Fluorouracil IV (5-FU, Adrucil)

DRUG TYPE
- A pyrimidine antagonist
- Classified as an antimetabolite antineoplastic agent

Indications
- Colorectal cancer
- Gastric cancer
- Metastatic breast carcinoma
- Metastatic colorectal cancer
- Pancreatic carcinoma
- Fluorouracil is also used when surgery or irradiation is not feasible for the palliative treatment of the following carcinomas
  - Breast
  - Stomach
  - Pancreas
  - Colon
  - Rectum

Unlabeled uses
- Biliary tract malignancy
- Carcinoid syndrome
- Localized malignant tumor of anus
- Locally advanced breast carcinoma
- Malignant esophagus neoplasm
- Malignant tumor of cervix
- Malignant tumor of head and neck
- Malignant tumor of urinary bladder
- Metastatic malignant tumor of anus
- Combination therapies for colorectal cancer
  - Fluorouracil is designated an orphan drug by the FDA for use in combination with leucovorin for the treatment of metastatic adenocarcinoma of the colon and rectum.

Mechanism of action
- Main mechanism thought to be the binding of deoxyribonucleotide of the drug (FdUMP) and the folate cofactor, N5–10-methylenetetrahydrofolate, to thymidylate synthase (TS) to form a covalently bound ternary complex, which inhibits the formation of thymidylate from uracil
  - Interferes with DNA synthesis
- Also, fluorouracil triphosphate (FUTP) can be incorporated into RNA in place of uridine triphosphate (UTP), producing a fraudulent RNA
  - Interferes with RNA processing and protein synthesis

Dosage and administration
- Fluorouracil is administered intravenously.
- Care should be taken to avoid extravasation of the drug.
- Adult dose
  - Minimum: 346.0 mg/1.73 m^2
  - Maximum: 865.0 mg/1.73 m^2
- Pediatric dose
  - Minimum: 346.0 mg/1.73 m^2
  - Maximum: 865.0 mg/1.73 m^2

Pregnancy and lactation
- Pregnancy category D
  - Fluorouracil may cause fetal harm when administered to a pregnant woman.
- Lactation
  - Absolute contraindication

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Cautions and adverse effects

- Toxicity depends on route and duration of treatment
- Adverse effects
  - Most frequent:
    - Dermatologic: Allergic dermatitis, palmar-plantar erythrodysesthesia syndrome (hand-foot syndrome), pruritus of skin, skin rash
    - Heme: Infection, leukopenia
    - Gastroinestinal: Anorexia, aphthous stomatitis, diarrhea, heartburn, nausea, vomiting
    - Others: Allergic reactions, alopecia, fatigue, general weakness
  - Less frequent:
    - Dry skin
    - Gastrointestinal ulcer
    - Thrombocytopenic disorder
  - Rare:
    - CNS: Acute cerebellar syndrome, ataxia, euphoria, headache disorder, impaired cognition, nystagmus
    - Others: Myocardial ischemia, pulmonary disease, sensation disturbance of limbs

Drug interactions

- Severe interaction:
  - Fluorouracil/metronidazole
  - Tinidazole capecitabine
  - Fluorouracil/selected anticoagulants
  - Live vaccines
  - Natalizumab
- Moderate interaction:
  - Fluorouracil and fluorouracil prodrugs/hydantoins

What to tell your patient

- You have been prescribed fluorouracil, which is an anti-cancer (antineoplastic or cytotoxic) chemotherapy drug. This medication is classified as an antimetabolite. Antimetabolites are very similar to normal substances within the cell. When the cells incorporate these substances into the cellular metabolism, they are unable to divide.
- Fluorouracil is given through a vein (intravenously or IV) as an infusion.
- The amount of fluorouracil that you receive depends on many factors, including your height and weight, your general health or other health problems, and the type of cancer that you have. Your doctor will determine your dose and schedule.
- Remember that your doctor has prescribed this medication because he or she has judged that the benefit is greater than the risk of side effects.
- Most people do not experience all of the side effects listed.
- Side effects are often predictable in terms of their onset and duration.
- Side effects are almost always reversible and will go away after treatment is complete.
- There are many ways to help minimize or prevent side effects.
- Common side effects
  - Diarrhea
  - Nausea and possible occasional vomiting
  - Mouth sores
  - Poor appetite
  - Watery eyes, sensitivity to light (photophobia)
  - Taste changes, metallic taste in mouth during infusion
  - Discoloration along vein through which the medication is given
  - Low blood counts
    - WBCs, RBCs, and platelets may temporarily decrease, increasing risk for infection, anemia and/or bleeding.
- Less common side effects:
  - Dry, cracking, peeling skin
  - Darkening of the skin (hyperpigmentation), darkening of the skin where previous radiation treatment was given (radiation recall)
  - Hair thinning
  - Nail discoloration, loss of nails
    - Hand-foot syndrome (palmar-plantar erythrodysesthesia [PPE])
    - Skin rash, swelling, redness, pain and/or peeling of the skin on the palms of hands and soles of feet
    - Usually mild, starting 5-6 weeks after initiation of treatment
    - May require lowering medication dose
- Contact your health care provider immediately, day or night, if you should experience fever of 100.5°F (38°C) or higher or chills (possible signs of infection), or any of the following:
  - Nausea that interferes with your ability to eat and unrelieved with prescribed medication
  - Vomiting: more than 4-5 times in a 24-hour period
  - Diarrhea: 4-6 episodes in a 24-hour period
  - Extreme fatigue: unable to carry on self-care activities
  - Mouth sores/skin rash: painful redness, swelling, or ulcers

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  - Eye irritation
  - Inability to eat or drink for 24 hours or experience signs of dehydration (tiredness, thirst, dry mouth, dark and decreased amount of urine, or dizziness)
- Serious adverse reactions to fluorouracil are chest pain, ECG changes, and increases in cardiac enzymes (may indicate problems with the heart). These symptoms are very rare but increased for patients with a prior history of heart disease.
- This is not a complete list of side effects and others may occur. Call your nurse or doctor for medical advice about side effects.
- Precautions
  - Before starting this treatment, make sure you tell your doctor about any other medications you are taking, including prescription, over-the-counter (OTC), vitamins, herbal remedies, etc.
  - Do not receive any kind of immunization or vaccination without your doctor's approval while taking this medication
  - Inform your nurse or doctor if you are pregnant or may be pregnant prior to starting this treatment. It is classified as Pregnancy Category D, which means fluorouracil may be hazardous to the fetus.
  - For both men and women: Do not conceive a child (get pregnant) while taking fluorouracil. Barrier methods of contraception, such as condoms, are recommended. Discuss with your doctor when you may safely become pregnant or conceive a child after therapy.
  - Do not breast-feed while taking this medication. ■

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