CAREPATHrx™
Specialty Pharmacy & Infusion Solutions

GUIDELINES FOR OUTPATIENT FULVESTRANT (FASLODEX) IM THERAPY

Section: Nursing
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
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Revised:
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I. BACKGROUND

Fulvestrant (Faslodex) is an analogue of 17β-oestradiol. 17β-oestradiol is the dominant circulating oestrogen, which controls the growth of many breast tumors. The estrogen receptor (ER) is expressed in the majority of breast tumors. When Oestradiol binds to the ER, the oestradiol/ER complex can exert its effects at both nuclear and cellular levels, initiating a cascade of events associated with proliferation, invasion, survival, and angiogenesis in breast cancer. Fulvestrant acts as an estrogen receptor antagonist by competitively binding to estrogen receptors on tumors and other tissue targets. This produces a nuclear complex that causes a dose-related down-regulation of estrogen receptors and inhibits tumor growth. The following outlines the procedures for servicing patients in need of outpatient Fulvestrant IM home injections.

II. PATIENT ACCEPTANCE CRITERIA

A. All candidates for home care service must be evaluated by the clinician(s) and deemed appropriate to receive home care based upon the dispensing pharmacy's admission criteria.

B. The decision to administer a first dose in the home by a field nurse will be determined on a case-by-case basis and reviewed by nursing and pharmacy management. The following criteria will be evaluated:
   1. Prescriber preference
   2. Allergy profile
   3. Age ≥18 years
   4. Ability to secure nursing for ongoing treatments
   5. Other relevant social and/or medical history

C. Physician orders for Fulvestrant must include:
   1. Drug and dose
   2. Route of administration
   3. Frequency of administration
   4. Emergency medications per protocol for first dose at home

D. Pregnancy testing within 7 days prior to Fulvestrant initiation

E. Dispensing pharmacy treatment protocol for hypersensitivity reactions with IM epinephrine will be instituted unless a physician provides more comprehensive patient-specific orders. (Appendix A)

III. PHARMACOLOGY OVERVIEW

A. Refer to manufacturer's full Prescribing Information for most up to date information

B. Indications and Dosing
    1. Dosing
        a. Monotherapy
            i. Breast cancer, advanced, monotherapy (postmenopausal women; HR positive):
                1) Initial: 500 mg on days 1, 15, and 29
                2) Maintenance: 500 mg once monthly
            ii. Breast cancer, advanced, monotherapy (postmenopausal women; HR positive, HER2 negative):
                1) Initial: 500 mg on days 1, 15, and 29
                2) Maintenance: 500 mg once monthly
        b. Combination therapy
            i. Breast cancer, advanced or metastatic, combination therapy (postmenopausal women; HR positive, HER2 negative):
                1) Initial: 500 mg on days 1, 15, and 29
                2) Maintenance: 500 mg once every 28 days
            ii. Breast cancer, advanced or metastatic, combination therapy (second-line endocrine-based combination therapy): Adult females (HR positive, HER2-negative):
                1) Initial: 500 mg on days 1, 15, and 29
                2) Maintenance: 500 mg once every 28 days.
        c. Refer to section IV for dose adjustment in hepatic insufficiency.

C. Contraindications
    1. Fulvestrant is contraindicated in patients with a known hypersensitivity to the drug or to any of its components.

D. Warnings and Precautions
    1. Risk of Bleeding
        a. Because Fulvestrant is administered intramuscularly, it should be used with caution in patients with bleeding diatheses, thrombocytopenia, or anticoagulant use.
    2. Increased Exposure in Patients with Hepatic Impairment
        a. The safety and pharmacokinetics of Fulvestrant were evaluated in a study in seven subjects with moderate hepatic impairment (Child-Pugh class B) and seven subjects with normal hepatic function. Exposure was increased in patients with moderate hepatic impairment; therefore, a dose of 250 mg is recommended. Fulvestrant has not been studied in patients with severe hepatic impairment
    3. Injection Site Reaction
        a. Injection site related events including sciatica, neuralgia, neuropathic pain, and peripheral neuropathy have been reported with Fulvestrant injection. Caution should

be taken while administering Fulvestrant at the dorsogluteal injection site due to the proximity of the underlying sciatic nerve.

4. Embryo-Fetal Toxicity
    a. Based on findings from animal studies and its mechanism of action, Fulvestrant can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of Fulvestrant to pregnant rats and rabbits during organogenesis resulted in embryo-fetal toxicity at daily doses that are significantly less than the maximum recommended human dose. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with Fulvestrant and for one year after the last dose
5. Immunoassay Measurement of Serum Estradiol
    a. Due to structural similarity of Fulvestrant and estradiol, Fulvestrant can interfere with estradiol measurement by immunoassay, resulting in falsely elevated estradiol levels.

E. Pharmacokinetics
1. Half-life: ~ 40 days
2. Volume of distribution: ~ 3 to 5 L/kg

F. Adverse Reactions
1. Endocrine & metabolic: Decreased serum glucose, hot flash, increased gamma-glutamyl transferase, decreased serum albumin, decreased serum phosphate, weight loss
2. Gastrointestinal: Abdominal pain, constipation, decreased appetite, diarrhea, nausea, stomatitis, vomiting
3. Hematologic & oncologic: Anemia, lymphocytopenia
4. Hepatic: Increased liver enzymes, increased serum alanine aminotransferase, increased serum aspartate aminotransferase
5. Infection
6. Local: Pain at injection site
7. Nervous system: Fatigue, headache, dizziness
8. Neuromuscular & skeletal: Arthralgia, musculoskeletal pain
9. Respiratory: Cough, dyspnea
10. Miscellaneous: Fever

G. Drug Interactions
1. Fluoroestradiol F18:
    a. Estrogen Receptor Antagonists may diminish the diagnostic effect of Fluoroestradiol F18.
    b. Consider Imaging patients with Fluoroestradiol F-18 prior to starting systemic endocrine therapies that block the estrogen receptor.

IV. ADMINISTRATIVE GUIDELINES

A. Administration
1. Administer 500 mg dose as two 5 mL IM injections (one in each buttock) slowly over 1 to 2 minutes per injection.
2. If administering at the dorsogluteal site, use caution during injection due to the proximity of underlying sciatic nerve.
3. This medication may meet the definitions of a hazardous drug as outlined by NIOSH
    a. Double gloving and a protective gown are recommended during administration.
    b. It is the responsibility of the dispensing pharmacy to ensure medication handling

follows organizational policies and procedures.

4. Do not administer IV, SQ, or intra-arterially.

B. Dosing
    1. For the 2 x 5 mL syringe package, the contents of both syringes must be injected to receive the 500 mg recommended dose.

C. Duration
    1. Continue until disease progression or unacceptable toxicity

D. Dose Adjustment
    1. There are no dosage adjustments for renal failure provided in the manufacturer's labeling
    2. Hepatic Failure Adjustments
        a. Mild impairment (Child-Pugh class A): No dosage adjustment necessary.
        b. Moderate impairment (Child-Pugh class B): Reduce initial and maintenance doses: Initial: 250 mg on days 1, 15, and 29; Maintenance: 250 mg once monthly.
        c. Severe impairment (Child-Pugh class C): There are no dosage adjustments provided in the manufacturer's labeling (use has not been evaluated)

E. Patient Monitoring
    1. Monitor for signs/symptoms of bleeding
    2. Monitor for signs/symptoms of disease progression
    3. Nurse to remain with the patient for at least 30 minutes following medication administration to monitor vital signs and response to therapy

V. NURSING PROCEDURE

A. If following NIOSH and USP <800> recommendations for handling, administration, and disposal, supplies may include but are not limited to:
    1. Alcohol Swabs
    2. Fulvestrant prefilled syringes with safety needles
    3. Chemo gloves/prep pad/ gown
    4. Chemo spill kit
    5. Chemo waste bin

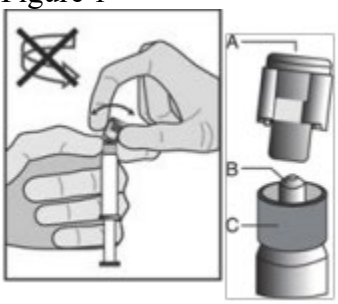
B. How Supplied
    1. Fulvestrant is supplied as two 5 mL clear neutral glass barrels, each containing 250 mg/5 mL of Fulvestrant solution for intramuscular injection and fitted with a tamper evident closure.
    2. The single-dose prefilled syringes are presented in a tray with polystyrene plunger rod and safety needles (SafetyGlide™) for connection to the barrel.

C. Storage and Handling
    1. Store in the original container between 36°F to 46°F (2°C to 8°C) until time of use. Protect from light. Discard each syringe after use.
    2. This medication may meet the definitions of a hazardous drug as outlined by NIOSH. It is the responsibility of the dispensing pharmacy to ensure medication handling is in compliance with organizational policies and procedures.

D. Procedures:

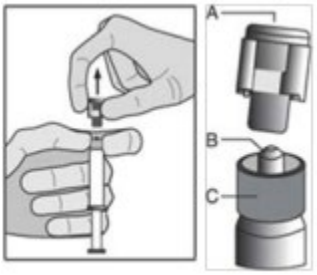
1. Explain the reasoning for visit and use of Fulvestrant.
2. Don gloves.
3. Counsel patient on warnings, precautions, and potential side effects.
4. Prepare Product
    a. Remove glass syringe barrel from tray and check that it is not damaged.
    b. Inspect drug product in glass syringe for any visible particulate matter or discoloration prior to use. Discard if particulate matter or discoloration is present.
    c. Peel open the safety needle outer packaging.
    d. Hold the syringe upright on the ribbed part (C). With the other hand, take hold of the cap (A) and carefully tilt cap back and forth (DO NOT TWIST CAP) until the cap disconnects for removal (see Figure 1).

Figure 1



    e. Pull the cap (A) off in a straight upward direction. DO NOT TOUCH THE STERILE SYRINGE TIP (Luer-Lok) (B) (see Figure 2).

Figure 2



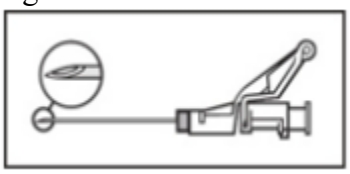
    f. Attach the safety needle to the syringe tip (Luer-Lok). Twist needle until firmly seated (see Figure 3). Confirm that the needle is locked to the Luer connector before moving or tilting the syringe out of the vertical plane to avoid spillage of syringe contents.

Figure 3

    g. For Administration:
        i. Pull shield straight off needle to avoid damaging needle point.

ii. Remove needle sheath.
iii. Expel excess gas from the syringe (a small gas bubble may remain).
iv. Administer intramuscularly slowly (1-2 minutes/injection) into the buttock (gluteal area). For user convenience, the needle 'bevel up' position is orientated to the lever arm, as shown in Figure 4.

Figure 4



v. After injection, immediately activate the lever arm to deploy the needle shielding by applying a single-finger stroke to the activation assisted lever arm to push the lever arm completely forward. Listen for a click. Confirm that the needle shielding has completely covered the needle (see Figure 5). NOTE: Activate away from self and others.

Figure 5

vi. Discard the empty syringe into a chemo sharps container
vii. Repeat steps Preparation and Administration steps 1 through 6 for second syringe.
viii. Nurse to remain with the patient for at least 30 minutes following medication administration to monitor vital signs and response to therapy

VI. CLINICAL MONITORING

A. Prior to starting therapy:
    1. Pregnancy test within 7 days of initiation of therapy

B. During therapy:
    1. Perform routine liver function tests
    2. Monitor for signs/symptoms of bleeding
    3. Monitor signs of tumor response for efficacy

Please refer to the package insert for the most up to date guidance on this medication.

REFERENCES:

A. Faslodex Prescribing Information. Wilmington, DE; AstraZeneca Pharmaceuticals LP. 2019.

B. Fulvestrant. Quick Answers. IBM Micromedex [database online]. Truven Health Analytics/IBM Watson Health; 2020. Accessed September, 19 2020. https://www.micromedexsolutions.com

C. Fulvestrant. In-Depth Answers. IBM Micromedex [database online]. Truven Health Analytics/IBM Watson Health; 2020. https://www.micromedexsolutions.com

APPENDIX A: EPINEPRINE KIT INSTRUCTIONS FOR SC INJECTION

Emergency Medication After Your Infusion

Please call 1-800-755-4704 if you have any questions or concerns. We are available 24 hours a day, 7 days a week. In the event of an emergency, always call 911.

Your nurse will tell you when you need to use Emergency Medications.

Start with a clean work surface and clean hands.

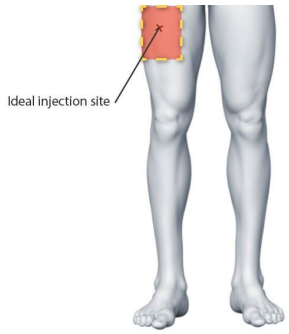
Open the supply bag labeled Epinephrine Kit Contents.

1. Remove 1 of each item
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

Prepare IM (intramuscular) injection of Epinephrine:

2. Attach the brown filtered needle to syringe
    a. Be careful to not touch the tip of the syringe or the needle.
3. Using an alcohol swab, wipe the neck of the epinephrine ampule
4. Holding the ampule upright, swirl and flick the ampule until all fluid flows to the bottom chamber (the top chamber should be empty).
5. Using a new alcohol wipe, grasp the neck of the ampule and with your other hand grasp the bottom chamber of the ampule. Quickly snap the top of the ampule off, directing the snap way from you.
6. Place the tip of the brown filter needle inside the ampule. Tilting the ampule, withdrawal all the medication into the syringe by gently pulling back on the plunger. Be careful to not pull the plunger out of the syringe.
7. Remove the needle from the ampule and hold the syringe upright with the needle pointing upward. Gently tap the side of the syringe to bring any air to the top of the syringe.
8. Push the air out of the syringe by gently pushing on the plunger.
9. Replace the cap on the brown filter needle.
10. Remove the brown filter needle and place the black safety needle onto the syringe.

Give your IM Epinephrine injection



2. Grasp your leg muscle at the outer mid-thigh and cleanse the area with a new alcohol wipe.
3. Push the needle into your leg muscle straight in at a 90-degree angle.
4. Inject the medication by depressing the plunger in a slow and steady motion.
5. Remove the needle and wipe the site with the alcohol wipe.

   Place all trash in the bag and take with you when you seek medical care. Give the bag to the nurse or EMT, so your doctor will know what medication you already took. They will properly dispose of the syringe and needles.

   Call 911 or have someone drive you to the emergency department.