

# FAVLYXA- fluorouracil injection, solution

## Avyxa Pharma, LLC

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### HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use FAVLYXA safely and effectively. See full prescribing information for FAVLYXA.

FAVLYXA™ (fluorouracil) injection, for intravenous use  
Initial U.S. Approval: 1962

#### **WARNING: SERIOUS ADVERSE REACTIONS OR DEATH IN PATIENTS WITH COMPLETE DPD DEFICIENCY**

- **Increased risk of serious adverse reactions or death in patients with complete DPD deficiency.**
- **Test patients for genetic variants of DPYD prior to initiating FAVLYXA unless immediate treatment is necessary. Avoid use of FAVLYXA in patients with certain homozygous or compound heterozygous DPYD variants that result in complete DPD deficiency. (5.1)**

#### **INDICATIONS AND USAGE**

FAVLYXA is a nucleoside metabolic inhibitor indicated for the treatment of patients with:

- Adenocarcinoma of the Colon and Rectum (1.1)
- Adenocarcinoma of the Breast (1.2)
- Gastric Adenocarcinoma (1.3)
- Pancreatic Adenocarcinoma (1.4)

#### **DOSAGE AND ADMINISTRATION**

- FAVLYXA is recommended for administration either as an intravenous bolus or as an intravenous infusion. (2.1)
- Adenocarcinoma of the Colon and Rectum
  - In combination with leucovorin or as a component of a multidrug chemotherapy regimen that includes leucovorin (infusional regimen): 400 mg/m<sup>2</sup> for one dose, followed by 2,400 mg/m<sup>2</sup> to 3,000 mg/m<sup>2</sup> over 46 hours on day 1 of each 2-week cycle or
  - In combination with leucovorin (bolus regimen): 500 mg/m<sup>2</sup> on days 1, 8, 15, 22, 29 and 36 of each 8-week cycle. (2.2)
- Adenocarcinoma of the Breast in combination with a cyclophosphamide-based multidrug regimen: 500 mg/m<sup>2</sup> or 600 mg/m<sup>2</sup> on days 1 and 8 of each 28-day cycle (bolus regimen). (2.2)
- Gastric Adenocarcinoma in combination with a platinum-containing multidrug regimen: 200 mg/m<sup>2</sup> to 1,000 mg/m<sup>2</sup> over 24 hours (infusional regimen). (2.2)
- Pancreatic Adenocarcinoma in combination with leucovorin or as a component of a multidrug chemotherapy regimen that includes leucovorin: 400 mg/m<sup>2</sup> on day 1, followed by 2,400 mg/m<sup>2</sup> over 46 hours every 2 weeks (infusional regimen). (2.2)
- Refer to Section 2.3 for dosage modifications due to adverse reactions.

#### **DOSAGE FORMS AND STRENGTHS**

Injection: 250 mg/10 mL (25 mg/mL) in a single-dose vial. (3)

#### **CONTRAINDICATIONS**

None. (4)

#### **WARNINGS AND PRECAUTIONS**

- **Cardiotoxicity:** FAVLYXA can cause cardiotoxicity, including angina, myocardial infarction/ischemia, arrhythmia, and heart failure. Withhold FAVLYXA for cardiac toxicity. (5.2)
- **Hyperammonemic Encephalopathy:** Altered mental status, confusion, disorientation, coma, or ataxia with elevated serum ammonia level can occur within 72 hours of initiation of FAVLYXA. Withhold FAVLYXA and initiate ammonia-lowering therapy. (5.3)
- **Neurologic Toxicity:** FAVLYXA can cause acute cerebellar syndrome, confusion, disorientation, ataxia, or visual disturbances. Withhold FAVLYXA for neurologic toxicity. (5.4)
- **Diarrhea:** FAVLYXA can cause severe diarrhea. Withhold FAVLYXA for severe diarrhea until resolved.

(5.5)

- Palmar-Plantar Erythrodysesthesia Syndrome: Based on severity, withhold FAVLYXA until resolved or decreased to Grade 1, then resume at a reduced dose. (5.6)
- Myelosuppression: FAVLYXA can cause severe and fatal myelosuppression. Withhold FAVLYXA until severe myelosuppression resolves, then resume at a reduced dose. (5.7)
- Mucositis: FAVLYXA can cause severe mucositis. Withhold FAVLYXA until resolved or decreased to Grade 1, then resume at a reduced dose. (5.8)
- Increased Risk of Bleeding with Concomitant Use of Warfarin: Concurrent administration with warfarin can result in clinically significant increases in coagulation parameters: Closely monitor INR and prothrombin time. (5.9)
- Embryofetal Toxicity: Can cause fetal harm. Advise females and males of reproductive potential of the potential risk to a fetus and to use effective contraception. (5.10, 8.1, 8.3)

-----**ADVERSE REACTIONS**-----

**To report SUSPECTED ADVERSE REACTIONS, contact Avyxa Pharma, LLC at 1-888-520-0954 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch). (6)**

-----**USE IN SPECIFIC POPULATIONS**-----

- Lactation: Advise not to breastfeed (8.2)
- Infertility: May impair fertility. (8.3)

**See 17 for PATIENT COUNSELING INFORMATION.**

**Revised: 2/2026**

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**FULL PRESCRIBING INFORMATION: CONTENTS\***

**1 INDICATIONS AND USAGE**

- 1.1 Adenocarcinoma of the Colon and Rectum
- 1.2 Adenocarcinoma of the Breast
- 1.3 Gastric Adenocarcinoma
- 1.4 Pancreatic Adenocarcinoma

**2 DOSAGE AND ADMINISTRATION**

- 2.1 Evaluation and Testing for DPD Deficiency Before Initiating FAVLYXA
- 2.2 Recommended Dosage
- 2.3 Dosage Modifications for Adverse Reactions
- 2.4 Preparation and Administration

**3 DOSAGE FORMS AND STRENGTHS**

**4 CONTRAINDICATIONS**

**5 WARNINGS AND PRECAUTIONS**

- 5.1 Serious Adverse Reactions or Death from Dihydropyrimidine Dehydrogenase (DPD) Deficiency
- 5.2 Cardiotoxicity
- 5.3 Hyperammonemic Encephalopathy
- 5.4 Neurologic Toxicity
- 5.5 Diarrhea
- 5.6 Palmar-Plantar Erythrodysesthesia (Hand-Foot Syndrome)
- 5.7 Myelosuppression
- 5.8 Mucositis
- 5.9 Increased Risk of Bleeding with Concomitant Use of Warfarin
- 5.10 Embryofetal Toxicity

**6 ADVERSE REACTIONS**

- 6.2 Postmarketing Experience

## **7 DRUG INTERACTIONS**

7.1 Effect of FAVLYXA on Other Drugs

## **8 USE IN SPECIFIC POPULATIONS**

8.1 Pregnancy

8.2 Lactation

8.3 Females and Males of Reproductive Potential

8.4 Pediatric Use

8.5 Geriatric Use

## **10 OVERDOSAGE**

## **11 DESCRIPTION**

## **12 CLINICAL PHARMACOLOGY**

12.1 Mechanism of Action

12.2 Pharmacodynamics

12.3 Pharmacokinetics

12.5 Pharmacogenomics

## **13 NONCLINICAL TOXICOLOGY**

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

## **15 REFERENCES**

## **16 HOW SUPPLIED/STORAGE AND HANDLING**

16.1 How Supplied

16.2 Storage

## **17 PATIENT COUNSELING INFORMATION**

\* Sections or subsections omitted from the full prescribing information are not listed.

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## **FULL PRESCRIBING INFORMATION**

### **WARNING: SERIOUS ADVERSE REACTIONS OR DEATH IN PATIENTS WITH COMPLETE DPD DEFICIENCY**

- Increased risk of serious adverse reactions or death in patients with complete DPD deficiency.
- Test patients for genetic variants of *DPYD* prior to initiating FAVLYXA unless immediate treatment is necessary. Avoid use of FAVLYXA in patients with certain homozygous or compound heterozygous *DPYD* variants that result in complete DPD deficiency [see *Warnings and Precautions (5.1)*].

## **1 INDICATIONS AND USAGE**

FAVLYXA is indicated for the treatment of patients with:

### **1.1 Adenocarcinoma of the Colon and Rectum**

### **1.2 Adenocarcinoma of the Breast**

### **1.3 Gastric Adenocarcinoma**

## 1.4 Pancreatic Adenocarcinoma

## 2 DOSAGE AND ADMINISTRATION

### 2.1 Evaluation and Testing for DPD Deficiency Before Initiating FAVLYXA

Prior to initiating FAVLYXA, test patients for genetic variants of the *DPYD* gene unless immediate treatment is necessary. An FDA-authorized test for the detection of the *DPYD* gene to identify patients at risk of serious adverse reactions with FAVLYXA is not currently available. Currently available tests used to identify *DPYD* variants may vary in accuracy and design (e.g., which *DPYD* variant(s) they identify).

Avoid use of FAVLYXA in patients known to have certain homozygous or compound heterozygous *DPYD* variants that result in complete DPD deficiency. No FAVLYXA dose has been proven safe for patients with complete DPD deficiency. For patients with partial DPD deficiency, individualize the dosage and modify based on tolerability and intent of treatment [see *Warnings and Precautions (5.1)*].

### 2.2 Recommended Dosage

FAVLYXA is recommended for administration either as an intravenous bolus or as an intravenous infusion. Dosage recommendations are in Table 1.

**Table 1: Recommended dosage of FAVLYXA**

<b>Indication</b>	<b>Recommended Dosage</b>	<b>Duration of Treatment</b>
<b>Adenocarcinoma of the Colon and Rectum</b>		
<i>In combination with leucovorin or as a component of a multidrug chemotherapy regimen that includes leucovorin</i>	400 mg/m <sup>2</sup> for one dose, followed by 2,400 mg/m <sup>2</sup> to 3,000 mg/m <sup>2</sup> over 46 hours on day 1 of each 2-week cycle	Until disease progression or unacceptable toxicity.
<i>In combination with leucovorin alone (bolus regimen)</i>	500 mg/m <sup>2</sup> on days 1, 8, 15, 22, 29 and 36 of each 8-week cycle	Until disease progression or unacceptable toxicity.
<b>Adenocarcinoma of the Breast</b>		
<i>In combination with cyclophosphamide-based multidrug regimen (bolus regimen)</i>	500 mg/m <sup>2</sup> or 600 mg/m <sup>2</sup> on days 1 and 8 of each 28-day cycle	Until disease progression or unacceptable toxicity or 6 cycles
<b>Gastric Adenocarcinoma</b>		
<i>In combination with a platinum-containing multidrug regimen</i>	200 mg/m <sup>2</sup> to 1,000 mg/m <sup>2</sup> over 24 hours	Frequency in each cycle and length of each cycle depend on dose of FAVLYXA and specific regimen
<b>Pancreatic Adenocarcinoma</b>		
<i>In combination with leucovorin or as a component</i>	400 mg/m <sup>2</sup> on day 1,	

leucovorin or as a component of a multidrug chemotherapy regimen that includes leucovorin followed by 2,400 mg/m<sup>2</sup> over 46 hours every 2 weeks Until disease progression or unacceptable toxicity.

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### 2.3 Dosage Modifications for Adverse Reactions

Withhold FAVLYXA for the following adverse reactions. Depending on the severity of the adverse reaction, either discontinue or resume FAVLYXA at a reduced dosage upon resolution or improvement to Grade 1:

- Grade 3 or 4 diarrhea [see *Warnings and Precautions (5.5)*]
- Grade 2 or 3 palmar-plantar erythrodysesthesia (hand-foot syndrome) [see *Warnings and Precautions (5.6)*]
- Grade 3 or 4 mucositis [see *Warnings and Precautions (5.8)*]
- Grade 4 myelosuppression [see *Warnings and Precautions (5.7)*]

There is no recommended dose for resumption of FAVLYXA administration following development of any of the following adverse reactions; consider permanent discontinuation of FAVLYXA following:

- Development of angina, myocardial infarction/ischemia, arrhythmia, or heart failure in patients with no history of coronary artery disease or myocardial dysfunction [see *Warnings and Precautions (5.2)*]
- Hyperammonemic encephalopathy [see *Warnings and Precautions (5.3)*]
- Neurologic toxicity including acute cerebellar syndrome [see *Warnings and Precautions (5.4)*]

### 2.4 Preparation and Administration

FAVLYXA is a hazardous drug. Follow applicable special handling and disposal procedures<sup>1</sup>.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

#### **For Direct Intravenous Bolus Injection**

##### Preparation

- Select the appropriate number of vial(s) based on the prescribed dose.
- Withdraw the calculated dose into a sterile syringe.
- Discard partially used or empty vials of FAVLYXA.

##### Administration

- Administer FAVLYXA as an intravenous bolus through an established intravenous line over 2 to 5 minutes.
- Do not administer in the same intravenous line concomitantly with other medicinal products.

##### Storage

- If the dose is not administered, attach a tip cap to the syringe prior to storage. The syringe can be stored at room temperature 20°C to 25°C (68°F to 77°F) for up to 4 hours.

## **For Intravenous Infusion**

### Preparation

- Select the appropriate number of vial(s) based on the prescribed dose.
- Withdraw the calculated dose into a sterile syringe.
- Dilute the calculated dose in an appropriate amount of 0.9% Sodium Chloride Injection, or 5% Dextrose Injection, to prepare an infusion solution with a final concentration ranging from 1.5 mg/mL to 10 mg/mL.

### Administration

- Do not administer in the same intravenous line concomitantly with other medicinal products.
- For intravenous infusion regimens, administer through a central venous line using an infusion pump.

### Storage

- If not used immediately, the diluted FAVLYXA can be stored at room temperature 20°C to 25°C (68°F to 77°F) for up to 24 hours.

## **3 DOSAGE FORMS AND STRENGTHS**

Injection: FAVLYXA contains 250 mg/10 mL (25 mg/mL) fluorouracil as colorless to light yellow clear solution in a single-dose vial.

## **4 CONTRAINDICATIONS**

None.

## **5 WARNINGS AND PRECAUTIONS**

### **5.1 Serious Adverse Reactions or Death from Dihydropyrimidine Dehydrogenase (DPD) Deficiency**

Patients with certain homozygous or compound heterozygous variants in the *DPYD* gene known to result in complete or near complete absence of DPD activity (complete DPD deficiency) are at increased risk for acute early-onset toxicity and serious, including fatal adverse reactions due to FAVLYXA (e.g., mucositis, diarrhea, neutropenia, and neurotoxicity). Patients with partial DPD activity (partial DPD deficiency) may also have increased risk of serious or fatal adverse reactions.

Prior to initiating FAVLYXA, test patients for genetic variants of the *DPYD* gene unless immediate treatment is necessary [see *Clinical Pharmacology (12.5)*]. Serious adverse reactions may still occur even if no *DPYD* variants are identified.

Avoid use of FAVLYXA in patients with certain homozygous or compound heterozygous *DPYD* variants that result in complete DPD deficiency.

Withhold or permanently discontinue FAVLYXA based on clinical assessment of the onset, duration, and severity of adverse events in patients with evidence of acute early-onset or unusually severe reactions. No fluorouracil dose has been proven safe for patients with complete DPD deficiency. For patients with partial DPD deficiency,

individualize the dosage and modify based on tolerability and intent of treatment.

An FDA-authorized test for the detection of genetic variants of the *DPYD* gene to identify patients at risk of serious adverse reactions with FAVLYXA treatment is not currently available. Currently available tests used to identify *DPYD* variants may vary in accuracy and design (e.g., which *DPYD* variant(s) they identify).

## **5.2 Cardiotoxicity**

FAVLYXA can cause cardiotoxicity, including angina, myocardial infarction/ischemia, arrhythmia, and heart failure, based on postmarketing reports. Reported risk factors for cardiotoxicity are administration by continuous infusion rather than intravenous bolus and presence of coronary artery disease. Withhold FAVLYXA for cardiotoxicity. The risks of resumption of FAVLYXA in patients with cardiotoxicity that has resolved have not been established [see *Dosage and Administration (2.3)*].

## **5.3 Hyperammonemic Encephalopathy**

FAVLYXA can cause hyperammonemic encephalopathy in the absence of liver disease or other identifiable cause, based on postmarketing reports. Signs or symptoms of hyperammonemic encephalopathy began within 72 hours after initiation of FAVLYXA infusion; these included altered mental status, confusion, disorientation, coma, or ataxia, in the presence of concomitant elevated serum ammonia level. Withhold FAVLYXA for hyperammonemic encephalopathy and initiate ammonia-lowering therapy. The risks of resumption of FAVLYXA in patients with hyperammonemic encephalopathy that has resolved have not been established [see *Dosage and Administration (2.3)*].

## **5.4 Neurologic Toxicity**

FAVLYXA can cause neurologic toxicity, including acute cerebellar syndrome and other neurologic events, based on postmarketing reports. Neurologic symptoms included confusion, disorientation, ataxia, or visual disturbances. Withhold FAVLYXA for neurologic toxicity. There are insufficient data on the risks of resumption of FAVLYXA in patients with neurologic toxicity that has resolved [see *Dosage and Administration (2.3)*].

## **5.5 Diarrhea**

FAVLYXA can cause severe diarrhea. Withhold FAVLYXA for Grade 3 or 4 diarrhea until resolved or decreased in intensity to Grade 1, then resume FAVLYXA at a reduced dose. Administer fluids, electrolyte replacement, or antidiarrheal treatments as necessary [see *Dosage and Administration (2.3)*].

## **5.6 Palmar-Plantar Erythrodysesthesia (Hand-Foot Syndrome)**

FAVLYXA can cause palmar-plantar erythrodysesthesia, also known as hand-foot syndrome (HFS). Symptoms of HFS include a tingling sensation, pain, swelling, and erythema with tenderness, and desquamation. HFS occurs more commonly when fluorouracil is administered as a continuous infusion than when fluorouracil is administered as a bolus injection, and has been reported to occur more frequently in patients with previous exposure to chemotherapy. HFS is generally observed after 8 to 9 weeks of fluorouracil administration but may occur earlier. Institute supportive measures for symptomatic relief of HFS. Withhold FAVLYXA administration for Grade 2 or 3 HFS; resume FAVLYXA at a reduced dose when HFS is completely resolved or

decreased in severity to Grade 1 [see *Dosage and Administration (2.3)*].

## **5.7 Myelosuppression**

FAVLYXA can cause severe and fatal myelosuppression which may include neutropenia, thrombocytopenia, and anemia. The nadir in neutrophil counts commonly occurs between 9 and 14 days after fluorouracil administration. Obtain complete blood counts prior to each treatment cycle, weekly if administered on a weekly or similar schedule, and as needed. Withhold FAVLYXA until Grade 4 myelosuppression resolves; resume FAVLYXA at a reduced dose when myelosuppression has resolved or improved to Grade 1 in severity [see *Dosage and Administration (2.3)*].

## **5.8 Mucositis**

FAVLYXA can cause mucositis, stomatitis or esophagopharyngitis, which may lead to mucosal sloughing or ulceration.

The incidence is reported to be higher with administration of fluorouracil by intravenous bolus compared with administration by continuous infusion. Withhold FAVLYXA administration for Grade 3 or 4 mucositis; resume FAVLYXA at a reduced dose once mucositis has resolved or decreased in severity to Grade 1 [see *Dosage and Administration (2.3)*].

## **5.9 Increased Risk of Bleeding with Concomitant Use of Warfarin**

Altered coagulation parameters and/or bleeding, including death, have been reported during concomitant use of warfarin and fluorouracil. Monitor INR more frequently and adjust the dose of warfarin in patients receiving concomitant warfarin [see *Drug Interactions (7)*].

## **5.10 Embryofetal Toxicity**

Based on its mechanism of action and animal reproduction studies, FAVLYXA can cause fetal harm when administered during pregnancy [see *Use in Specific Populations (8.1)*, and *Clinical Pharmacology (12.1)*]. Advise females of reproductive potential to use effective contraception during treatment with FAVLYXA and for 6 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with FAVLYXA and for 3 months after the last dose [see *Use in Specific Populations (8.3)*].

## **6 ADVERSE REACTIONS**

The following adverse reactions are discussed in more detail in other sections of the labeling:

- Serious adverse reactions or death from Dihydropyrimidine Dehydrogenase (DPD) deficiency [see *Warnings and Precautions (5.1)*]
- Cardiotoxicity [see *Warnings and Precautions (5.2)*]
- Hyperammonemic encephalopathy [see *Warnings and Precautions (5.3)*]
- Neurologic toxicity [see *Warnings and Precautions (5.4)*]
- Diarrhea [see *Warnings and Precautions (5.5)*]
- Palmar-plantar erythrodysesthesia (hand-foot syndrome) [see *Warnings and Precautions (5.6)*]

- Myelosuppression [see Warnings and Precautions (5.7)]
- Mucositis [see Warnings and Precautions (5.8)]
- Increased risk of bleeding with concomitant use of warfarin [see Warnings and Precautions (5.9)]

## 6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of fluorouracil. 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.

*Hematologic:* pancytopenia [see Warnings and Precautions (5.7)]

*Gastrointestinal:* gastrointestinal ulceration, nausea, vomiting

*Allergic Reactions:* anaphylaxis and generalized allergic reactions

*Neurologic:* nystagmus, headache

*Dermatologic:* dry skin; fissuring; photosensitivity, as manifested by erythema or increased pigmentation of the skin; vein pigmentation

*Ophthalmic:* lacrimal duct stenosis, visual changes, lacrimation, photophobia

*Psychiatric:* euphoria

*Miscellaneous:* thrombophlebitis, epistaxis, nail changes (including loss of nails)

## 7 DRUG INTERACTIONS

### 7.1 Effect of FAVLYXA on Other Drugs

#### Vitamin K Antagonists

Monitor INR and PT more frequently in patients receiving FAVLYXA and warfarin. Elevated INR and PT have been reported in patients taking fluorouracil concomitantly with warfarin.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

#### Risk Summary

Based on mechanism of action and animal reproduction studies, FAVLYXA can cause fetal harm when administered during pregnancy [see *Clinical Pharmacology (12.1)*]. Available data from observational studies with intravenous administration of fluorouracil during pregnancy are insufficient to identify a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes.

Administration of fluorouracil to rats and mice during selected periods of organogenesis, at doses lower than a human dose of 12 mg/kg, caused embryoletality and teratogenicity. Malformations included cleft palate and skeletal defects. In monkeys, maternal doses of fluorouracil higher than an approximate human dose of 12 mg/kg

resulted in abortion (see *Data*).

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2–4% and 15–20%, respectively.

## Data

### *Animal Data*

Malformations including cleft palate, skeletal defects and deformed appendages (paws and tails) were observed when fluorouracil was administered by intraperitoneal injection to mice at doses at or above 10 mg/kg (approximately 0.06 times a human dose of 12 mg/kg on a mg/m<sup>2</sup> basis) for 4 days during the period of organogenesis. Similar results were observed in hamsters administered fluorouracil intramuscularly at doses lower than those administered in commonly used clinical treatment regimens. In rats, administration of fluorouracil by intraperitoneal injection at doses greater than 15 mg/kg (approximately 0.2 times a human dose of 12 mg/kg on a mg/m<sup>2</sup> basis) for a single day during organogenesis resulted in delays in growth and malformations including micro-anophthalmos. In monkeys, administration of fluorouracil during organogenesis at doses approximately equal to a human dose of 12 mg/kg on a mg/m<sup>2</sup> basis resulted in abortion; at a 50% lower dose, resorptions and decreased fetal body weights were reported.

## **8.2 Lactation**

### Risk Summary

There are no data on the presence of fluorouracil or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in the breastfed child, advise patients not to breastfeed during treatment with FAVLYXA and for 1 week after the last dose.

## **8.3 Females and Males of Reproductive Potential**

FAVLYXA can cause fetal harm when administered to a pregnant woman [*see Use in Specific Populations (8.1)*].

### Pregnancy Testing

Verify that females of reproductive potential are not pregnant prior to initiating FAVLYXA [*see Warnings and Precautions (5.10), Use in Specific Populations (8.1, 8.3)*].

### Contraception

#### *Females*

Advise females of reproductive potential to use effective contraception during treatment with FAVLYXA and for 6 months after the last dose.

#### *Males*

Based on genotoxicity findings, advise males with female partners of reproductive potential to use effective contraception during treatment with FAVLYXA and for 3 months after the last dose [*see Nonclinical Toxicology (13.1)*].

### Infertility

Based on animal studies, FAVLYXA may impair fertility in females and males of

reproductive potential [see *Nonclinical Toxicology (13.1)*].

## 8.4 Pediatric Use

The safety and effectiveness of FAVLYXA in pediatric patients have not been established.

## 8.5 Geriatric Use

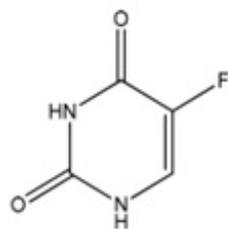
Reported clinical experience has not identified differences in safety or effectiveness between the elderly and younger patients.

## 10 OVERDOSAGE

Administer uridine triacetate within 96 hours following the end of FAVLYXA infusion for management of fluorouracil overdose.

## 11 DESCRIPTION

FAVLYXA injection contains fluorouracil, a nucleoside metabolic inhibitor. Fluorouracil, a fluorinated pyrimidine, has a chemical name of 5-fluoro-2,4 (1*H*,3*H*)-pyrimidinedione. Its structural formula is:



Molecular formula: C<sub>4</sub>H<sub>3</sub>FN<sub>2</sub>O<sub>2</sub>

Molecular weight: 130.08 g/mole

FAVLYXA injection 250 mg/10 mL is a sterile, colorless to light yellow clear solution available in single-dose vials for intravenous bolus or infusion administration. Each mL contains 25 mg fluorouracil in water for injection. Sodium hydroxide is added to adjust the pH to 8.6 to 9.4.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Fluorouracil is a nucleoside metabolic inhibitor that interferes with the synthesis of deoxyribonucleic acid (DNA) and to a lesser extent inhibits the formation of ribonucleic acid (RNA); these affect rapidly growing cells and may lead to cell death. Fluorouracil is converted to three main active metabolites: 5-fluoro-2'-deoxyuridine-5'-monophosphate (FdUMP), 5-fluorouridine-5'-triphosphate (FUTP) and 5-fluoro-2'-deoxyuridine-5'-triphosphate (FdUTP). These metabolites have several effects including the inhibition of thymidylate synthase by FdUMP, incorporation of FUTP into RNA and incorporation of FdUTP into DNA.

## 12.2 Pharmacodynamics

Fluorouracil exposure-response relationships and the time course of the pharmacodynamic response are unknown.

## 12.3 Pharmacokinetics

### *Distribution*

Following bolus intravenous injection, fluorouracil distributes throughout the body including the intestinal mucosa, bone marrow, liver, cerebrospinal fluid and brain tissue.

### *Elimination*

Following bolus intravenous injection, 5 to 20% of the parent drug is excreted unchanged in the urine in six hours. The remaining percentage of the administered dose is metabolized, primarily in the liver. The metabolites of fluorouracil (e.g., urea and  $\alpha$ -fluoro- $\beta$ -alanine) are excreted in the urine over 3 to 4 hours.

Following bolus intravenous injection of fluorouracil, as a single agent, the elimination half-life increased with dose from 8 to 20 minutes.

## 12.5 Pharmacogenomics

The *DPYD* gene encodes the enzyme DPD, which is responsible for the catabolism of >80% of fluorouracil. Approximately 3 to 5% of White populations have partial DPD deficiency and 0.2% of White populations have complete DPD deficiency, which may be due to certain genetic no function or decreased function variants in *DPYD* resulting in partial to complete or near complete absence of enzyme activity. DPD deficiency is estimated to be more prevalent in Black or African American populations compared to White populations. Insufficient information is available to estimate the prevalence of DPD deficiency in other populations.

Patients who are homozygous or compound heterozygous for no function *DPYD* variants (i.e., carry two *DPYD* variants that result in no DPD enzyme activity) or are compound heterozygous for a no function *DPYD* variant plus a decreased function *DPYD* variant have complete DPD deficiency and are at increased risk for acute early-onset of toxicity and serious life-threatening, or fatal adverse reactions due to increased systemic exposure to fluorouracil. Partial DPD deficiency can result from the presence of either two decreased function *DPYD* variants or one normal function plus either a decreased function or a no function *DPYD* variant. Patients with partial DPD deficiency may also be at an increased risk for toxicity from fluorouracil.

Several *DPYD* variants observed with variability across populations have been associated with reduced or no DPD activity, especially when present as homozygous or compound heterozygous variants. These include c.1905+1G>A (*DPYD* \*2A), c.1679T>G (*DPYD* \*13), c.2846A>T, and c.1129-5923C>G (Haplotype B3). *DPYD*\*2A and *DPYD*\*13 are no function variants, and c.2846A>T, c.1129-5923C>G, and c557A>G are decreased function variants. This is not a complete listing of all *DPYD* variants that may result in DPD deficiency [see *Warnings and Precautions* (5.1)].

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies have not been performed with fluorouracil. Fluorouracil was mutagenic *in vitro* in the bacterial reverse mutation (Ames) assay and induced chromosomal aberrations in hamster fibroblasts *in vitro* and in mouse bone marrow in the *in vivo* mouse micronucleus assay.

Administration of fluorouracil intraperitoneally to male rats at dose levels equal to or greater than 1.7-fold the human dose of 12 mg/kg induced chromosomal aberrations in spermatogonia and inhibition of spermatogonia differentiation resulting in transient infertility. In female rats, intraperitoneal administration of fluorouracil during the pre-ovulatory phases of oogenesis at dose levels equal to or greater than 0.33 times a human dose of 12 mg/kg resulted in decreased incidence of fertile matings, increased pre-implantation loss, and fetotoxicity.

## 15 REFERENCES

"OSHA Hazardous Drugs." *OSHA*.  
<http://www.osha.gov/SLTC/hazardousdrugs/index.html>

## 16 HOW SUPPLIED/STORAGE AND HANDLING

### 16.1 How Supplied

FAVLYXA™ Injection is a sterile colorless to light yellow clear solution available in single-dose vials individually packaged in a carton as follows:

NDC Number	Strength	Package
83831-143-01	250 mg/10 mL (25 mg/mL)	1 single-dose vial in 1 carton

### 16.2 Storage

Store at 20°C to 25°C (68°F to 77°F); excursions permitted from 15°C to 30°C (59°F to 86°F). [see USP Controlled Room Temperature]. Protect from light. Retain in carton until time of use.

Fluorouracil is a hazardous drug. Follow applicable special handling and disposable procedures [see *References (15)*].

## 17 PATIENT COUNSELING INFORMATION

Advise patients of the following:

### Serious Adverse Reactions or Death from Dihydropyrimidine Dehydrogenase (DPD) Deficiency

Prior to initiating FAVLYXA treatment, inform patients of the potential for serious or fatal adverse reactions due to DPD deficiency and testing for genetic variants of *DPYD*. Advise patients to immediately contact their healthcare provider if symptoms of severe mucositis, diarrhea, neutropenia, and neurotoxicity occur [see *Warnings and*

*Precautions (5.1) and Clinical Pharmacology (12.5)].*

### Cardiotoxicity

Advise patients of the risk of cardiotoxicity and to immediately contact their healthcare provider for new onset of chest pain, shortness of breath, dizziness, or lightheadedness [*see Warnings and Precautions (5.2)*].

### Hyperammonemic Encephalopathy and Neurologic Toxicity

Advise patients to immediately contact their healthcare provider or go to an emergency room for new onset of confusion, disorientation, or otherwise altered mental status; difficulty with balance or coordination; or visual disturbances [*see Warnings and Precautions (5.3, 5.4)*].

### Diarrhea

Inform patients experiencing grade 2 or higher diarrhea (an increase of 4 to 6 stools/day or nocturnal stools) or experiencing severe bloody diarrhea with severe abdominal pain and fever to immediately contact their health care provider. Advise patients on the use of antidiarrheal treatments (e.g., loperamide) to manage diarrhea [*see Warnings and Precautions (5.5)*].

### Palmar-Plantar Erythrodysesthesia Syndrome

Instruct patients experiencing grade 2 palmar-plantar erythrodysesthesia syndrome or greater to stop taking FAVLYXA immediately and to contact their healthcare provider. Inform patients that initiation of symptomatic treatment is recommended, and hand-and-foot syndrome can lead to loss of fingerprints which could impact personal identification [*see Warnings and Precautions (5.6)*].

### Myelosuppression

Inform patients who develop a fever of 100.5°F or greater or other evidence of potential infection to immediately contact their healthcare provider [*see Warnings and Precautions (5.7)*].

### Mucositis

Inform patients experiencing grade 2 stomatitis (painful erythema, edema or ulcers of the mouth or tongue, but able to eat) or greater to contact their healthcare provider [*see Adverse Reactions (5.8)*].

### Increased Risk of Bleeding with Concomitant Warfarin

Advise patients taking warfarin, that they are at an increased risk of severe bleeding while taking FAVLYXA. Advise these patients that INR should be monitored more frequently, and dosage modifications of warfarin may be required, while taking and after discontinuation of FAVLYXA. Advise these patients to immediately contact their healthcare provider if signs or symptoms of bleeding occur [*see Warnings and Precautions (5.9)*].

### Embryo-Fetal Toxicity

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to inform their healthcare provider of a known or suspected pregnancy [*see Warnings and Precautions (5.10), Use in Specific Populations (8.1)*].

Advise females of reproductive potential to use effective contraception during treatment with FAVLYXA and for 6 months after the last dose [see *Use in Specific Populations (8.3)*].

Advise males with female partners of reproductive potential to use effective contraception during treatment with FAVLYXA and for 3 months after the last dose [see *Use in Specific Populations (8.3)*].

#### Lactation

Advise females not to breastfeed during treatment with FAVLYXA and for 1 week after the last dose [see *Use in Specific Populations (8.2)*].

#### Infertility

Advise males and females of reproductive potential that FAVLYXA may impair fertility [see *Use in Specific Populations (8.3)*].

#### Drug interactions

Advise patients to notify their healthcare provider of all drugs they are taking, including warfarin or other coumarin-derivative anticoagulants. Advise patients of the importance of keeping appointments for blood tests [see *Warnings and Precautions (5.9), Drug Interactions (7.1)*].

#### **Rx Only**

#### **Manufactured for:**

Avyxa Pharma, LLC  
New Jersey 07054, USA

Made in China



Revised: 02/2026

#### **PACKAGE LABEL.PRINCIPAL DISPLAY PANEL**

**NDC 83831-143-01**

**FAVLYXA™**  
**(fluorouracil)**  
**Injection, USP**

**250 mg/10 mL**

(25 mg/mL)

**For Intravenous Use**

**WARNING: Hazardous Drug**

**One 10 mL Single-Dose Vial**

Rx Only

## Vial-Label

NDC 83831-143-01

**FAVLYXA™**  
(fluorouracil)  
Injection, USP

**250 mg/10 mL**  
(25 mg/mL)

**For Intravenous Use**

**WARNING: Hazardous Drug**

One 10 mL Single-Dose Vial

Rx Only

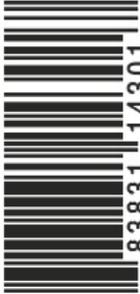
**Sterile**  
Each mL contains: 25 mg fluorouracil in water for injection. Sodium hydroxide is added to adjust the pH to 8.6 to 9.4

**Recommended Dosage:** see Prescribing Information.  
**Store at 20°C to 25°C (68°F to 77°F); excursions permitted from 15°C to 30°C (59°F to 86°F).** [See USP Controlled Room Temperature]. **Protect from light. Retain in carton until time of use. Discard unused portion.**

**Manufactured for:**  
Avyxa Pharma, LLC  
New Jersey 07054, USA  
Made in China  
143-01 v1/02-2026



  
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3 83831 14301 7

Lot: \_\_\_\_\_  
EXP: \_\_\_\_\_

Unvarnished Area

EXP: YYYY-MM-DD

## Carton-Label



## FAVLYXA

fluorouracil injection, solution

### Product Information

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:83831-143
<b>Route of Administration</b>	INTRAVENOUS		

### Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
<b>FLUOROURACIL</b> (UNII: U3P01618RT) (FLUOROURACIL - UNII:U3P01618RT)	FLUOROURACIL	25 mg in 1 mL

### Inactive Ingredients

Ingredient Name	Strength
<b>WATER</b> (UNII: 059QF0KO0R)	

**SODIUM HYDROXIDE** (UNII: 55X04QC32I)

### Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:83831-143-01	1 in 1 CARTON	02/20/2026	
1		10 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product		

### Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA220201	02/20/2026	

**Labeler** - Avyxa Pharma, LLC (128918748)

**Registrant** - Avyxa Holdings, LLC (119187191)

### Establishment

Name	Address	ID/FEI	Business Operations
Sichuan Huiyu Pharmaceutical Co., Ltd.		421266477	MANUFACTURE(83831-143)

Revised: 3/2026

Avyxa Pharma, LLC