physicians should use caution in treating patients with extensive prior irradiation (e.g. > 25% of bone marrow irradiated and within 6 weeks prior to start of treatment with irinotecan). Dosing adjustment may apply to this population.

Cardiac disorders

Myocardial ischemic events have been observed following irinotecan therapy predominately in patients with underlying cardiac disease, other known risk factors for cardiac disease, or previous cytotoxic chemotherapy.
Consequently, patients with known risk factors should be closely monitored, and action should be taken to try to minimize all modifiable risk factors (e.g. smoking, hypertension, and hyperlipidaemia).

Vascular disorders

Irinotecan has been rarely associated with thromboembolic events (pulmonary embolism, venous thrombosis, and arterial thromboembolism) in patients presenting with multiple risk factors in addition to the underlying neoplasm.

Others

Infrequent cases of renal insufficiency, hypotension or circulatory failure have been observed in patients who experienced episodes of dehydration associated with diarrhoea and/or vomiting, or sepsis.

Contraception in women of childbearing potential/men:

Due to the potential for genotoxicity, advise female patients of reproductive potential to use highly effective contraception during treatment and for 6 months after the last dose of irinotecan. Due to the potential for genotoxicity, advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of irinotecan.

Pregnancy

There are limited data from the use of irinotecan in pregnant women. Irinotecan has been shown to be embryotoxic and teratogenic in animals. Therefore, based on results from animal studies and the mechanism of action of irinotecan, irinotecan should not be used during pregnancy unless clearly necessary.
Women of childbearing potential should not be started on irinotecan until pregnancy is excluded. Pregnancy should be avoided if either partner is receiving irinotecan.

Breast-feeding

Due to the potential for adverse reactions in nursing infants, breast-feeding should be discontinued for the duration of irinotecan therapy.
Concomitant administration of irinotecan with a strong inhibitor (e.g. ketoconazole) or inducer (e.g. rifampicin, carbamazepine, phenobarbital, phenytoin, apalutamide) of CYP3A4 may alter the metabolism of irinotecan and should be avoided.
This medicine contains sorbitol. Sorbitol is a source of fructose. Patients with hereditary fructose intolerance (HFI) must not be given this medicine unless strictly necessary.
Babies and young children (below 2 years of age) may not yet be diagnosed with HFI. Medicines (containing fructose) given intravenously may have life-threatening effects in individuals with HFI and should not be administered in this population unless there is an overwhelming clinical need and no alternatives are available.
A detailed history with regard to HFI symptoms has to be taken of each patient prior to being given this medicinal product.

SIDE EFFECTS

The following adverse reactions have been identified during post approval use of Irinotecan. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
Myocardial ischemic events have been observed following Irinotecan therapy. Thromboembolic events have been observed in patients receiving Irinotecan.

Symptomatic pancreatitis, asymptomatic pancreatic enzyme elevation have been reported. Increases in serum levels of transaminases (i.e., AST and ALT) in the absence of progressive liver metastasis have been observed.

Hyponatremia, mostly with diarrhea and vomiting, has been reported.

Transient dysarthria has been reported in patients treated with Irinotecan; in some cases, the event was attributed to the cholinergic syndrome observed during or shortly after infusion of irinotecan.

Interaction between Irinotecan and neuromuscular blocking agents cannot be ruled out. Irinotecan has anticholinesterase activity, which may prolong the neuromuscular blocking effects of suxamethonium and the neuromuscular blockade of non-depolarizing drugs may be antagonized.

DRUG INTERACTIONS

Concomitant use contraindicated

Saint John's Wort: Decrease in the active metabolite of irinotecan, SN-38, plasma levels. In a small pharmacokinetic study (n = 5), in which irinotecan 350 mg/m2 was co-administered with St. John's Wort (Hypericum perforatum) 900 mg, a 42% decrease in the active metabolite of irinotecan, SN-38, plasma concentrations was observed. As a result, St. John's Wort should not be administered with irinotecan.

Live attenuated vaccines (e.g. yellow fever vaccine): Risk of generalised reaction to vaccines, possibly fatal. Concomitant use is contraindicated during treatment with irinotecan and for 6 months following discontinuation of chemotherapy. Killed or inactivated vaccines may be administered; however, the response to such vaccines may be diminished.

Concomitant use not recommended

Concurrent administration of irinotecan with strong inhibitors or inducers of cytochrome P450 3A4 (CYP3A4) may alter the metabolism of irinotecan and should be avoided.

Strong CYP3A4 and/or UGT1A1 inducing medicinal products (e.g. rifampicin, carbamazepine, phenobarbital, phenytoin or apalutamide): Risk of reduced exposure to irinotecan, SN-38 and SN-38 glucuronide and reduced pharmacodynamic effects. Several studies have shown that concomitant administration of CYP3A4-inducing anticonvulsant medicinal products leads to reduced exposure to irinotecan, SN-38 and SN-38 glucuronide and reduced pharmacodynamic effects. The effects of such anticonvulsant medicinal products were reflected by a decrease in AUC of SN-38 and SN-38G by 50% or more. In addition to induction of CYP3A4 enzymes, enhanced glucuronidation and enhanced biliary excretion may play a role in reducing exposure to irinotecan and its metabolites.

Additionally with phenytoin: Risk of exacerbation of convulsions resulting from the decrease of phenytoin digestive absorption by cytotoxic medicinal products.

Strong CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, voriconazole, posaconazole, protease inhibitors, clarithromycin, erythromycin, telithromycin): A study has shown that the co-administration of ketoconazole resulted in a decrease in the AUC of APC of 87% and in an increase in the AUC of SN-38 of 109% in comparison to irinotecan given alone.

UGT1A1 inhibitors (e.g. atazanavir, ketoconazole, regorafenib): Risk to increase systemic exposure to SN-38, the active metabolite of irinotecan. Physicians should take this into consideration if the combination is unavoidable.

Other CYP3A4 inhibitors (e.g. crizotinib, idelalisib): Risk of increase in irinotecan toxicity, due to a decrease in irinotecan metabolism by crizotinib or idelalisib.

Caution for use

Vitamin K antagonists: Increased risk of haemorrhage and thrombotic events in tumoural diseases. If vitamin K antagonists are indicated, an increased frequency in the monitoring of INR (International Normalised Ratio) is required.

Concomitant use to take into consideration

Immunodepressant agents (e.g. ciclosporine, tacrolimus): Excessive immunosuppression with risk of lymphoproliferation.

Neuromuscular blocking agents: Interaction between irinotecan and neuromuscular blocking agents cannot be ruled out. Since irinotecan has anticholinesterase activity, medicinal products with anticholinesterase activity may prolong the neuromuscular blocking effects of suxamethonium and the neuromuscular blockade of non-depolarising medicinal products may be antagonised.

Other combinations

5-fluorouracil/folinic acid: Co-administration of 5-fluorouracil/folinic acid in the combination regimen does not change the pharmacokinetics of irinotecan.

Bevacizumab: Results from a dedicated drug-drug interaction trial demonstrated no significant effect of bevacizumab on the pharmacokinetics of irinotecan and its active metabolite SN-38. However, this does not preclude any increase of toxicities due to their pharmacological properties.

Cetuximab: There is no evidence that the safety profile of irinotecan is influenced by cetuximab or vice versa.

Antineoplastic agents (including flucytosine as a prodrug for 5-fluorouracil): Adverse effects of irinotecan, such as myelosuppression, may be exacerbated by other antineoplastic agents having a similar adverse-effect profile.

OVERDOSE

Symptoms

There have been reports of overdose, with doses up to approximately twice the recommended therapeutic dose, which may be fatal. The most significant adverse reactions reported were severe neutropenia and severe diarrhea.

Management

There is no known antidote for irinotecan. Maximum supportive treatment should be initiated to prevent dehydration due to diarrhea and to treat any infectious complications.

CONTRAINDICATIONS

Irinotecan Injection is contraindicated in patients with a known hypersensitivity to the drug or its excipients.

STORAGE & INSTRUCTIONS:

Store below 25°C.
Protect from heat, sunlight and moisture. Do not freeze.
Keep out of the reach of children.
CONTAINS NO ANTIMICROBIAL PRESERVATIVES.
Single use Vial. Discard unused portion.
For Intravenous use only.

CAUTION: IT IS DANGEROUS TO TAKE THIS MEDICATION EXCEPT UNDER STRICT MEDICAL SUPERVISION.

WARNING: To be sold on the prescription of a registered oncologist or on demand from cancer hospitals and institutions only.

HOW SUPPLIED

1 Vial.

خوراک وہدایت:

سرطان کے ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:

دوا کو ۲۵ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

دھوپ، گرمی، نمی اور منجمد ہونے سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

صرف ایک بار استعمال کے لیے ہے۔ صرف وریدی استعمال کے لیے ہے۔

انتباہ: صرف مستند اونکولوجسٹ یا کینسر ہسپتال کے نسخے پر فروخت کریں۔

Manufactured by:

PHARMASOL
PRIVATE LIMITED
Plot # 549,Sundar Industrial Estate,
Lahore, Pakistan.