Regimen Monograph

A - Regimen Name

FLVS Regimen

Fulvestrant

Disease Site	Breast
Intent	Palliative
Regimen Category	**Evidence-Informed :** Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.
Rationale and Uses	For the treatment of metastatic or locally advanced hormone receptor-positive (ER+ and/or PR+) breast cancer
Supplementary Public Funding	**fulvestrant** ODB - General Benefit (fulvestrant)

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B - Drug Regimen

fulvestrant	500 mg	IM	Days 1, 15 and 29, then every 28 days

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C - Cycle Frequency

REPEAT EVERY 28 DAYS
Until evidence of disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Not applicable

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Dosage with toxicity

Toxicity	Action
Hypersensitivity	Consider discontinuing if severe.
Mild hepatotoxicity	Hold until recovery and then restart.
Moderate to severe hepatotoxicity	Discontinue.

Hepatic Impairment

Fulvestrant is metabolized primarily in the liver. There are no efficacy and safety data in patients with breast cancer and hepatic impairment. Decreased clearance (by 2.2 fold) and changes in exposure (↑ 70%) were observed in women with moderate hepatic impairment compared to patients with normal hepatic function.

Hepatic Impairment	Fulvestrant Dose
Mild to Moderate (Child-Pugh Class A or B)	Use with caution. No dose adjustment required.
Severe (Child-Pugh Class C)	Not studied. Use not recommended.

Renal Impairment

Creatinine Clearance (mL/min)	Fulvestrant Dose
≥ 30	No dosage adjustment required.
< 30	Use with caution; no data.

Dosage in the Elderly

No dosage adjustment required.

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F - Adverse Effects

Refer to fulvestrant drug monograph(s) for additional details of adverse effects.

Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Joint disorders, musculoskeletal pain • Injection site reaction (may be severe) • Increased LFTs (may be severe) • Fatigue • Nausea, vomiting	• Arterial / venous thromboembolism • Hypersensitivity • Thrombocytopenia • Estrogen deprivation symptoms • Osteoporosis

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G - Interactions

Refer to fulvestrant drug monograph(s) for additional details.

- Fulvestrant may interfere with estradiol immunoassay measurements (falsely elevated estradiol levels) due to its structural similarity with estradiol.

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H - Drug Administration and Special Precautions

Refer to fulvestrant drug monograph(s) for additional details.

Administration:

- Each dose consists of 2 pre-filled syringes (250 mg/5mL). Administer each pre-filled syringe as SLOW intramuscular injection (1-2 minutes per injection) into EACH buttock.
- Caution should be taken due to proximity of the sciatic nerve and large blood vessels.
- Administer according to local guidelines at the Cancer Centre or physician's office.
- Store refrigerated at 2 to 8°C in original package.

Contraindications:

- Patients with known hypersensitivity to the drug or to any of the formulation or container
- Pregnant and breastfeeding women

Warnings/Precautions:

- Due to the route of administration, use with caution in patients with bleeding disorders or on anticoagulants.
- Exercise caution when driving or operating machinery due to fatigue.
- There is a potential osteoporosis risk due to fulvestrant's mechanism of action.

Pregnancy/Lactation:

- Fulvestrant is **contraindicated** in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least **2 years** after the last dose.
- Breastfeeding: **Contraindicated**
- Fertility effects: Probable

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Recommended Clinical Monitoring

- Liver function tests; Baseline and as clinically indicated
- Clinical assessment of injection site reactions, hypersensitivity, estrogen deprivation symptoms, fatigue, thromboembolism and musculoskeletal effects; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Renal function tests; Baseline and repeat as clinically indicated

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J - Administrative Information

Outpatient prescription; drug administration at Cancer Centre or physician's office

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K - References

Chia S, Gradishar W, Mauriac L, et al. Double-blind, randomized placebo controlled trial of fulvestrant compared with exemestane after prior nonsteroidal aromatase inhibitor therapy in postmenopausal women with hormone receptor-positive, advanced breast cancer: results from EFECT. J Clin Oncol 2008; 26:1664-70.

Di Leo A, Jerusalem G, Petruzelka L, et al. Results of the CONFIRM phase III trial comparing fulvestrant 250 mg with fulvestrant 500 mg in postmenopausal women with estrogen receptor-positive advanced breast cancer. J Clin Oncol 2010;28(30):4594-600.

Fulvestrant drug monograph, Ontario Health (Cancer Care Ontario).

Howell A, Pippen J, Elledge RM, et al. Fulvestrant versus anastrozole for the treatment of advanced breast carcinoma: a prospectively planned combined survival analysis of two multicenter trials. Cancer 2005;104(2):236-9.

Howell A, Robertson JF, Abram P, et al. Comparison of fulvestrant versus tamoxifen for the treatment of advanced breast cancer in postmenopausal women previously untreated with endocrine therapy: A multinational, double-blind, randomized trial. J Clin Oncol 2004;22:1605-13.

Howell A, Robertson JFR, Quersma Albano J, et al. Fulvestrant, formerly ICI182,870 is as effective as anastrozole in postmenopausal women with advanced breast cancer progressing after prior endocrine treatment. JCO 2002;20:3396-403.

McCormack P, Sapunar F. Pharmacokinetic profile of the fulvestrant loading dose regimen in postmenopausal women with hormone receptor-positive advanced breast cancer. Clin Breast Cancer 2008;8(4):347-51.

Osborne CK, Pippen J, Jones SE et al. Double-blind, randomized trial comparing the efficacy and tolerability of fulvestrant versus anastrozole in postmenopausal women with advanced breast cancer progressing on prior endocrine therapy: results of a North American trial. J Clin Oncol 2002;20:3386-95.

Robertson JFR, Bondarenko IM, Trishkina E, et al. Fulvestrant 500 mg versus anastrozole 1 mg for hormone receptor-positive advanced breast cancer (FALCON): an international, randomised, double-blind, phase 3 trial. Lancet. 2016 Dec 17;388(10063):2997-3005.

Robertson JFR, Osborne CK, Howell A et al. Fulvestrant versus anastrozole for the treatment of advanced breast carcinoma in postmenopausal women: a prospective combined analysis of two multicentre trials. Cancer 2003;98:229-38.

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

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