

Irinotecan Hydrochloride

IRINON

100 mg/5 mL Concentrate for Solution
for Infusion



Description: Pale yellow clear aqueous solution filled into amber vial with rubber stopper and aluminium seal.

Product Name
Irinotecan Hydrochloride 100 mg/5 mL Concentrate for Solution for Infusion

Name and Strength of Active Substance(s)
Irinotecan 100 mg/5 mL.

Pharmacodynamic Properties

Pharmacotherapeutic group: 16.1.4 – Antineoplastic and immunomodulating agents; Cytotoxics; Topoisomerase I inhibitor.

Mechanism of Action

Irinotecan is a semi-synthetic derivative of camptothecin. It is an antineoplastic agent which acts as a specific inhibitor of DNA topoisomerase I. It is metabolized by carboxylesterase in most tissues to SN-38, which was found to be more active than irinotecan in purified topoisomerase I and more cytotoxic than irinotecan against several murine and human tumour cell lines. The inhibition of DNA topoisomerase I by irinotecan or SN-38 induces single-strand DNA lesions which blocks the DNA replication fork and are responsible for the cytotoxicity. This cytotoxic activity was found time-dependent and was specific to the S phase.

In vitro, irinotecan and SN-38 were not found to be significantly recognised by the P-glycoprotein MDR, and displays cytotoxic activities against doxorubicin and vinblastine resistant cell lines.

Furthermore, irinotecan has a broad antitumor activity against murine tumour models (P03 pancreatic ductal adenocarcinoma, MA16/C mammary adenocarcinoma, C38 and C51 colon adenocarcinomas) and against human xenografts (Co-4 colon adenocarcinoma, Mx-1 mammary adenocarcinoma, ST-15 and SC-16 gastric adenocarcinomas). Irinotecan is also active against tumours expressing the P-glycoprotein MDR (vincristine- and doxorubicin-resistant P388 leukaemia). Beside the antitumor activity of irinotecan, the most relevant pharmacological effect of irinotecan is the inhibition of acetyl cholinesterase.

Pharmacokinetics

In a phase I study in 60 patients with a dosage regimen consisting of a 30-minute intravenous infusion of 100 to 750 mg/m² every three weeks, irinotecan showed a biphasic or triphasic elimination profile. The mean plasma clearance was 15 L/h/m² and the volume of distribution at steady state (Vss): 157 L/m². The mean plasma half-life of the first phase of the triphasic model was 12 minutes, of the second phase 2.5 hours, and the terminal phase half-life was 14.2 hours. SN-38 showed a biphasic elimination profile with a mean terminal elimination half-life of 13.8 hours. At the end of the infusion, at the recommended dose of 350 mg/m², the mean peak plasma concentrations of irinotecan and SN-38 were 7.7 µg/ml and 56 ng/ml, respectively and the mean area under the curve (AUC) values were 34 µg.h/ml and 451 ng.h/ml, respectively. A large interindividual variability in pharmacokinetic parameters is generally observed for SN-38.

A population pharmacokinetic analysis of irinotecan has been performed in 148 patients with metastatic colorectal cancer, treated with various schedules and at different doses in phase II trials. Pharmacokinetic parameters estimated with a three compartment model were similar to those observed in phase I studies. All studies have shown that irinotecan (CPT-11) and SN-38 exposure increase proportionally with the CPT-11 administered dose; their pharmacokinetics are independent of the number of previous cycles and of the administration schedule.

In vitro, plasma protein binding was approximately 65 % for irinotecan and 95% for SN-38.

Mass balance and metabolism studies with 14 C-labelled drug have shown that more than 50% of an intravenously administered dose of irinotecan is excreted as unchanged drug, with 33% in the faeces mainly via the bile and 22% in urine.

Two metabolic pathways account each for at least 12% of the dose:

- hydrolysis by carboxylesterase into active metabolite SN-38. SN-38 is mainly eliminated by glucuronidation, and further by biliary and renal excretion (less than 0.5 % of the irinotecan dose). The SN-38 glucuronite is subsequently probably hydrolysed in the intestine.
- Cytochrome P450 3A -dependent oxidation, resulting in opening of the outer piperidine ring with formation of APC (aminopentanoic acid derivate) and NPC (primary amine derivate) (see section 4.5).

Unchanged irinotecan is the major entity in plasma, followed by APC, SN-38 glucuronide and SN-38. Only SN-38 has significant cytotoxic activity.

Irinotecan clearance is decreased by about 40% in patients with bilirubinemia between 1.5 and 3 times the upper normal limit. In these patients a 200 mg/m² irinotecan dose leads to plasma drug exposure comparable to that observed at 350 mg/m² in cancer patients with normal liver parameters.

Indication

Irinotecan is indicated for the treatment of patients with advanced colorectal cancer:

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

Irinotecan in combination with cetuximab is indicated for the treatment of patients with epidermal growth factor receptor (EGFR) - expressing KRAS wild-type metastatic colorectal cancer, who had not received prior treatment for metastatic disease or after failure of Irinotecan-including cytotoxic therapy.

Irinotecan in combination with 5-fluorouracil, folinic acid and bevacizumab is indicated for first-line treatment of patients with metastatic carcinoma of the colon or rectum.

Irinotecan in combination with Capecitabine with or without bevacizumab is indicated for first-line treatment of patients with metastatic colorectal carcinoma.

Recommended Dosage

In monotherapy (for previously treated patient):

The recommended dosage of Irinotecan is 350 mg/m², administered as an intravenous infusion over a 30 to 90 minute period; every three weeks.

In combination therapy (for previously untreated patient):

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

- Irinotecan plus 5-FU/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 infusion of folinic acid and 5-fluorouracil.

For the posology and method of administration of concomitant cetuximab, refer to the product information for this medicinal product.

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.

For the posology and method of administration of bevacizumab, refer to the bevacizumab summary product of characteristics.

For the posology and method of administration of Capecitabine combination, please see section 5.1 and refer to the appropriate sections in the Capecitabine summary of product characteristics.

Mode of Administration

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

At the start of a subsequent infusion of therapy, the dose of Irinotecan, and 5-FU 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 5-FU 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/m² twice daily is recommended according to the summary of product characteristics for Capecitabine. Refer also to the recommendations for dose modifications in combination regimen given in the summary of product characteristics for Capecitabine.

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 hyperbilirubinemia and a prothrombin time greater than 50%, the clearance of Irinotecan is reduced 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 up to 1.5 times the upper limit of the normal range (ULN), the recommended dosage of Irinotecan is 350 mg/m²,
- In patients with bilirubin ranging from 1.5 to 3 times the ULN, the recommended dosage of Irinotecan is 200 mg/m²,
- Patients with bilirubin beyond to 3 times the ULN should not be treated with Irinotecan.

No data are available in patients with hepatic impairment treated by 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 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.

Contraindications

- History of severe hypersensitivity reactions to Irinotecan hydrochloride trihydrate or to one of the excipients of Irinotecan.
- Chronic inflammatory bowel disease and/or bowel obstruction.
- Lactation.
- Bilirubin > 3 times the upper limit of the normal range.
- Severe bone marrow failure.
- WHO performance status > 2.
- Concomitant use with St John's Wort.

For additional contraindications of cetuximab or bevacizumab or Capecitabine, refer to the product information for these medicinal products.

Warnings and Precautions

The use of Irinotecan should be confined to units specialised 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 weighted against the possible therapeutic risks:

- In patients presenting 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 antidiarrheal treatment, combined with high fluid intake at onset of delayed diarrhoea). Strict hospital supervision is recommended for such patients.

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

Statement on Usage during Pregnancy and Lactation

Pregnancy:

There is no information on the use of irinotecan in pregnant women. Irinotecan was embryotoxic and teratogenic in animals. Based on results from animal studies and the mechanism of action of irinotecan, this medicine must not be used during pregnancy unless clearly necessary.

Women of child-bearing potential/Contraception in males and females:

Women of child-bearing potential and men have to use effective contraception during and up to 1 month and 3 months after treatment respectively.

Fertility

There are no human data on the effect of irinotecan on fertility. In animals adverse effects of irinotecan on the fertility of offspring has been documented.

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Acute cholinergic syndrome
Severe transient acute cholinergic syndrome was observed in 1.4 % of patients treated in combination therapy.

Asthenia was severe in 6.2 % of patients treated in combination therapy. The causal relationship to irinotecan has not been clearly established. Fever in the absence of infection and without concomitant severe neutropenia, occurred in 6.2 % of patients treated in combination therapy.

Laboratory tests

Transient serum levels (grades 1 and 2) of either SGPT, SGOT, alkaline phosphatase or bilirubin were observed in 15%, 11%, 11% and 10% of the patients, respectively, in the absence of progressive liver metastasis. Transient grade 3 were observed in 0%, 0%, 0% and 1% of the patients, respectively. No grade 4 was observed.

Increases of amylase and/or lipase have been very rarely reported.

Rare cases of hypokalemia and hyponatremia mostly related with diarrhea and vomiting have been reported.

OTHER ADVERSE EVENTS REPORTED IN CLINICAL STUDIES WITH THE WEEKLY REGIMEN FOR IRINOTECAN

The following additional drug-related events have been reported in clinical studies with irinotecan: pain, sepsis, rectal disorder, GI monilia, hypomagnesemia, rash, cutaneous signs, abnormal gait, confusion, headache, syncope, flushing, bradycardia, urinary tract infection, breast pain, increased GGTP, extravasation, and tumour lysis syndrome, cardiovascular disorders (angina pectoris, heart arrest, myocardial infarction, myocardial ischaemia, peripheral vascular disorder, vascular disorder), and thromboembolic events (arterial thrombosis, cerebral infarction, cerebrovascular accident, deep thrombophlebitis, embolus of the lower extremity, pulmonary embolus, thrombophlebitis, thrombosis, and sudden death).

POST-MARKETING SURVEILLANCE

Frequencies from post-marketing surveillance are not known (cannot be estimated from available data).

MedDRA System Organ Class	Preferred Term
Infections and infestations	• Pseudomembranous colitis one of which has been documented bacteriologically (<i>Clostridium difficile</i>) • Sepsis • Fungal infections ^a • Viral infections ^b
Blood and lymphatic system disorders	• Peripheral thrombocytopenia with antiplatelet antibodies
Metabolism and nutrition disorders	• Dehydration (due to diarrhoea and vomiting) • Hypovolaemia
Immune system disorders	• Hypersensitivity reaction • Anaphylactic reaction
Nervous system disorders	• Speech disorders generally transient in nature, in some cases, the event was attributed to the cholinergic syndrome observed during or shortly after infusion of irinotecan • Paraesthesia
Cardiac disorders	• Hypertension (during or after infusion) • Cardio circulatory failure^c
Respiratory, thoracic and mediastinal disorders	• Interstitial pulmonary disease presenting as pulmonary infiltrates is uncommon during irinotecan therapy; Early effects such as dyspnoea have been reported.
	• Dyspnoea • Hiccups

Breastfeeding:

In lactating rats, 14C-irinotecan was detected in milk. It is unknown if irinotecan is excreted in human breast milk. Consequently, because of the potential for adverse reactions in nursing infants, breastfeeding is contraindicated during therapy with Irinotecan.

Adverse Effects / Undesirable Effects
CLINICAL STUDIES

Adverse reaction data have been extensively collected from studies in metastatic colorectal cancer; the frequencies are presented below. The adverse reactions for other indications are expected to be similar to those for colorectal cancer.

The most common (≥1/10), dose-limiting adverse reactions of irinotecan are delayed diarrhoea (occurring more than 24 hours after administration) and blood disorders including neutropenia, anaemia and thrombocytopenia.

Neutropenia is a dose-limiting toxic effect. Neutropenia was reversible and not cumulative; the median day to nadir was 8 days whatever the use in monotherapy or in combination therapy. Very commonly severe transient acute cholinergic syndrome was observed.

The main symptoms were defined as early diarrhoea and various other symptoms such as abdominal pain, sweating, myosis and increased salivation occurring during or within the first 24 hours after the infusion of irinotecan. These symptoms disappear after atropine administration.

MONOTHERAPY

The following adverse reactions considered to be possibly or probably related to the adminis- tration of irinotecan have been reported from 765 patients at the recommended dose of 350 mg/m² in monotherapy. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), and very rare (<1/10,000).

Adverse Reactions Reported with irinotecan in Monotherapy (350 mg/ m² every 3 weeks schedule)		
MedDRA System Organ Class	Frequency Category	Preferred Term
Infections and infestations	Common	Infection
	Very common	Neutropenia
	Very common	Anaemia
	Common	Thrombocytopenia
Blood and lymphatic system disorders	Common	Febrile neutropenia
	Very common	Decreased appetite
	Very common	Cholinergic syndrome
	Very common	Diarrhoea
Metabolism and nutrition disorders	Very common	Vomiting
	Very common	Nausea
	Very common	Abdominal pain
	Common	Constipation
Nervous system disorders	Very common	Alopecia (reversible)
	Very common	Mucosal inflammation
	Very common	Pyrexia
	Very common	Asthenia
Gastrointestinal disorders	Common	Blood creatinine increased
	Common	Transaminases (SGPT and SGOT) increased
	Common	Bilirubin increased
	Common	Blood alkaline phosphatase increased

Description of selected adverse reactions (monotherapy)

Severe diarrhoea was observed in 20% of patients who follow recommendations for the management of diarrhoea. Of the evaluable cycles, 14% have severe diarrhoea. The median time of onset of the first liquid stool was on day 5 after the infusion of irinotecan.

Nausea and vomiting were severe in approximately 10% of patients treated with anti- emetics.

Constipation has been observed in less than 10% of patients.

Neutropenia was observed in 78.7% of patients and was severe (neutrophil count < 500 cells/ mm3) in 22.6% of patients. Of the evaluable cycles, 18 % had a neutrophil count below 1,000 cells/mm³ including 7.6% with a neutrophil count < 500 cells/mm³.

Total recovery was usually reached by day 22.

Fever with severe neutropenia was reported in 6.2% of patients and in 1.7% of cycles.

Infectious episodes occurred in about 10.3% of patients (2.5% of cycles) and were associated with severe neutropenia in about 5.3% of patients (1.1% of cycles), and resulted in death in 2 cases.

Anaemia was reported in about 58.7% of patients (8% with haemoglobin < 8 g/dl and 0.9% with haemoglobin < 6.5 g/dl).

Thrombocytopenia (< 100,000 cells/mm³) was observed in 7.4 % of patients and 1.8% of cycles with 0.9% with platelets count ≤ 50,000 cells/mm3 and 0.2% of cycles.

Nearly all the patients showed a recovery by day 22.

Acute cholinergic syndrome

Severe transient acute cholinergic syndrome was observed in 9 % of patients treated in mono- therapy.

Asthenia was severe in less than 10 % of patients treated in monotherapy. The causal re- lationship to irinotecan has not been clearly established. Fever in the absence of infection and without concomitant severe neutropenia, occurred in 12 % of patients treated in monotherapy.

Laboratory tests

Transient and mild to moderate increases in serum levels of either transaminases, alkaline phos- phatase or bilirubin were observed in 9.2 %, 8.1 % and 1.8 % of the patients, respectively, in the absence of progressive liver metastasis.

Transient and mild to moderate increases of serum levels of creatinine have been observed in 7.3 % of the patients.

COMBINATION THERAPY

Adverse reactions detailed in this section refer to irinotecan. There is no evidence that the safety profile of irinotecan is influenced by cetuximab or vice versa. In combination with cetuximab, additional reported adverse reactions were those expected with

cetuximab (such as acneform rash 88%). For information on adverse reactions on irinotecan in combination with cetuximab, also refer to their respective summary of product characteristics.

Adverse drug reactions reported in patients treated with capecitabine in combination with irinotecan in addition to those seen with capecitabine monotherapy or seen at a higher frequency grouping compared to capecitabine monotherapy include: *Very common, all grade adverse drug reactions:* thrombosis/embolism; *Common, all grade adverse drug reactions:* hypersensitivity reaction, cardiac ischemia/infarction; *Common, grade 3 and grade 4 adverse drug reactions:* febrile neutropenia. For complete information on adverse reactions of capecitabine, refer to the capecitabine summary product of characteristics.

Grade 3 and Grade 4 adverse drug reactions reported in patients treated with capecitabine in combination with irinotecan and bevacizumab in addition to those seen with capecitabine monotherapy or seen at a higher frequency grouping compared to capecitabine monotherapy in- clude: *Common, grade 3 and grade 4 adverse drug reactions:* neutropenia, thrombosis/embolism, hypertension, and cardiac ischemia/infarction. For complete information on adverse reactions of capecitabine and bevacizumab, refer to the respective capecitabine and bevacizumab summary of product characteristics.

Grade 3 hypertension was the principal significant risk involved with the addition of bevacizumab to bolus irinotecan/5-FU/FA. In addition, there was a small increase in the grade 3/4 chemotherapy adverse events of diarrhoea and leukopenia with this regimen compared to patients receiving bolus irinotecan/5-FU/FA alone. For other information on adverse reactions in combination with bevacizumab, refer to the bevacizumab summary of product characteristics.

Irinotecan has been studied in combination with 5-FU and FA for metastatic colorectal cancer.

Safety data of adverse reactions from clinical studies demonstrate very commonly observed NCI Grade 3 or 4 possibly or probably-related adverse events in the blood and the lymphatic system disorders, gastrointestinal disorders, and skin and subcutaneous tissue disorders MedDRA System Organ Classes.

The following adverse reactions considered to be possibly or probably related to the adminis- tration of irinotecan have been reported from 145 patients treated by irinotecan in combination therapy with 5FU/FA in every 2 weeks schedule at the recommended dose of 180 mg/m².

Adverse Reactions Reported with irinotecan in Combination Therapy (180 mg/m² every 2 weeks schedule)		
MedDRA System Organ Class	Frequency Category	Preferred Term
Infections and infestations	Common	Infection
	Very common	Thrombocytopenia
	Very common	Neutropenia
	Very common	Anaemia
Blood and lymphatic system disorders	Common	Febrile neutropenia
	Very common	Decreased appetite
	Very common	Cholinergic syndrome
	Very common	Diarrhoea
Metabolism and nutrition disorders	Very common	Vomiting
	Very common	Nausea
	Common	Abdominal pain
	Common	Constipation
Nervous system disorders	Very common	Alopecia (reversible)
	Very common	Mucosal inflammation
	Very common	Pyrexia
	Very common	Asthenia
Gastrointestinal disorders	Common	Blood creatinine increased
	Common	Transaminases (SGPT and SGOT) increased
	Common	Bilirubin increased
	Common	Blood alkaline phosphatase increased

Description of selected adverse reactions (combination therapy)

Severe diarrhoea was observed in 13.1 % of patients who follow recommendations for the management of diarrhoea. Of the evaluable cycles, 3.9 % have a severe diarrhoea.

A lower incidence of severe **nausea and vomiting** was observed (2.1 % and 2.8 % of patients respectively).

Constipation relative to irinotecan and/or loperamide has been observed in 3.4 % of patients.

Neutropenia was observed in 82.5% of patients and was severe (neutrophil count < 500 cells/ mm3) in 9.8% of patients. Of the evaluable cycles, 67.3% had a neutrophil count below 1,000 cells/mm³ including 2.7% with a neutrophil count < 500 cells/mm³. Total recovery was usually reached within 7-8 days.

Fever with severe neutropenia was reported in 3.4% of patients and in 0.9% of cycles. Infectious episodes occurred in about 2% of patients (0.5% of cycles) and were associated with severe neutropenia in about 2.1% of patients (0.5% of cycles), and resulted in death in 1 case.

Anaemia was reported in 97.2% of patients (2.1% with haemoglobin < 8 g/dl).

Thrombocytopenia (< 100,000 cells/mm³) was observed in 32.6% of patients and 21.8% of cycles. No severe thrombocytopenia (< 50,000 cells/mm³) has been observed.

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Gastrointestinal disorders	• Intestinal obstruction • Ileus: cases of ileus without preceding colitis have also been reported • Megacolon • Gastrointestinal haemorrhage • Colitis: In some cases, colitis was complicated by ulceration, bleeding, ileus, or infection. • Typhlitis • Ischemic colitis • Ulcerative colitis • Gastrointestinal bleeding • Symptomatic or asymptomatic elevated pancreatic enzymes • Intestinal perforation
	• Hepatic steatosis • Steatohepatitis
Skin and subcutaneous tissue disorders	• Skin reactions
General disorders and ad- ministration site conditions	• Infusion site reactions
Investigations	• Blood amylase increased • Lipase increased • Hypokalaemia • Hyponatraemia mostly related with diarrhoea and vomiting • Increases in serum levels of transaminases (i.e., AST and ALT) in the absence of progressive liver metastasis have been very rarely reported.
Musculoskeletal and con- nective tissue disorders	• Muscular contraction or cramps
Renal and urinary disorders	• Renal impairment and acute renal failure generally in patients who become infected and/or volume depleted from severe gastrointestinal toxicities.* • Renal insufficiency†
Vascular Disorders	• Hypotension†

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

a. e.g. Pneumocystis jirovecii pneumonia, bronchopulmonary aspergillosis, systemic candida.

b. e.g. Hepes zoster, influenza, hepatitis B reactivation, cytomegalovirus colitis.

Overdose and Treatment

There have been reports of over dosage at doses up to approximately twice the recommended therapeutic dose, which may be fatal. The most significant adverse reactions were severe neu- tropenia and severe diarrhoea. There is no known antidote for Irinotecan. Maximum supportive care should be instituted to prevent dehydration due to diarrhoea and to treat any infectious complications.

Caution

Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

Storage Condition:

Store at temperatures not exceeding 30°C.

Store in the original package in order to protect from light.

Packing Available

One vial of 5 mL contains 100 mg of Irinotecan hydrochloride trihydrate (100 mg/5 mL)

“For suspected adverse drug reaction, report to pr@biocarelifesciences.com”

Manufactured by:
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