**Fluorouracil**

**Generic name:** Fluorouracil

**Brand name:** NECIL®

**Dosage form:** Solution for injection 50 mg/ml (250, 500 & 1000 mg)

**Drug class:** Pyrimidine antagonist; antimetabolite; antineoplastic agent.

**Indications:**

* in the treatment of metastatic colorectal cancer
* as adjuvant treatment in colon and rectal cancer
* in the treatment of advanced gastric cancer,
* in the treatment of advanced pancreatic cancer,
* in the treatment of advanced oesophageal cancer,
* in the treatment of advanced or metastatic breast cancer,
* as adjuvant treatment in patients with operable primary invasive breast cancer,
* in the treatment of inoperable locally advanced squamous cell carcinoma of the head and neck in previously untreated patients
* in the treatment of locally recurrent or metastatic squamous cell carcinoma of the head and neck.

**Contraindications**

NECIL® should not be prescribed for patients with the following conditions:

* In patients with a known hypersensitivity or allergy to Fluorouracil or any of the other ingredients of NECIL®.
* Pregnancy or breastfeeding.
* Dihydropyrimidine Dehydrogenase (DPD) deficiency
* Serious infections (e.g. Herpes zoster, chickenpox).
* Seriously debilitated patients.
* Bone marrow depression after radiotherapy or treatment with other antineoplastic agents.
* Management of non-malignant disease
* Serious liver impairment
* • Fluorouracil (5-FU) must not be given to patients homozygotic for dihydropyrimidine dehydrogenase (DPD).

**Mechanism of action**

5FU is converted to Fluorodeoxyuridine monophosphate (FdUMP), which forms a stable complex with thymidylate synthase (TS), and thus inhibits deoxythymidine mono-phosphate (dTMP) production. dTMP is essential for DNA replication and repair and its depletion therefore causes cytotoxicity. Dihydropyrimidine dehydrogenase (DPD)-mediated conversion of 5FU to dihydrofluorouracil (DHFU) is the rate-limiting step of 5-FU catabolism in normal and tumor cells.

**Warning and precautions**

* This medicine is prescribed for your current condition. So do not use it in similar cases or recommend it to others.
* Take this medicine according to the treatment plan prescribed by the doctor and with the strict observance of the hours and intervals mentioned.
* Discontinue the use of medication only with a doctor and avoid abstinence.
* Fluorouracil should not be given to patients who are allergic to Fluorouracil or any of the other ingredients of this product.
* This medication should only be prescribed by specialist physicians. The injection of this drug should be done at approved centers for the administration of oncological drugs.
* It should be treated with this drug in accordance with the instructions for use with cytotoxic drugs.
* This medicine may cause fatigue, dizziness, and changes in vision. Take caution when driving or doing things that require vigilance.
* Fluorouracil can harm an unborn baby or cause birth defects if the mother or the father is using this medicine.
* If you have blood disorders. Your doctor will check your blood before each treatment with NECIL®.
* If you get heart problems during treatment with NECIL®. Your doctor should check the functioning of your heart before starting the next treatment with NECIL®.
* If you get marked allergic reactions (e.g. shortness of breath, low blood pressure, facial swelling or rash)
* If you experience or have experienced persistent numbness or tingling or pain in hands or feet (peripheral neuropathy), a dose reduction of NECIL® may be necessary.
* If your liver function is severely impaired, using of NECIL® is not recommended.
* If you get diarrhea during or shortly after treatment with NECIL®; your colon could be inflamed (pseudomembranous colitis). Your doctor should be aware of this risk.
* If your lungs are irradiated concomitantly. You may develop pneumonia (interstitial pneumonitis)
* If you have any problems with your kidneys.
* If you have had high-dose pelvic radiation.
* If you know that you have a partial deficiency in the activity of the enzyme dihydropyrimidine dehydrogenase (DPD).
* If you have a family member who has partial or complete deficiency of the enzyme dihydropyrimidine dehydrogenase (DPD). It is recommended to test you for DPD deficiency before start of treatment.
* If you suffer from inflammation of the mucosa (mucositis); a dose reduction of NECIL® may be necessary.
* This medicine can produce adverse event on nervous system and visual changes which could interfere driving or the usage of heavy machinery.so, It is recommended not to drive or use machines immediately after a course of treatment. As in all cases, you should not drive a car or use machines if you feel dizzy or light-headed.
* You may be at risk of infection, so wash your hands often and try to avoid contact with people who have colds, flu or infections.
* NECIL® may have unsafe effects on the bone marrow. The bone marrow may not be able to make cells found in the blood as well as it used to for a few weeks. That is why it is necessary to do regular blood tests to continue your treatment. If your white blood cell count is too low, your doctor may stop the treatment so long as there is enough white blood cell count.
* Consult your doctor about all the medications you are taking. NECIL® may interact with other medications.
* Keep a list with you of all the medicines you use (including any prescription or nonprescription medicine, herbal preparation and vitamins) and show this list your doctor.
* Do not receive any kind of vaccination without your doctor’s approval while taking NECIL® and after the end of the treatment (at least for three months after completion of treatment).
* Avoid coming into contact with anyone who has recently received a live vaccine. If it is not possible, wear a mask and cover your nose and mouth.
* Talk with your doctor before using products that have aspirin, blood thinners, garlic, Ginseng, Ginkgo, Ibuprofen, pain killers, or vitamin E and similar products. These medications may increase the risk of bleeding with NECIL® concomitant use.
* Avoid alcohol drinks.
* Avoid smoking and tobacco.
* Talk with your doctor if you often use grapefruit or its juice in your diet.
* You may bleed more easily. Be careful and avoid injury.
* Be careful using sharp objects such as razors or nail clippers and during the brushing or dental flossing or toothpicks. Use a soft toothbrush and an electric razor.
* Avoid exercise in which there is a risk of injury or bruising.
* Consult with your doctor before you receive any dental care.
* Use birth control that you can trust to stop pregnancy while taking this medication.
* If you are a man and have sex, protect your partner from pregnancy. Use birth control that you can trust.
* During infusion do not touch your eyes or the inside of your nose and mouth. Wash your hands with soap after infusion session.

**How is Fluorouracil given?**

Fluorouracil is given as an infusion into a vein. A healthcare provider will give you this injection.

You may receive your first dose in a hospital or clinic setting to quickly treat any serious side effects.

Fluorouracil is often given in a treatment cycle, and you may need to use the medicine only on certain days of each cycle. Fluorouracil is sometimes given in a continuous infusion over 24 to 46 hours.

How often you need fluorouracil injections will depend on many factors, including side effects and how your body responds to the medicine. Your doctor will determine how long to treat you with this medicine.

Tell your caregivers if you feel any burning, [pain](https://www.drugs.com/cg/pain-management.html), or swelling around the IV needle when fluorouracil is injected.

Fluorouracil can increase your risk of bleeding or [infection](https://www.drugs.com/condition/infection-bacterial-fungal-protozoal-viral.html). You will need frequent medical tests. Your cancer treatments may be delayed based on the results of these tests.

Recommended posology:

*Colorectal cancer:*

5-fluorouracil is used in the treatment of colon and rectal cancers in a number of treatment regimens. 5-fluorouracil is preferably used along with folinic acid. Commonly used treatment regimens also combine 5-fluorouracil and folinic acid with other chemotherapeutic agents such as Irinotecan, Oxaliplatin or both Irinotecan and Oxaliplatin.

The commonly used dose range of 5-fluorouracil varies from 200-600mg/m2of body surface. The dose also varies depending administration as intravenous bolus or as continuous intravenous infusion.

The dose schedules also vary depending on the chemotherapy regimen, and 5-fluorouracil dose could be repeated weekly, bimonthly or monthly.

The number of cycles varies with the treatment regimens used and also depends on the clinical decision based on treatment success and tolerability.

*Breast cancer:*

5-fluorouracil is commonly used in chemotherapy regimens in combination with cyclophosphamide and methotrexate (CMF), or epirubicin, cyclophosphamide (FEC) or methotrexate and leucovorin (MFL). The usual dose range is 500- 600 mg/m2 body surface as an intravenous bolus and repeated every 3–4 weeks as necessary. In adjuvant treatment of primary invasive breast cancer, duration of treatment will usually continue for 6 cycles.

*Gastric cancer and cancer of gastroesophageal junction:*

Peri-operative chemotherapy with ECF regimen (epirubicin, cisplatin, 5-fluorouracil) is currently recommended. The recommended dose of 5-fluorouracil is 200 mg/m2body surface per day given as continuous intravenous infusion for 3 weeks. 6 cycles are recommended but this depends on treatment success and tolerability of medicinal product by the patient.

*Oesophageal cancer:*

5-fluorouracil is commonly used in combination with cisplatin; or cisplatin and epirubicin; or epirubicin and oxaliplatin. Dose varies between 200- 1000 mg/m2body surface per day as continuous intravenous infusion over several days and repeated cyclically depending upon regimen.

For cancers involving lower part of oesophagus, peri-operative chemotherapy with ECF regimen (epirubicin, cisplatin, 5-fluorouracil) is commonly recommended. The recommended dose of 5-fluorouracil is 200 mg/m2body surface per day given as continuous intravenous infusion for 3 weeks and repeated cyclically.

Concerning administration of 5-fluorouracil/cisplatin in combination with radiotherapy, please refer to the literature.

*Pancreatic cancer:*

5-fluorouracil is preferably used in combination with folinic acid or gemcitabine. Dose varies between 200- 500 mg/m2body surface per day as intravenous bolus injection or intravenous infusion, depending on the regimen and repeated cyclically.

*Head and neck cancer:*

5-fluorouracil is preferably used in combination with cisplatin or carboplatin. Dose varies between 600- 1200 mg/m2body surface per day as continuous intravenous infusion over several days and repeated cyclically depending upon regimen.

Concerning administration of 5-fluorouracil/ cisplatin or carboplatin in combination with radiotherapy, please refer to the literature.

**What should I avoid while receiving** **Fluorouracil?**

* Avoid being near people who are sick or have infections. Tell your doctor at once if you develop signs of infection.
* Avoid coming into contact with anyone who has recently received a live vaccine. If it is not possible, wear a mask and cover your nose and mouth.
* Avoid drive a car or use machines if you feel dizzy or light-headed.
* Avoid beer, wine, or mixed drinks.
* Avoid smoking and tobacco.
* You may bleed more easily. Be careful and avoid injury.
* Avoid exercise in which there is a risk of injury or bruising.

**Fluorouracil side effects**

Taking any medication may cause side effects. In some cases, patients do not experience any side effects or the side effects of the drug disappear after a short time of taking the drug. Talk to your doctor if you experience any side effects while taking this medicine.

Like all medicines, NECIL® can cause side effects, although not everybody gets them.

Get emergency medical help if you have signs of an allergic reaction including hives, difficult breathing, swelling of your face, lips, tongue, or throat.

Fluorouracil may cause serious side effects. Call your doctor at once if you have:

* Fever (take your temperature each day while receiving Fluorouracil)
* Severe or ongoing diarrhea
* Vision problems
* Confusion, problems with balance or muscle movement
* Painful mouth sores, red or swollen gums, trouble swallowing, talking, or eating
* Bone marrow suppression. dizziness, pale lips or fingernail beds, fast heart rate, getting easily tired or short of breath
* "Hand and foot syndrome”, pain, blisters, bleeding, or severe rash on the palms of your hands or the soles of your feet
* Heart problems. Chest pain or pressure, pain spreading to your jaw or shoulder, irregular heartbeats, nausea, sweating, feeling dizzy or short of breath.

**Common side effects of fluorouracil may include:**

* diarrhea
* mouth sores
* heart problems
* Bone marrow suppression.

Along with its needed effects, fluorouracil may cause some unwanted effects. Although not all of these side effects may occur, if they do occur they may need medical attention.

Also, because of the way these medicines act on the body, there is a chance that they might cause other unwanted effects that may not occur until months or years after the medicine is used. These delayed effects may include certain types of cancer, such as [leukemia](https://www.drugs.com/health-guide/leukemia.html). Discuss these possible effects with your doctor.

**Check with your doctor immediately** if any of the following side effects occur while taking Fluorouracil:

**More common**

* [Diarrhea](https://www.drugs.com/cg/acute-diarrhea.html)
* [heartburn](https://www.drugs.com/cg/gerd-gastroesophageal-reflux-disease.html)
* sores in mouth and on lips

**Less common**

* Black, tarry stools
* Cough or hoarseness, accompanied by [fever](https://www.drugs.com/cg/fever-in-adults.html) or chills
* Fever or chills
* Lower back or side [pain](https://www.drugs.com/cg/pain-management.html), accompanied by fever or chills
* [Nausea and vomiting](https://www.drugs.com/mcs/nausea-and-vomiting) (severe)
* Painful or difficult urination, accompanied by fever or chills
* Stomach cramps

**Rare**

* Blood in urine or stools
* pinpoint red spots on skin
* unusual bleeding or bruising

Check with your doctor as soon as possible if any of the following side effects occur while taking Fluorouracil:

**Rare**

* Chest pain
* Cough
* Shortness of breath
* Tingling of hands and feet, followed by pain, redness, and swelling
* Trouble with balance

**Drug Interactions**

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. Interaction means that different medicines may influence each other.

* Methotrexate (an anti-cancer medicine)
* Metronidazole (an antibiotic)
* Calcium leucovorin (also called calcium folinate - used to reduce the harmful effects of anti-cancer medicines)
* Allopurinol (used to treat gout)
* Cimetidine (used to treat stomach ulcers)
* Warfarin (used to treat blood clots)
* Interferon alpha 2a; brivudin, sorivudin and analogues (an antiviral)
* Cisplatin (an anticancer medicine)
* Phenytoin (used to control epilepsy/fits and irregular heart rhythm)
* Vaccines
* Vinorelbine (an anti-cancer medicine)
* Cyclophosphamide (an anti-cancer medicine)
* Levamisol (medicine used to treat worm infection)
* Tamoxifen (an anti-cancer medicine), These medicines affect the effect of NECIL®.

Keep a list with you of all the medicines you use (including any prescription or nonprescription medicine, herbal preparation and vitamins) and show this list your doctor.

**Fluorouracil use while Pregnancy and Breastfeeding**

Pregnancy: Category D

Pregnancy during or directly following chemotherapy is strongly discouraged and you should take precautions to avoid pregnancy. Female and male patients of fertile age, or their partners, should use contraceptives for at least 6 months after treatment with Fluorouracil. If pregnancy occurs, inform your doctor immediately. You must not breast-feed your baby when you are treated with NECIL®. Do not restart breast-feeding, unless your doctor has allowed you to.

**Storage conditions**

* Store the medicine at temperatures below 30° C and stored away from light and moisture.
* Keep the medicine out of the reach of children.
* Single use only. Discard any unused portion.
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* Shelf Life after dilution: Chemical and physical in-use stability has been demonstrated for 24 hours at 25°C with Glucose 5% or Sodium Chloride 0.9% Injection or Water for Injections at concentration 0.98 mg/ml of Fluorouracil.
* 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.
* The product should be discarded if it appears brown or dark yellow in solution.