When FASLODEX is used in combination with abemaciclib, the recommended dose of abemaciclib is 150 mg orally, twice daily. Abemaciclib may be taken with or without food. Refer to the Full Prescribing Information for abemaciclib.

When FASLODEX is used in combination with ribociclib, the recommended dose of ribociclib is 600 mg taken orally, once daily for 21 consecutive days followed by 7 days off treatment resulting in a complete cycle of 28 days. Ribociclib can be taken with or without food. Refer to the Full Prescribing Information for ribociclib.

Pre/perimenopausal women treated with the combination of FASLODEX plus palbociclib, abemaciclib, or ribociclib, should be treated with luteinizing hormone-releasing hormone (LHRH) agonists according to current clinical practice standards *[see Clinical Studies (14)]*.

2.2 Dose Modification

Monotherapy

Hepatic Impairment:

A dose of 250 mg is recommended for patients with moderate hepatic impairment (Child-Pugh class B) to be administered intramuscularly into the buttock (gluteal area) slowly (1 - 2 minutes) as one 5 mL injection on Days 1, 15, 29, and once monthly thereafter.

FASLODEX has not been evaluated in patients with severe hepatic impairment (Child-Pugh class C) *[see Warnings and Precautions (5.2) and Use in Specific Populations (8.6)]*.

Combination Therapy

When FASLODEX is used in combination with palbociclib, abemaciclib, or ribociclib, refer to monotherapy dose modification instructions for FASLODEX.

Refer to the Full Prescribing Information of co-administered palbociclib, abemaciclib, or ribociclib for dose modification guidelines in the event of toxicities, for use with concomitant medications, and other relevant safety information.

2.3 Administration Technique

Administer the injection according to the local guidelines for performing large volume intramuscular injections.

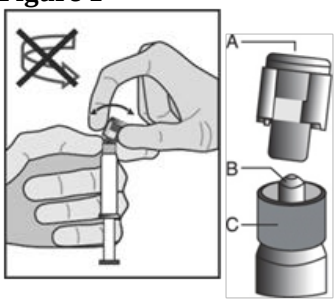
NOTE: Due to the proximity of the underlying sciatic nerve, caution should be taken if administering FASLODEX at the dorsogluteal injection site *[see Warnings and Precautions (5.3) and Adverse Reactions (6.1)]*.

The proper method of administration of FASLODEX for intramuscular use is described in the following instructions.

For each single-dose prefilled syringe:

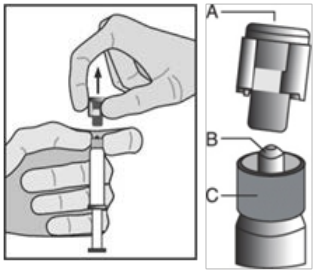
1. Remove glass syringe barrel from tray and check that it is not damaged.
2. Remove perforated patient record label from syringe.
3. Inspect drug product in glass syringe for any visible particulate matter or discoloration prior to use. Discard if particulate matter or discoloration is present.
4. Peel open the safety needle (SafetyGlide™) outer packaging.
5. 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



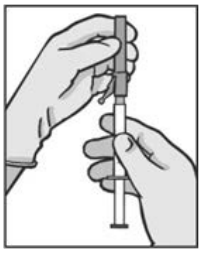
6. Pull the cap (A) off in a straight upward direction. DO NOT TOUCH THE STERILE SYRINGE TIP (Luer-Lok) (B) (see Figure 2).

Figure 2



7. 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.

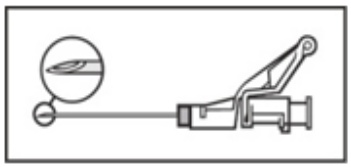
Figure 3



For Administration:

8. Pull shield straight off needle to avoid damaging needle point.
9. Remove needle sheath.
10. Expel excess gas from the syringe (a small gas bubble may remain).
11. 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



12. 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

13. Discard the empty syringe into an approved sharps collector in accordance with applicable regulations and institutional policy.
14. Repeat steps 1 through 13 for second syringe.

How To Use FASLODEX

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

SAFETYGLIDE™ INSTRUCTIONS FROM BECTON DICKINSON

SafetyGlide™ is a trademark of Becton Dickinson and Company.

Important Administration Information

To help avoid HIV (AIDS), HBV (Hepatitis), and other infectious diseases due to accidental needlesticks, contaminated needles should not be recapped or removed, unless there is no alternative or that such action is required by a specific medical procedure. Hands must remain behind the needle at all times during use and disposal.

Do not autoclave SafetyGlide™ Needle before use.

Becton Dickinson guarantees the contents of their unopened or undamaged packages to be sterile, non-toxic, and non-pyrogenic.

3 DOSAGE FORMS AND STRENGTHS

FASLODEX, an injection for intramuscular administration, is supplied as 5-mL single-dose prefilled syringes containing 250 mg/5 mL fulvestrant.

4 CONTRAINDICATIONS

FASLODEX is contraindicated in patients with a known hypersensitivity to the drug or to any of its components. Hypersensitivity reactions, including urticaria and angioedema, have been reported in association with FASLODEX *[see Adverse Reactions (6.2)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Bleeding

Because FASLODEX is administered intramuscularly, it should be used with caution in patients with bleeding diatheses, thrombocytopenia, or anticoagulant use.

5.2 Increased Exposure in Patients with Hepatic Impairment

The safety and pharmacokinetics of FASLODEX 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 *[see Dosage and Administration (2.2)]*.

FASLODEX has not been studied in patients with severe hepatic impairment (Child-Pugh class C) *[see Use in Specific Populations (8.6)]*.

5.3 Injection Site Reaction

Injection site related events including sciatica, neuralgia, neuropathic pain, and peripheral neuropathy have been reported with FASLODEX injection. Caution should be taken while administering FASLODEX at the dorsogluteal injection site due to the proximity of the underlying sciatic nerve *[see Dosage and Administration (2.3) and Adverse Reactions (6.1)]*.

5.4 Embryo-Fetal Toxicity

Based on findings from animal studies and its mechanism of action, FASLODEX 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 FASLODEX and for one year after the last dose *[see Use in Specific Populations (8.1), (8.3) and Clinical Pharmacology (12.1)]*.

5.5 Immunoassay Measurement of Serum Estradiol

Due to structural similarity of fulvestrant and estradiol, FASLODEX can interfere with estradiol measurement by immunoassay, resulting in falsely elevated estradiol levels.

6 ADVERSE REACTIONS

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

- Risk of Bleeding *[see Warnings and Precautions (5.1)]*
- Increased Exposure in Patients with Hepatic Impairment *[see Warnings and Precautions (5.2)]*
- Injection Site Reaction *[see Warnings and Precautions (5.3)]*
- Embryo-Fetal Toxicity *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, the adverse reaction rates observed cannot be directly compared to rates in other trials and may not reflect the rates observed in clinical practice.

Monotherapy

Comparison of FASLODEX 500 mg and FASLODEX 250 mg (CONFIRM)

The following adverse reactions (ARs) were calculated based on the safety analysis of CONFIRM comparing the administration of FASLODEX 500 mg intramuscularly once a month with FASLODEX 250 mg intramuscularly once a month. The most frequently reported adverse reactions in the FASLODEX 500 mg group were injection site pain (11.6% of patients), nausea (9.7% of patients), and bone pain (9.4% of patients); the most frequently reported adverse reactions in the FASLODEX 250 mg group were nausea (13.6% of patients), back pain (10.7% of patients), and injection site pain (9.1% of patients).

Table 1 lists adverse reactions reported with an incidence of 5% or greater, regardless of assessed causality, from CONFIRM.

Table 1: Adverse Reactions in CONFIRM (≥5% in Either Treatment Group)

Adverse Reactions	FASLODEX 500 mg N=361 %	FASLODEX 250 mg N=374 %
Body as a Whole		
Injection Site Pain[1]	12	9
Headache	8	7
Back Pain	8	11
Fatigue	8	6
Pain in Extremity	7	7
Asthenia	6	6
Vascular System		
Hot Flash	7	6
Digestive System		

Adverse Reactions	FASLODEX 500 mg N=361 %	FASLODEX 250 mg N=374 %
Nausea	10	14
Vomiting	6	6
Anorexia	6	4
Constipation	5	4
Musculoskeletal System		
Bone Pain	9	8
Arthralgia	8	8
Musculoskeletal Pain	6	3
Respiratory System		
Cough	5	5
Dyspnea	4	5

[1.] Including more severe injection site related sciatica, neuralgia, neuropathic pain, and peripheral neuropathy.

In the pooled safety population (N=1127) from clinical trials comparing FASLODEX 500 mg to FASLODEX 250 mg, post-baseline increases of ≥1 CTC grade in either AST, ALT, or alkaline phosphatase were observed in >15% of patients receiving FASLODEX. Grade 3-4 increases were observed in 1-2% of patients. The incidence and severity of increased hepatic enzymes (ALT, AST, ALP) did not differ between the 250 mg and the 500 mg FASLODEX arms.

Comparison of FASLODEX 500 mg and Anastrozole 1 mg (FALCON)

The safety of FASLODEX 500 mg versus anastrozole 1 mg was evaluated in FALCON. The data described below reflect exposure to FASLODEX in 228 out of 460 patients with HR-positive advanced breast cancer in postmenopausal women not previously treated with endocrine therapy who received at least one (1) dose of treatment in FALCON.

Permanent discontinuation associated with an adverse reaction occurred in 4 of 228 (1.8%) patients receiving FASLODEX and in 3 of 232 (1.3%) patients receiving anastrozole. Adverse reactions leading to discontinuation for those patients receiving FASLODEX included drug hypersensitivity (0.9%), injection site hypersensitivity (0.4%), and elevated liver enzymes (0.4%).

The most common adverse reactions (≥10%) of any grade reported in patients in the FASLODEX arm were arthralgia, hot flash, fatigue, and nausea.

Adverse reactions reported in patients who received FASLODEX in FALCON at an incidence of ≥5% in either treatment arm are listed in Table 2, and laboratory abnormalities are listed in Table 3.

Table 2: Adverse Reactions in FALCON

Adverse Reactions	FASLODEX 500 mg N=228		Anastrozole 1 mg N=232	
	All Grades %	Grade 3 or 4 %	All Grades %	Grade 3 or 4 %
Vascular Disorders				
Hot flash	11	0	10	0
Gastrointestinal Disorders				
Nausea	11	0	10	<1

8.2 Lactation

Risk Summary

There is no information regarding the presence of fulvestrant in human milk, nor of its effects on milk production or breastfed infant. Fulvestrant can be detected in rat milk *[see Data]*. Because of the potential for serious adverse reactions in breastfed infants from FASLODEX, advise a lactating woman not to breastfeed during treatment with FASLODEX and for one year after the final dose.

Data

Levels of fulvestrant were approximately 12-fold higher in milk than in plasma after exposure of lactating rats to a dose of 2 mg/kg. Drug exposure in rodent pups from fulvestrant-treated lactating dams was estimated as 10% of the administered dose. In a study in rats of fulvestrant at 10 mg/kg given twice or 15 mg/kg given once (less than the recommended human dose based on mg/m^2) during lactation, offspring survival was slightly reduced.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Pregnancy testing is recommended for females of reproductive potential within seven days prior to initiating FASLODEX.

Contraception

Females

FASLODEX can cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]*. Advise females of reproductive potential to use effective contraception during treatment and for one year after the last dose.

Infertility

Based on animal studies, FASLODEX may impair fertility in females and males of reproductive potential. The effects of fulvestrant on fertility were reversible in female rats *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established. A multi-center, single-arm, open-label, study of fulvestrant was conducted in 30 girls with McCune-Albright Syndrome (MAS) associated with Progressive Precocious Puberty (PPP). The median age at informed consent was 6 years old (range: 1 to 8).

The first 10 patients initially received fulvestrant 2 mg/kg. Based on PK data from the first 6 patients, all 10 patients receiving 2 mg/kg were escalated to a dose of 4 mg/kg and all other patients received 4 mg/kg from study entry.

Baseline measurements for vaginal bleeding days, bone age, growth velocity, and Tanner staging for at least 6 months prior to study entry were provided retrospectively by the parent, guardian, or local

compared to patients with normal hepatic function. AUC was positively correlated with total bilirubin concentration (p=0.012). FASLODEX has not been studied in patients with severe hepatic impairment (Child-Pugh class C).

A dose of FASLODEX 250 mg is recommended in patients with moderate hepatic impairment (Child-Pugh class B) *[see Dosage and Administration (2.2) and Warnings and Precautions (5.2)]*.

8.7 Renal Impairment

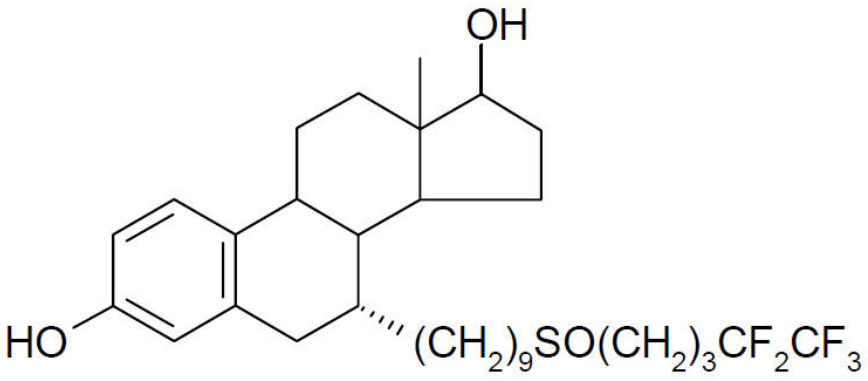
Negligible amounts of fulvestrant are eliminated in urine; therefore, a study in patients with renal impairment was not conducted. In the advanced breast cancer trials, fulvestrant concentrations in women with estimated creatinine clearance as low as 30 mL/min were similar to women with normal creatinine.

10 OVERDOSAGE

Human experience of overdose with FASLODEX is limited. There are isolated reports of overdose with FASLODEX in humans. No adverse reactions were seen in healthy male and female volunteers who received intravenous fulvestrant, which resulted in peak plasma concentrations at the end of the infusion, that were approximately 10 to 15 times those seen after intramuscular injection. The potential toxicity of fulvestrant at these or higher concentrations in cancer patients who may have additional comorbidities is unknown. There is no specific treatment in the event of fulvestrant overdose, and symptoms of overdose are not established. In the event of an overdose, healthcare practitioners should follow general supportive measures and should treat symptomatically.

11 DESCRIPTION

FASLODEX® (fulvestrant) injection for intramuscular administration is an estrogen receptor antagonist. The chemical name is 7-alpha-[9-(4,4,5,5,5-penta fluoropentylsulphinyl) nonyl]estra-1,3,5-(10)- triene-3,17-beta-diol. The molecular formula is $C_{32}H_{47}F_5O_3S$ and its structural formula is:



Fulvestrant is a white powder with a molecular weight of 606.77. The solution for injection is a clear, colorless to yellow, viscous liquid.

Each injection contains as inactive ingredients: 10% w/v Alcohol, USP, 10% w/v Benzyl Alcohol, NF, and 15% w/v Benzyl Benzoate, USP, as co-solvents, and made up to 100% w/v with Castor Oil, USP as a co-solvent and release rate modifier.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Many breast cancers have estrogen receptors (ER) and the growth of these tumors can be stimulated by estrogen. Fulvestrant is an estrogen receptor antagonist that binds to the estrogen receptor in a competitive manner with affinity comparable to that of estradiol and downregulates the ER protein in human breast cancer cells.

In vitro studies demonstrated that fulvestrant is a reversible inhibitor of the growth of tamoxifen-resistant, as well as estrogen-sensitive human breast cancer (MCF-7) cell lines. In *in vivo* tumor studies, fulvestrant delayed the establishment of tumors from xenografts of human breast cancer MCF-7 cells in nude mice. Fulvestrant inhibited the growth of established MCF-7 xenografts and of tamoxifen-resistant breast tumor xenografts.

Fulvestrant showed no agonist-type effects in *in vivo* uterotrophic assays in immature or ovariectomized mice and rats. In *in vivo* studies in immature rats and ovariectomized monkeys, fulvestrant blocked the uterotrophic action of estradiol. In postmenopausal women, the absence of changes in plasma concentrations of FSH and LH in response to fulvestrant treatment (250 mg monthly) suggests no peripheral steroidal effects.

12.2 Pharmacodynamics

In a clinical study in postmenopausal women with primary breast cancer treated with single doses of FASLODEX 15-22 days prior to surgery, there was evidence of increasing down-regulation of ER with increasing dose. This was associated with a dose-related decrease in the expression of the progesterone receptor, an estrogen-regulated protein. These effects on the ER pathway were also associated with a decrease in Ki67 labeling index, a marker of cell proliferation.

12.3 Pharmacokinetics

Absorption:

The single dose and multiple dose PK parameters for the 500 mg dosing regimen with an additional dose (AD) at Day 15 are reported in Table 11. The additional dose of FASLODEX given two weeks after the initial dose allows for steady state concentrations to be reached within the first month of dosing.

Table 11: Summary of Fulvestrant Pharmacokinetic Parameters [gMean (CV%)] in Postmenopausal Advanced Breast Cancer Patients after Intramuscular Administration 500 mg + AD Dosing Regimen

		C_{max} (ng/mL)	C_{min} (ng/mL)	AUC (ng.hr/mL)
500 mg + AD[1]	Single dose	25.1 (35.3)	16.3 (25.9)	11400 (33.4)
	Multiple dose steady state[2]	28.0 (27.9)	12.2 (21.7)	13100 (23.4)

1. Additional 500 mg dose given on Day 15
2. Month 3

studied, but in a 6-month toxicology study, male rats treated with intramuscular doses of 15 mg/kg/30 days, 10 mg/rat/30 days, or 10 mg/rat/15 days fulvestrant showed a loss of spermatozoa from the seminiferous tubules, seminiferous tubular atrophy, and degenerative changes in the epididymides. Changes in the testes and epididymides had not recovered 20 weeks after cessation of dosing. These fulvestrant doses correspond to 1.3-, 1.2-, and 3.5-fold the systemic exposure [$AUC_{0\text{-}30\ days}$] achieved in women receiving the recommended dose of 500 mg/month.

14 CLINICAL STUDIES

The efficacy of FASLODEX 500 mg versus FASLODEX 250 mg was compared in CONFIRM. The efficacy of FASLODEX 250 mg was compared to 1 mg anastrozole in Studies 0020 and 0021. The efficacy of FASLODEX 500 mg was compared to 1 mg anastrozole in FALCON. The efficacy of FASLODEX 500 mg in combination with palbociclib 125 mg was compared to FASLODEX 500 mg plus placebo in PALOMA-3. The efficacy of FASLODEX 500 mg in combination with abemaciclib 150 mg was compared to FASLODEX 500 mg plus placebo in MONARCH 2. The efficacy of FASLODEX 500 mg in combination with ribociclib 600 mg was compared to FASLODEX 500 mg plus placebo in MONALEESA-3.

Monotherapy

Comparison of FASLODEX 500 mg and FASLODEX 250 mg (CONFIRM)

A randomized, double-blind, controlled clinical trial (CONFIRM, NCT00099437) was completed in 736 postmenopausal women with advanced breast cancer who had disease recurrence on or after adjuvant endocrine therapy or progression following endocrine therapy for advanced disease. This trial compared the efficacy and safety of FASLODEX 500 mg (n=362) with FASLODEX 250 mg (n=374).

FASLODEX 500 mg was administered as two 5 mL injections each containing FASLODEX 250 mg/5 mL, one in each buttock, on Days 1, 15, 29, and every 28 (+/- 3) days thereafter. FASLODEX 250 mg was administered as two 5 mL injections (one containing FASLODEX 250 mg/5 mL injection plus one placebo injection), one in each buttock, on Days 1, 15 (2 placebo injections only), 29, and every 28 (+/- 3) days thereafter.

The median age of study participants was 61 years. All patients had ER+ advanced breast cancer. Approximately 30% of subjects had no measurable disease. Approximately 55% of patients had visceral disease.

Results of CONFIRM are summarized in Table 12. The efficacy of FASLODEX 500 mg was compared to that of FASLODEX 250 mg. Figure 6 shows a Kaplan-Meier plot of the Progression Free Survival (PFS) data after a minimum follow-up duration of 18 months demonstrating statistically significant superiority of FASLODEX 500 mg vs. FASLODEX 250 mg. In the initial Overall Survival (OS) analysis after a minimum follow-up duration of 18 months, there was no statistically significant difference in OS between the two treatment groups. After a minimum follow-up duration of 50 months, an updated OS analysis was performed. Figure 7 shows a Kaplan-Meier plot of the updated OS data.

Table 12: Efficacy Results in CONFIRM (Intent-To-Treat (ITT) Population)

Endpoint	FASLODEX 500 mg (N=362)	FASLODEX 250 mg (N=374)
PFS[1] Median (months)	6.5	5.4
Hazard Ratio[2] (95% CI[3])	0.80 (0.68-0.94)	
p-value	0.006	
OS[4] **Updated Analysis**[5] (% patients who died)	261 (72.1%)	293 (78.3%)
Median OS (months)	26.4	22.3
Hazard Ratio[2] (95% CI[3])[6]	0.81 (0.69-0.96)	
ORR[7] (95% CI[3])	13.8% (9.7%, 18.8%) (33/240)	14.6% (10.5%, 19.4%) (38/261)

1. PFS (Progression Free Survival)=the time between randomization and the earliest of progression or death from any cause. Minimum follow-up duration of 18 months.
2. Hazard Ratio <1 favors FASLODEX 500 mg.
3. CI=Confidence Interval
4. OS=Overall Survival
5. Minimum follow up duration of 50 months.
6. Not statistically significant as no adjustments were made for multiplicity.
7. ORR (Objective Response Rate), as defined as number (%) of patients with complete response or partial response, was analyzed in the evaluable patients with measurable disease at baseline (fulvestrant 500 mg N=240; fulvestrant 250 mg N=261). Minimum follow-up duration of 18 months.

Figure 6 Kaplan-Meier PFS: CONFIRM ITT Population

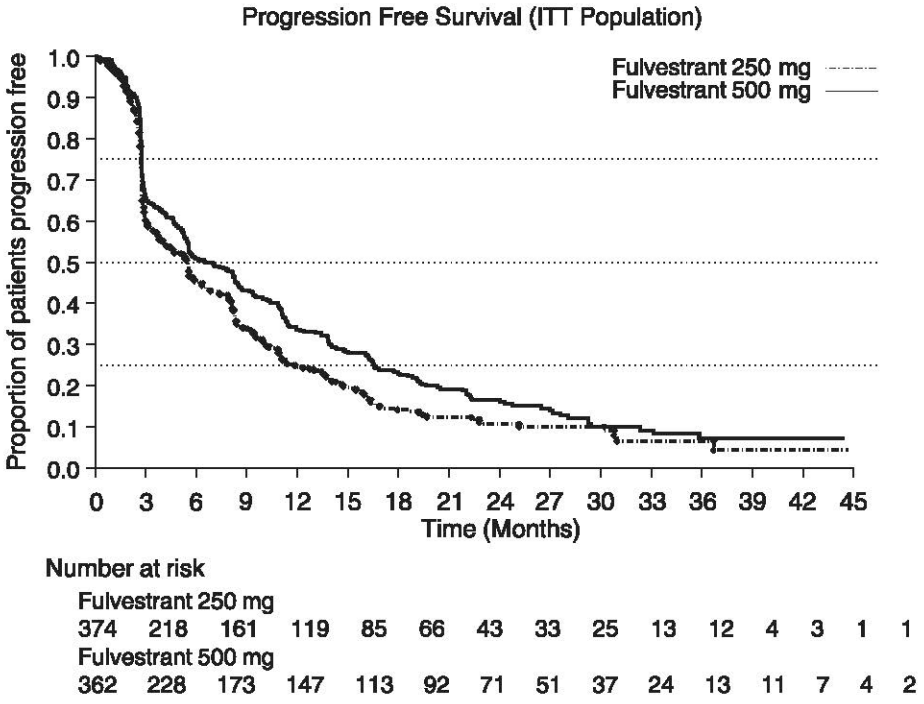
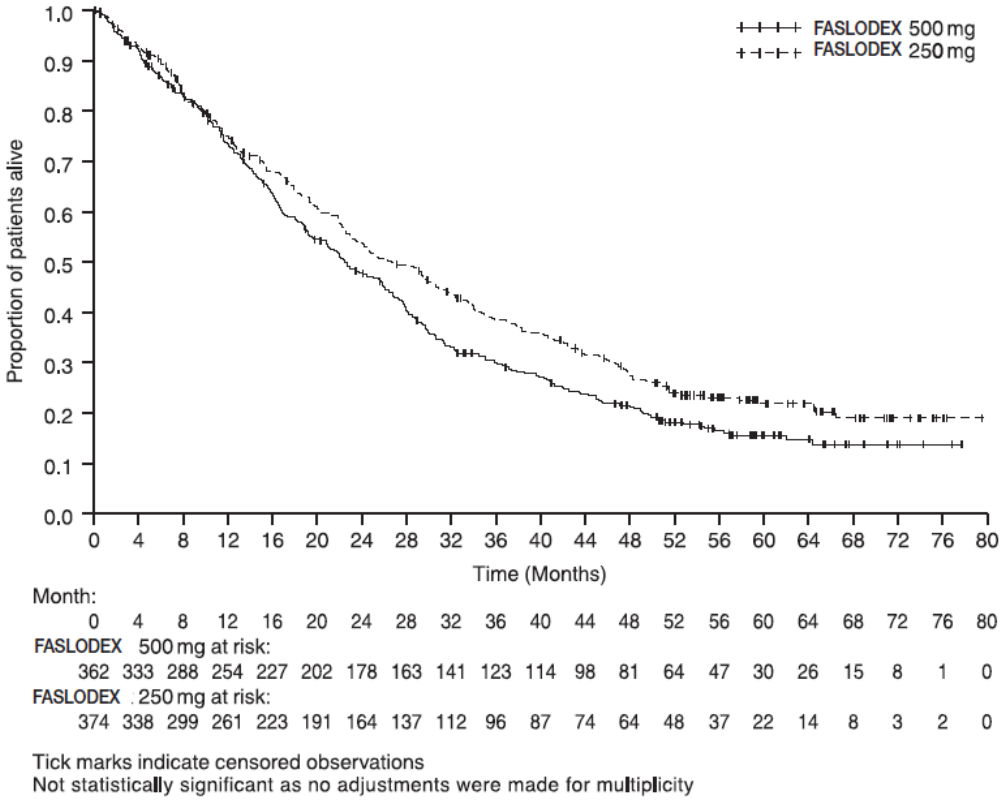


Figure 7 Kaplan-Meier OS (Minimum Follow-up Duration of 50 Months): CONFIRM ITT Population



Comparison of FASLODEX 500 mg and Anastrozole 1 mg (FALCON)

A randomized, double-blind, double-dummy, multi-center study (FALCON, NCT01602380) of FASLODEX 500 mg versus anastrozole 1 mg was conducted in postmenopausal women with ER-positive and/or PgR-positive, HER2-negative locally advanced or metastatic breast cancer who had not previously been treated with any hormonal therapy. A total of 462 patients were randomized 1:1 to receive administration of FASLODEX 500 mg as an intramuscular injection on Days 1, 15, 29, and every 28 (+/- 3) days thereafter or daily administration of 1 mg of anastrozole orally. This study compared the efficacy and safety of FASLODEX 500 mg and anastrozole 1 mg.

Randomization was stratified by disease setting (locally advanced or metastatic), use of prior chemotherapy for advanced disease, and presence or absence of measurable disease.

The major efficacy outcome measure of the study was investigator-assessed progression-free survival (PFS) evaluated according to RECIST v.1.1 (Response Evaluation Criteria in Solid Tumors). Key secondary efficacy outcome measures included overall survival (OS), objective response rate (ORR), and duration of response (DoR).

Patients enrolled in this study had a median age of 63 years (range 36-90). The majority of patients (87%) had metastatic disease at baseline. Fifty-five percent (55%) of patients had visceral metastasis at baseline. A total of 17% of patients had received one prior chemotherapy regimen for advanced disease; 84% of patients had measurable disease. Sites of metastases were as follows: musculoskeletal 59%, lymph nodes 50%, respiratory 40%, liver (including gall bladder) 18%.

The single-dose prefilled syringes are presented in a tray with polystyrene plunger rod and safety needles (SafetyGlide™) for connection to the barrel.

Discard each syringe after use. If a patient dose requires only one syringe, unused syringe should be stored as directed below.

Storage:

REFRIGERATE, 2°-8°C (36°-46°F). TO PROTECT FROM LIGHT, STORE IN THE ORIGINAL CARTON UNTIL TIME OF USE.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Monotherapy

Risk of Bleeding:

- Because FASLODEX is administered intramuscularly, it should be used with caution in patients with bleeding disorders, decreased platelet count, or in patients receiving anticoagulants (for example, warfarin) *[see Warnings and Precautions (5.1)].*

Embryo-Fetal Toxicity:

- Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment with FASLODEX and for one year after the last dose. Advise females to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions (5.4) and Use in Specific Populations (8.1), (8.3)].*

Lactation:

- Advise women not to breastfeed during treatment with FASLODEX and for one year after the last dose *[see Use in Specific Populations (8.2)].*

Combination Therapy

When FASLODEX is used in combination with palbociclib, abemaciclib, or ribociclib, refer to the respective Full Prescribing Information for Patient Counseling Information.

Distributed by:
AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850

FASLODEX is a registered trademark of the AstraZeneca group of companies

PATIENT INFORMATION
FASLODEX® (faz-lo-dex)
(fulvestrant)
injection

What is FASLODEX?
FASLODEX is a prescription medicine used to treat advanced breast cancer or breast cancer that has spread to other parts of the body (metastatic).

FASLODEX may be used alone, if you have gone through menopause, and your advanced breast cancer is:

- hormone receptor (HR)-positive and human epidermal growth factor receptor 2 (HER2)-negative and has not been previously treated with endocrine therapy
  or
- HR-positive and has progressed after endocrine therapy.

FASLODEX may be used in combination with ribociclib, if you have gone through menopause, and your advanced or metastatic breast cancer is HR-positive and HER2-negative, and has not been previously treated with endocrine therapy or has progressed after endocrine therapy.

FASLODEX may be used in combination with palbociclib or abemaciclib if your advanced or metastatic breast cancer is HR-positive and HER2-negative, and has progressed after endocrine therapy.

When FASLODEX is used in combination with palbociclib, abemaciclib, or ribociclib, also read the Patient Information for the prescribed product.

It is not known if FASLODEX is safe and effective in children.

It is not known if FASLODEX is safe and effective in people with severe liver problems.

Who should not receive FASLODEX?
Do not receive FASLODEX if you have had an allergic reaction to fulvestrant or any of the ingredients in FASLODEX. See the end of this leaflet for a list of the ingredients in FASLODEX.
Symptoms of an allergic reaction to FASLODEX may include:

- itching or hives
- swelling of your face, lips, tongue, or throat
- trouble breathing

What should I tell my healthcare provider before receiving FASLODEX?
Before receiving FASLODEX, tell your healthcare provider about all of your medical conditions, including if you:

- have a low level of platelets in your blood or bleed easily.
- have liver problems.
- are pregnant or plan to become pregnant. FASLODEX can harm your unborn baby.
  Females who are able to become pregnant:
  - Your healthcare provider may perform a pregnancy test within 7 days before you start FASLODEX.
  - You should use effective birth control during treatment with FASLODEX and for one year after the last dose of FASLODEX.
  - Tell your healthcare provider right away if you become pregnant or think you are pregnant during treatment with FASLODEX.
- are breastfeeding or plan to breastfeed. It is not known if FASLODEX passes into your breast milk. Do not breastfeed during your treatment with FASLODEX and for one year after the final dose of FASLODEX. Talk to your healthcare provider about the best way to feed your baby during this time.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. FASLODEX may affect the way other medicines work, and other medicines may affect how FASLODEX works.
Especially tell your healthcare provider if you take a blood thinner medicine.

How will I receive FASLODEX?

- Your healthcare provider will give you FASLODEX by injection into the muscle of each buttock.
- Your healthcare provider may change your dose of FASLODEX if needed.

What are the possible side effects of FASLODEX?

FASLODEX may cause serious side effects, including:

- **Injection site related nerve damage.** Call your healthcare provider if you develop any of the following symptoms in your legs following a FASLODEX injection:
  - numbness
  - tingling
  - weakness

The most common side effects of FASLODEX include:

- injection site pain
- nausea
- muscle, joint, and bone pain
- headache
- back pain
- tiredness
- pain in arms, hands, legs, or feet
- hot flashes
- vomiting
- loss of appetite
- weakness
- cough
- shortness of breath
- constipation
- increased liver enzymes
- diarrhea

FASLODEX may cause fertility problems in males and females. Talk to your healthcare provider if you plan to become pregnant.
Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all of the possible side effects with FASLODEX. For more information, ask your healthcare provider or pharmacist.
Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of FASLODEX

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about FASLODEX that is written for health professionals.

What are the ingredients in FASLODEX?

Active ingredient: fulvestrant.
Inactive ingredients: alcohol, benzyl alcohol, benzyl benzoate, and castor oil.

Distributed by:
AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850
Manufactured for:
AstraZeneca UK Limited
Macclesfield, Cheshire, England
By: Vetter Pharma-Fertigung GMBH & Co. KG
Ravensburg, Germany
For more information, go to www.FASLODEX.com or call 1-800-236-9933.

This Patient Information has been approved by the U.S. Food and Drug Administration Revised: 1/2021