Fulvestrant: Drug information

(For additional information see "Fulvestrant: Patient drug information" and see "Fulvestrant: Pediatric drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

Special Alerts

Faslodex Safety Alert October 2016

Health Canada is warning that *Faslodex* (fulvestrant) can interfere with antibody-based estradiol measurement by immunoassay due to the structural similarity of fulvestrant and estradiol. This can result in falsely elevated estradiol levels, which may lead to misinterpretation of the menopausal status of women and can put patients at risk for unnecessary surgery or endocrine therapy modification. New warnings have been added to the Canadian product monograph for *Faslodex* advising of this risk.

Health care providers should consider reassessing the menopausal status of *Faslodex* patients previously tested using antibody-based estradiol assays. Alternative methods for measuring estradiol levels (such as liquid chromatography-mass spectrometry) should be considered in patients receiving *Faslodex*. When requesting blood tests that include estradiol, providers should indicate if the patient is taking *Faslodex*. Patients should contact their health care provider for more information.

Further information can be found at http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2016/60590a-eng.php.

Brand Names: US

Faslodex

Brand Names: Canada

Faslodex

Pharmacologic Category

Antineoplastic Agent, Estrogen Receptor Antagonist

Dosing: Adult

Breast cancer, metastatic (postmenopausal women; HR positive): IM: Initial: 500 mg on days 1, 15, and 29; Maintenance: 500 mg once monthly. In studies, the 500 mg once monthly dose was administered at 28 days ± 3 days (Di Leo 2014).

Breast cancer, advanced or metastatic (second-line endocrine-based combination therapy): Adult females (HR positive, HER-2 negative): IM: Initial: 500 mg on days 1, 15, and 29; Maintenance: 500 mg once every 28 days. Administer in combination with palbociclib (and an LHRH agonist [eg, goserelin] if

pre- or perimenopausal); continue until disease progression or unacceptable toxicity (Turner 2015).
Note: Refer to Palbociclib monograph for dosing in combination with fulvestrant.

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

There are no dosage adjustments provided in the manufacturer's labeling (has not been studied). However, renal elimination of fulvestrant is negligible.

Dosing: Hepatic Impairment

Mild impairment (Child-Pugh class A): No dosage adjustment is necessary.

Moderate impairment (Child-Pugh class B): Reduce initial doses and maintenance dose to 250 mg.

Severe impairment (Child-Pugh class C): There are no dosage adjustments provided in the manufacturer's labeling (use has not been evaluated).

Dosage Forms

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Intramuscular:

Faslodex: 250 mg/5 mL (5 mL) [contains alcohol, usp, benzyl alcohol, benzyl benzoate]

Generic Equivalent Available (US)

No

Administration

For IM administration only. Administer 500 mg dose as two 5 mL IM injections (one in each buttocks [gluteal area]) slowly over 1 to 2 minutes per injection. If administering at the dorsogluteal site, use caution during injection due to the proximity of underlying sciatic nerve. Refer to facility policy for IM administration of large volumes. To prepare each syringe for administration, hold syringe upright; carefully tilt syringe cap back and forth (without twisting) until the cap disconnects for removal; pull cap off by pulling up without touching the syringe tip (to maintain sterility); attach safety needle to syringe tip and twist firmly to lock. Remove needle cap by pulling straight off to avoid damaging needle point, remove needle sheath and expel excess air from syringe prior to administration. Refer to product labeling for detailed instructions.

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends double gloving, a protective gown, ventilated engineering controls (a class II biological safety cabinet or a compounding aseptic containment isolator), and closed system transfer devices (CSTDs) for preparation. Double gloving and a protective gown are recommended during administration (NIOSH 2016).

Use

Breast cancer, metastatic: Treatment of hormone-receptor (HR)-positive metastatic breast cancer (as monotherapy) in postmenopausal women with disease progression following antiestrogen therapy

Breast cancer, advanced or metastatic (second-line endocrine-based combination therapy): Treatment of HR-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer (in combination with palbociclib) in women with disease progression following endocrine therapy

Adverse Reactions

Adverse reactions reported with 500 mg dose.

>10%:

Central nervous system: Fatigue (8% to 29%), headache (8% to 20%)

Gastrointestinal: Nausea (10% to 28%), diarrhea (19%), constipation (5% to 16%), stomatitis (13%)

Hematologic & oncologic: Anemia (13% to 40%; grade 3: 2%)

Hepatic: Increased liver enzymes (>15%; grades 3/4: 1% to 2%)

Infection: Infection (31%; including nasopharyngitis, upper respiratory infection, urinary tract infection, influenza, bronchitis, rhinitis, conjunctivitis, pneumonia, sinusitis, cystitis, oral herpes, respiratory tract infection)

Local: Pain at injection site (12%; including neuralgia, peripheral neuropathy, sciatica)

1% to 10%:

Dermatologic: Alopecia (6%), skin rash (6%), xeroderma (1%)

Endocrine & metabolic: Hot flash (7%)

Gastrointestinal: Decreased appetite (8%), anorexia (6%), vomiting (6%), dysgeusia (3%)

Hematologic & oncologic: Decreased platelet count (10%), leukopenia (5%; grade 3: 1%; grade 4: 1%), neutropenia (4%; grade 3: 1%), febrile neutropenia (1%; grade 4: 1%)

Neuromuscular & skeletal: Ostealgia (9%), arthralgia (8%), back pain (8%), limb pain (7%), musculoskeletal pain (6%), weakness (5% to 6%)

Ophthalmic: Blurred vision (2%), dry eye syndrome (2%), increased lacrimation (1%)

Respiratory: Cough (5%), dyspnea (4%), epistaxis (2%)

<1%, postmarketing, and/or case reports (reported with 250 or 500 mg dose): Angioedema, hepatic failure, hepatitis, hypersensitivity reaction, increased gamma-glutamyl transferase, increased serum bilirubin, myalgia, thrombosis, urticaria, vaginal hemorrhage, vertigo

Contraindications

Known hypersensitivity to fulvestrant or any component of the formulation

Canadian labeling: Additional contraindications (not in US labeling): Pregnant or lactating women

Warnings/Precautions

Concerns related to adverse effects:

• Hypersensitivity: Hypersensitivity reactions, including urticaria and angioedema, have been reported.

• Injection-site related events: Events related to injection site, including sciatica, neuralgia, neuropathic pain, and peripheral neuropathy, have been reported with fulvestrant administration. Due to the proximity of underlying sciatic nerve, use caution if administering at the dorsogluteal site.

Disease-related concerns:

• Bleeding disorders: Use with caution in patients with a history of bleeding disorders (including thrombocytopenia) and/or patients on anticoagulant therapy; bleeding/hematoma may occur from IM administration.

• Hepatic impairment: Exposure is increased and dosage adjustment is recommended in patients with moderate impairment. Safety and efficacy have not been established in severe impairment.

Dosage form specific issues:

• Benzyl alcohol and derivatives: Some dosage forms may contain benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates; the "gasping syndrome" consists of metabolic acidosis, respiratory distress, gasping respirations, CNS dysfunction (including convulsions, intracranial hemorrhage), hypotension and cardiovascular collapse (AAP ["Inactive" 1997]; CDC, 1982); some data suggests that benzoate displaces bilirubin from protein binding sites (Ahlfors 2001); avoid or use dosage forms containing benzyl alcohol with caution in neonates. See manufacturer's labeling.

Metabolism/Transport Effects

Substrate of CYP3A4 (minor); **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

There are no known significant interactions.

Pregnancy Implications

Adverse events were observed in animal reproduction studies. Based on the mechanism of action, fulvestrant may cause fetal harm if administered during pregnancy. For females of reproductive potential, pregnancy testing is recommended within 7 days prior to initiation of fulvestrant and effective contraception should be used during treatment and for 1 year after the last fulvestrant dose. Animal data suggest that fulvestrant may affect female and male fertility (although not approved for use in men).

Breast-Feeding Considerations

It is not known if fulvestrant is excreted into breast milk. Because of the potential for serious adverse reactions in the nursing infant, lactating women should not breast-feed during treatment and for 1 year after the final fulvestrant dose.

Monitoring Parameters

Liver function tests; pregnancy testing is recommended within 7 days prior to fulvestrant initiation (for females of reproductive potential); monitor for signs/symptoms of bleeding

Mechanism of Action

Estrogen receptor antagonist; competitively binds to estrogen receptors on tumors and other tissue targets, producing a nuclear complex that causes a dose-related down-regulation of estrogen receptors and inhibits tumor growth.

Pharmacodynamics/Kinetics

Duration: IM: Steady state concentrations reached within first month, when administered with additional dose given 2 weeks following the initial dose; plasma levels maintained for at least 1 month

Distribution: V_d: ~3 to 5 L/kg

Protein binding: 99%; to plasma proteins (VLDL, LDL and HDL lipoprotein fractions)

Metabolism: Hepatic via multiple biotransformation pathways (CYP3A4 substrate involved in oxidation pathway, although relative contribution to metabolism unknown); metabolites formed are either less active or have similar activity to parent compound

Half-life elimination:

Children 1 to 10 years: 70.4 ± 8.1 days (Sims 2012)

Adults 250 mg: ~40 days

Excretion: Feces (~90%); urine (<1%)

Clearance: Children 1 to 8 years (based on a 4 mg/kg dose): Decreased by 32% compared to adults

Pricing: US

Solution (Faslodex Intramuscular)

250 mg/5 mL (5 mL): $1123.65

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names

Faslodex (AR, AT, AU, BE, BG, BR, CH, CL, CN, CO, CR, CU, CY, CZ, DE, DK, DO, EE, ES, FI, FR, GB, GR, GT, HK, HN, HR, HU, IE, IL, IN, IS, IT, JP, KR, LB, LT, LU, LV, MT, MX, MY, NI, NL, NO, PA, PE, PH, PL, PT, QA, RO, RU, SE, SG, SI, SK, SV, TH, TR, TW, UY, VE, VN, ZA); Fazlodeks (UA); Fulvenat (IN); Fulvetraz (IN); Nilgaban (AR); Olvestran (AR)

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