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Before you contact this company: often several companies will market medicines with the same active ingredient. Please check that this is the correct company before contacting them. **Why?**

Summary of Product Characteristics last updated on the eMC: 24/08/2011

SPC Fluorouracil 50 mg/ml Injection

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Legal Categories

POM – Prescription Only Medicine

Active Ingredients/Generics

fluorouracil

1. NAME OF THE MEDICINAL PRODUCT

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Fluorouracil 50mg/ml Injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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Each 1 ml contains 50 mg of fluorouracil.

Presentations:	250 mg/5 ml	500 mg/10 ml	1 g120 ml	2.5 g/50 ml	5g/100ml
Amount fluorouracil present (as sodium salt) per vial	250 mg	500 mg	1 g	2.5 g	5 g

For excipients see 6.1

3. PHARMACEUTICAL FORM

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Solution for injection.

Clear, colourless or slightly yellow solution.

4. CLINICAL PARTICULARS

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4.1 Therapeutic indications

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Fluorouracil may be used alone, or in combination for its palliative action in the management of common malignancies particularly cancer of the colon and breast, either as a single agent or in combination with other cytotoxic agents.

4.2 Posology and method of administration Go to top of the page

Selection of an appropriate dose and treatment regime will depend upon the condition of the patient, the type of carcinoma being treated and whether Fluorouracil is to be administered alone or in combination with other therapy. Initial treatment should be given in hospital and the total daily dose should not exceed 1 gram. It is customary to calculate the dose in accordance with patient's actual weight unless there is obesity, oedema or some other form of abnormal fluid retention such as ascites. In this case, ideal weight should be used as the basis for the calculation. Reduction of the dose is advisable in patients with any of the following:

1) Cachexia

2) Major surgery within preceding 30 days

3) Reduced bone marrow function

4) Impaired hepatic or renal function

Fluorouracil injection can be given by intravenous injection or, intravenous or intra-arterial infusion.

Adult Dose

The following regimen have been recommended for use as a single agent:

Initial Treatment: This may be in the form of an infusion or an injection, the former usually being preferred because of lesser toxicity.

Intravenous infusion: 15mg/kg bodyweight but not more than 1g per infusion, diluted in 500ml of 5% glucose or 0.9% NaCl injection and given by intravenous infusion at a rate of 40 drops per minute over 4 hours. Alternatively the daily dose may be infused over 30 - 60 minutes or may be given as a continuous infusion over 24 hours. The infusion may be repeated daily until there is evidence of toxicity or a total dose of 12 - 15g has been reached.

Intravenous Injection: 12mg/kg bodyweight may be given daily for 3 days and then, if there is no evidence of toxicity, 6mg/kg on alternate days for 3 further doses. An alternative regimen is 15mg/kg as a single intravenous injection once a week throughout the course.

Intra-arterial Infusion: 5/7.5mg/kg may be given by 24 hour continuous intra-arterial infusion.

Maintenance Therapy: An initial intensive course may be followed by maintenance therapy providing there are no significant toxic effects. In all instances, toxic side effects must disappear before maintenance therapy is started.

The initial course of fluorouracil can be repeated after an interval of 4 to 6 weeks from the last dose or, alternatively, treatment can be continued with intravenous injections of 5-15mg/kg bodyweight at weekly intervals.

This sequence constitutes a course of therapy. Some patients have received up to 30g at a maximum rate of 1 g daily. A more recent alternative method is to give 15mg/kg IV once a week throughout the course of treatment. This obviates the need for an initial period of daily administration.

In combination with Irradiation: Irradiation combined with 5FU has been found to be useful in the treatment of certain types of metastatic lesions in the lungs and for the relief of pain caused by recurrent, inoperable growth. The standard dose of 5FU should be used.

Children

No recommendations are made regarding the use of Fluorouracil in children.

Elderly

Fluorouracil should be used in the elderly with similar considerations as with normal adult dosages.

4.3 Contraindications Go to top of the page

Fluorouracil is contraindicated in seriously debilitated patients or those with bone marrow depression after radiotherapy or treatment with other antineoplastic agents.

Fluorouracil is strictly contraindicated in pregnant or breast feeding women.

Flourouracil should not be used in the management of non-malignant disease.

4.4 Special warnings and precautions for use Go to top of the page

It is recommended that Fluorouracil be given only by, or under the strict supervision of, a qualified physician who is conversant with the use of potent antimetabolites.

All patients should be admitted to hospital for initial treatment.

Adequate treatment with Fluorouracil is usually followed by leucopenia, the lowest white blood cell (W.B.C) count commonly being observed between the 7th and 14th day of the first course, but occasionally being delayed for as long as 20 days. The count usually returns to normal by the 30th day. Daily monitoring of platelet and W.B.C count is recommended and treatment should be stopped if platelets fall below 100,000 per mm^3 or the W.B.C. count falls below 3,500 per mm^3. If the total count is less than 2000mm^3, and especially if there is granulocytopenia, it is recommended that the patient be placed in protective isolation in the hospital and treated with appropriate measures to prevent systemic infection.

Treatment should be stopped at the first sign of oral ulceration or if there is evidence of gastrointestinal side effects such as stomatitis, diarrhoea, bleeding from the G.I. tract of haemorrhage at any site. The ratio between effective and toxic dose is small and therapeutic response is unlikely without some degree of toxicity. Care must be taken therefore, in the selection of patients and adjustment of dosage.

Flourouracil should be used with caution in patients with reduced renal or liver function or jaundice. Isolated cases of angina, ECG abnormalities and rarely, myocardial infarction have been reported following administration of Fluorouracil. Care should be therefore be exercised in treating patients who experience chest pain during courses of treatment, or patients with a history of heart disease.

There have been reports of increased toxicity in patients who have reduced activity/deficiency of the enzyme

dihydropyrimidine dehydrogenase (DPD).

4.5 Interaction with other medicinal products and other forms of interaction Go to top of the page

Various agents have been reported to biochemically modulate the antitumour efficacy or toxicity of Fluorouracil, common drugs include Methotrexate, Metronidazole, Leucovorin as well as Allopurinol and Cimetidine which can affect the availability of the active drug.

Marked elevations of prothrombin time and INR have been reported in a few patients stabilised on warfarin therapy following initiation of fluorouracil regimes.

A clinically significant interaction between the antiviral sorivudine and fluorouracil prodrugs, resulting from inhibition of dihydropyrimidine dehydrogenase by sorivudine or chemically related analogues. Caution should be taken when using fluorouracil in conjunction with medications which may affect dihydropyrimidine dehydrogenase activity.

4.6 Pregnancy and lactation Go to top of the page

Flourouracil is strictly contraindicated in pregnant and breast feeding women.

4.7 Effects on ability to drive and use machines Go to top of the page

Not applicable.

4.8 Undesirable effects Go to top of the page

Diarrhoea, nausea and vomiting are observed quite commonly during therapy and may be treated symptomatically. An anti-emetic may be given for nausea and vomiting.

Alopecia may be seen in a substantial number of cases, particularly females, but is reversible. Other side effects include dermatitis, pigmentation, changes in nails, ataxia and fever.

There have been reports of chest pain, tachycardia, breathlessness and E.C.G. changes after administration of Fluorouracil. Special attention is advisable in treating patients with a history of heart disease or those who develop chest pain during treatment.

Leucopenia is common and the precautions described above should be followed.

Systemic fluorouracil treatment has been associated with various types of ocular toxicity. Peripheral neuropathy may occur.

A transient reversible cerebellar syndrome has been reported following fluorouracil treatment. Rarely, a reversible confusional state may occur. Cases of leucoencephalopathy have also been reported.

Additionally several other reports have been noted including:

Incidences of excessive lacrimation dacryostenosis, visual changes and photophobia.

Palmar-Plantar Erythrodysesthesia Syndrome has been reported as an unusual complication of high dose bolus or protracted continuous therapy for 5-fluorouracil.

Thrombophlebitis / Vein Tracking.

4.9 Overdose Go to top of the page

The symptoms and signs of overdosage are qualitatively similar to the adverse reactions and should be managed as indicated under "Other Undesirable Effects" and "Special Warnings and Precautions".

5. PHARMACOLOGICAL PROPERTIES Go to top of the page

5.1 Pharmacodynamic properties Go to top of the page

Fluorouracil is an analogue of uracil, a component of ribonucleic acid. The drug is believed to function as an antimetabolite. After intracellular conversion to the active deoxynucleotide, it interferes with the synthesis of DNA by blocking the conversion of deoxyuridylic acid to thymidylic acid by the cellular enzyme thymidylate synthetase. Flourouracil may also interfere with RNA synthesis.

5.2 Pharmacokinetic properties Go to top of the page

After intravenous administration, Flourouracil is distributed through the body water and disappears from the blood within 3 hours. It is preferentially taken up by actively dividing tissues and tumours after conversion to its nucleotide. Fluorouracil ready enters the C.S.F and brain tissue.

Following IV administration, the plasma elimination half-life averages about 16 minutes and is dose dependant. Following a single intravenous dose of Fluorouracil approximately 15% of the dose is excreted unchanged in the urine within 6 hours; over 90% of this is excreted in the first hour. The remainder is mostly metabolised in the liver by the usual body mechanisms for uracil.

5.3 Preclinical safety data Go to top of the page

Preclinical information has not been included because the toxicity profile of fluorouracil has been established after many years of clinical use. Please refer to section 4.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

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Sodium Hydroxide

Water for Injections

6.2 Incompatibilities

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Fluorouracil is incompatible with Carboplatin, Cisplatin, Cytarabine, Diazepam, Doxorubicin, other Anthracyclines and possibly Methotrexate.

Formulated solutions are alkaline and it is recommended that admixture with acidic drugs or preparations should be avoided.

6.3 Shelf life

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Before use: 18 months for 2.5 g/50 ml and 1 g/20 ml Onco-Vial® presentation,

24 months for all other presentations.

In use: Chemical and physical in-use stability has been demonstrated for 5 days at 20-21°C.

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 2-8°C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

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Do not store above 25°C. Do not refrigerate or freeze. Keep container in the outer carton

The pH of fluorouracil injection is 8.9 and the drug has maximal stability over the pH range 8.6 to 9.0.

If a precipitate has formed as a result of exposure to low temperatures, redissolve by heating to 60°C accompanied by vigorous shaking. Allow to cool to body temperature prior to use.

The product should be discarded if it appears brown or dark yellow in solution.

6.5 Nature and contents of container

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Type 1 clear glass vial (CGV) with rubber closures

Type 1 clear Onco-Tain® with rubber closures

Type 1 glass, Onco•Vial® with rubber closures

CGV and Onco-Tain®:

250 mg/5 ml: Pack Size 5.

500 mg/10 ml: Pack Size 5.

1 g/20 ml: Pack Size 5

2.5 g/50 ml: Pack Size 10's

5 g/100 ml: Pack Size singles

Onco-Vial®:

500 mg/10 ml: Pack Size singles

1 g/20 ml: Pack Size singles

2.5 g/50 ml: Pack Size singles

6.6 Special precautions for disposal and other handling

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Cytotoxic Handling Guidelines

Should be administered only by or under the direct supervision of a qualified physician who is experienced in the use of cancer chemotherapeutic agents.

Fluorouracil Injection should only be prepared for administration by professionals who have been trained in the safe use of the preparation. Preparation should only be carried out in an aseptic cabinet or suite dedicated for the assembly of cytotoxics.

In the event of spillage, operators should put on gloves, face mask, eye protection and disposable apron and mop up the spilled material with a absorbent material kept in the area for that purpose. The area should then be cleaned and all contaminated material transferred to a cytotoxic spillage bag or bin and sealed for incineration.

Contamination

Fluorouracil is an irritant, contact with skin and mucous membranes should be avoided.

In the event of contact with the skin or eyes, the affected area should be washed with copious amounts of water or normal saline. A bland cream may be used to treat the transient stinging of the skin. Medical advice should be sought if the eyes are affected or if the preparation is inhaled or ingested.

Please refer to company for COSHH hazard datasheets.

Preparation Guidelines

a) Chemotherapeutic agents should be prepared for administration only by professionals who have been trained in the safe use of the preparation.

b) Operations such as reconstitution of powder and transfer to syringes should be carried out only under aseptic conditions in a suite or cabinet dedicated for the assembly of cytotoxics.

c) The personnel carrying out these procedures should be adequately protected with clothing, gloves and eye shield.

d) Pregnant personnel are advised not to handle chemotherapeutic agents.

Disposal

Syringes, Onco•Vials® and adaptors containing remaining solution, absorbent materials, and any other contaminated material should be placed in a thick plastic bag or other impervious container and incinerated at 700°C.

Diluents

Fluorouracil Injection may be diluted with Glucose 5% Injection or Sodium Chloride 0.9% Injection or Water for Injections immediately before parenteral use.

Directions for use of the Onco•Vial®

Onco•Vial® should be used with an appropriate Mayne administration device.

7. MARKETING AUTHORISATION HOLDER

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Hospira UK Limited

Queensway

Royal Leamington Spa

Warwick,

CV31 3RW

8. MARKETING AUTHORISATION NUMBER(S)

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PL 04515/0088

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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19 July 2004

10. DATE OF REVISION OF THE TEXT

Go to top of the page

12 August 2011

More information about this product

- Patient Information Leaflets (PILs):
  Fluorouracil 50 mg/ml Injection

Link to this document from your website: http://www.medicines.org.uk/emc/medicine/636/SPC/

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