Proposed packaging material		
Code	FASLODEX 500 (2s) PFS-PI-01.04	
Submission	☐NDA ☐Renewal ☑Variation change detail no.: -	
Code of previous version	N/A	
Changes	Additional Indication – Combination with Abemaciclib and Ribociclib	
Reference	☑CDS version: CDS Faslodex V.5.0 / Doc ID-003518776 ☐CPIL version:	☐SmPC country/version/date: ☑GRL approval: 24 June 2022
Name & Date	FTA – 5 Juli 2024	

FASLODEX 500 mg

Fulvestrant

Solution for injection

Qualitative and quantitative composition

One pre-filled syringe contains 250 mg fulvestrant in 5 ml solution.

Pharmaceutical form

Solution for injection. Clear, colourless to yellow, viscous solution.

Therapeutic indications

Monotherapy

- Treatment of postmenopausal women with estrogen receptor positive, locally advanced or metastatic breast cancer for disease relapse on or after adjuvant anti-estrogen therapy or disease progression on therapy with an anti-estrogen.
- Treatment of estrogen receptor-positive, human epidermal growth receptor 2 (HER2) - negative locally advanced or metastatic breast cancer in postmenopausal women not previously treated with endocrine therapy.

Combination Therapy

FASLODEX is indicated in combination with abemaciclib for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer in women with disease progression after endocrine therapy.

In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinising hormone releasing hormone (LHRH) agonist.

Note: for women < 60 years old, serum FSH and estradiol should be measured to assure postmenopausal status, unless bilateral oophorectomy has been done.

FASLODEX is indicated in combination with ribociclib for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in postmenopausal women, as initial endocrine based therapy or after disease progression following endocrine therapy.

Posology and method of administration

Posology

Monotherapy

Adult females (including Elderly)

The recommended dose is 500 mg at intervals of one month, with an additional 500 mg dose given two weeks after the initial dose.

Combination therapy

When FASLODEX is used in combination with abemaciclib, or ribociclib, the recommended dose of FASLODEX is 500 mg to be administered intramuscularly on Days 1, 15, 29, and once monthly thereafter.

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.

Prior to the start of treatment with the combination of FASLODEX plus abemaciclib, and throughout its duration, pre/perimenopausal women should be treated with LHRH agonists according to local clinical practice.

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

Special populations

Renal impairment

No dose adjustments are recommended for patients with mild to moderate renal impairment (creatinine clearance ≥ 30 ml/min). Safety and efficacy have not been evaluated in patients with severe renal impairment (creatinine clearance < 30 ml/min), and, therefore, caution is recommended in these patients (see section Special warnings and precautions for use).

Hepatic impairment

No dose adjustments are recommended for patients with mild to moderate hepatic impairment. However, as fulvestrant exposure may be increased, Faslodex should be used with caution in these patients. There are no data in patients with severe hepatic impairment (see sections Contraindications, Special warning and precautions for use and Pharmacokinetic properties).

Paediatric population

The safety and efficacy of Faslodex in children from birth to 18 years of age have not been established. Currently available data are described in sections Pharmacodynamic propertiesand Pharmacokinetic properties, but no recommendation on a posology can be made.

Method of administration

Faslodex should be administered as two consecutive 5 ml injections by slow intramuscular injection (1-2 minutes/injection), one in each buttock (gluteal area).
Caution should be taken if injecting Faslodex at the dorsogluteal site due to the proximity of the underlying sciatic nerve.

For detailed instructions for administration, see section Special precautions for disposal and other handling.

Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section List of excipients.
Pregnancy and lactation (see section Fertility, pregnancy, and lactation).
Severe hepatic impairment (see sections Special warning and precautions for use and Pharmacokinetic properties).

See abemaciclib local Prescribing Information for Contraindications.

See ribociclib local Prescribing Information for Contraindications.

Special warnings and precautions for use

Faslodex should be used with caution in patients with mild to moderate hepatic impairment (see sections Posology and method of administration, Contraindications and Pharmacokinetic properties).

Faslodex should be used with caution in patients with severe renal impairment (creatinine clearance less than 30 ml/min).

Due to the intramuscular route of administration, Faslodex should be used with caution if treating patients with bleeding diatheses, thrombocytopenia or those taking anticoagulant treatment.

Thromboembolic events are commonly observed in women with advanced breast cancer and have been observed in clinical studies with Faslodex (see section Undesirable effects). This should be taken into consideration when prescribing Faslodex to patients at risk.

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 sections Posology and method of administration and Undesirable effects).

There are no long-term data on the effect of fulvestrant on bone. Due to the mechanism of action of fulvestrant, there is a potential risk of osteoporosis.

Ethanol: Faslodex contains 10% w/v ethanol (alcohol) as an excipient, i.e. up to 500 mg per injection, equivalent to 10 ml beer or 4 ml. This may be harmful for those suffering from alcoholism and should be taken into account in high risk groups such as patients with liver disease and epilepsy.

Benzyl alcohol: Faslodex contains benzyl alcohol as an excipient which may cause allergic reactions.

Interference with estradiol antibody assays

Due to the structural similarity of fulvestrant and estradiol, fulvestrant may interfere with antibody based-estradiol assays and may result in falsely increased levels of estradiol.

Paediatric population

Faslodex is not recommended for use in children and adolescents as safety and efficacy have not been established in this group of patients (see section Pharmacodynamic properties).

See abemaciclib local Prescribing Information for Special warnings and precautions for use.

See ribociclib local Prescribing Information for Special warnings and precautions for use.

Interaction with other medicinal products and other forms of interaction

A clinical interaction study with midazolam (substrate of CYP3A4) demonstrated that fulvestrant does not inhibit CYP3A4. Clinical interaction studies with rifampicin (inducer of CYP3A4) and ketoconazole (inhibitor of CYP3A4) showed no clinically relevant change in fulvestrant clearance. Dose adjustment is therefore not necessary in patients who are receiving fulvestrant and CYP3A4 inhibitors or inducers concomitantly.

Fertility, pregnancy and lactation

Women of childbearing potential

Patients of child-bearing potential should use effective contraception during treatment with Faslodex and for 2 years after the last dose.

Pregnancy

Faslodex is contraindicated in pregnancy (see section Contraindications). Fulvestrant has been shown to cross the placenta after single intramuscular doses in rat and rabbit. Studies in animals have shown reproductive toxicity including an increased incidence of foetal abnormalities and deaths (see section Preclinical safety data). If pregnancy occurs while taking Faslodex, the patient must be informed of the potential hazard to the foetus and potential risk for loss of pregnancy.

Breast-feeding

Breast-feeding must be discontinued during treatment with Faslodex. Fulvestrant is excreted in milk in lactating rats. It is not known whether fulvestrant is excreted in human milk. Considering the potential for serious adverse reactions due to fulvestrant in breast-fed infants, use during lactation is contraindicated (see section Contraindications).

Fertility

The effects of Faslodex on fertility in humans has not been studied.

Effects on ability to drive and use machines

Faslodex has no or negligible influence on the ability to drive or use machines. However, since asthenia has been reported very commonly with Faslodex, caution should be observed by those patients who experience this adverse reaction when driving or operating machinery.

Undesirable effects

This section provides information based on all adverse reactions from clinical studies, post-marketing studies or spontaneous reports. The most frequently reported adverse reactions are injection site reactions, asthenia, nausea, and increased hepatic enzymes (ALT, AST, ALP).

The following frequency categories for adverse drug reactions (ADRs) were calculated based on the Faslodex 500 mg treatment group in pooled safety analyses of studies that compared Faslodex 500 mg with Faslodex 250 mg [CONFIRM (Study D6997C00002), FINDER 1 (Study D6997C00004), FINDER 2 (Study D6997C00006), and NEWEST (Study D6997C00003) studies], or from FALCON (Study D699BC00001) alone that compared Faslodex 500 mg with anastrozole 1 mg. Where frequencies differ between the pooled safety analysis and FALCON, the highest frequency is presented. The frequencies in the following table were based on all reported adverse drug reactions, regardless of the investigator assessment of causality.

Adverse reactions listed below are classified according to frequency and System Organ Class (SOC). Frequency groupings are defined according to the following convention: Very common (≥1/10), Common (≥1/100 to <1/10), Uncommon (≥1/1,000 to <1/100). Within each frequency grouping adverse reactions are reported in order of decreasing seriousness.

Table 1 Adverse Drug Reactions

Adverse reactions by system organ class and frequency

Infections and infestations	Common	Urinary tract infections
Blood and lymphatic system disorders	Common	Reduced platelet count[e]
Immune system disorders	Very common	Hypersensitivity reactions[e]
Metabolism and nutrition disorders	Common	Anorexia[a]
Nervous system disorders	Common	Headache
Vascular disorders	Very common	Hot flushes[e]
	Common	Venous thromboembolism[a]
Gastrointestinal disorders	Very common	Nausea
	Common	Vomiting, diarrhoea
Hepatobiliary disorders	Very common	Elevated hepatic enzymes (ALT, AST, ALP)[a]
	Common	Elevated bilirubin[a]
	Uncommon	Hepatic failure[c, f], hepatitis[f], elevated gamma-GT[f]
Skin and subcutaneous tissue disorders	Very common	Rash[e]
Musculoskeletal and connective tissue disorders	Very common	Joint and musculoskeletal pain[d]
	Common	Back pain[a]
Reproductive system and breast disorders	Common	Vaginal haemorrhage[e]
	Uncommon	Vaginal moniliasis[f], leukorrhea[f]
General disorders and administration site conditions	Very common	Asthenia[a], injection site reactions[b]
	Common	Neuropathy peripheral[e], sciatica[e]
	Uncommon	Injection site haemorrhage[f], injection site haematoma[f], neuralgia[c,f]

[a] Includes adverse drug reactions for which the exact contribution of Faslodex cannot be assessed due to the underlying disease.

[b] The term injection site reactions does not include the terms injection site haemorrhage, injection site haematoma, sciatica, neuralgia and neuropathy peripheral.

[c] The event was not observed in major clinical studies (CONFIRM, FINDER 1, FINDER 2, NEWEST). The frequency has been calculated using the upper limit of the 95% confidence interval for the point estimate. This is calculated as 3/560 (where 560 is the number of patients in the major clinical studies), which equates to a frequency category of 'uncommon'.

[d] Includes: arthralgia, and less frequently musculoskeletal pain, myalgia and pain in extremity.

[e] Frequency category differs between pooled safety dataset and FALCON.

[f] ADR was not observed in FALCON.

Description of selected adverse reactions

The descriptions included below are based on the safety analysis set of 228 patients who received at least one (1) dose of fulvestrant and 232 patients who received at least one (1) dose of anastrozole, respectively in the Phase 3 FALCON study.

Joint and musculoskeletal pain
In the FALCON study, the number of patients who reported an adverse reaction of joint and musculoskeletal pain was 65 (31.2%) and 48 (24.1%) for fulvestrant and anastrozole arms, respectively. Of the 65 patients in the Faslodex arm, 40% (26/65) of patients reported joint and musculoskeletal pain within the first month of treatment, and 66.2% (43/65) of patients within the first 3 months of treatment. No patients reported events that were CTCAE Grade ≥3 or that required a dose reduction, dose interruption, or discontinued treatment due to these adverse reactions.

See abemaciclib local Prescribing Information for Undesirable effects.
See ribociclib local Prescribing Information for Undesirable effects.

Overdose
There are isolated reports of overdose with Faslodex in humans. If overdose occurs, symptomatic supportive treatment is recommended. Animal studies suggest that no effects other than those related directly or indirectly to antiestrogenic activity were evident with higher doses of fulvestrant (see section Preclinical safety data).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:
Pusat Farmakovigilans/MESO Nasional
Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif Badan Pengawas Obat dan Makanan
Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext.1079
Website: https://e-meso.pom.go.id/ADR

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties
Pharmacotherapeutic group: Endocrine therapy, Antiestrogens, ATC code: L02BA03

Mechanism of action and pharmacodynamic effects
Fulvestrant is a competitive estrogen receptor (ER) antagonist with an affinity comparable to estradiol. Fulvestrant blocks the trophic actions of estrogens without any partial agonist (estrogen-like) activity. The mechanism of action is associated with downregulation of estrogen receptor protein levels. Clinical studies in postmenopausal women with primary breast cancer have shown that fulvestrant significantly downregulates ER protein in ER positive tumours compared with placebo. There was also a significant decrease in progesterone receptor expression consistent with a lack of intrinsic estrogen agonist effects. It has also been shown that fulvestrant 500 mg downregulates ER and the proliferation marker Ki67, to a greater degree than fulvestrant 250 mg in breast tumours in postmenopausal neoadjuvant setting.

Clinical efficacy and safety in advanced breast cancer
Two phase III clinical trials Studies 9238IL/0020 and 9238IL/0021 were completed in a total of 851 postmenopausal women with advanced breast cancer who had disease recurrence on or after adjuvant endocrine therapy or progression following endocrine therapy for advanced disease. 77% of the study population had estrogen receptor positive breast cancer. These trials compared the safety and efficacy of monthly administration of Faslodex 250 mg versus the daily administration of 1 mg anastrozole (aromatase inhibitor). Overall, Faslodex at the 250 mg monthly dose was at least as

effective as anastrozole in terms of progression-free survival, objective response, and time to death. There were no statistically significant differences in any of these endpoints between the two treatment groups. Progression-free survival was the primary endpoint. Combined analysis of both trials showed that 83% of patients who received Faslodex progressed, compared with 85% of patients who received anastrozole. Combined analysis of both trials showed the hazard ratio of Faslodex 250 mg to anastrozole for progression-free survival was 0.95 (95% CI 0.82 to 1.10). The objective response rate for Faslodex 250 mg was 19.2% compared with 16.5% for anastrozole. The median time to death was 27.4 months for patients treated with Faslodex and 27.6 months for patients treated with anastrozole. The hazard ratio of Faslodex 250 mg to anastrozole for time to death was 1.01 (95% CI 0.86 to 1.19).

A Phase 3 clinical study 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. The study included 423 patients whose disease had recurred or progressed during antiestrogen therapy (AE subgroup) and 313 patients whose disease had recurred or progressed during aromatase inhibitor therapy (AI subgroup). This study compared the efficacy and safety of Faslodex 500 mg (n=362) with Faslodex 250 mg (n=374). Progression-free survival (PFS) was the primary endpoint; key secondary efficacy endpoints included objective response rate (ORR), clinical benefit rate (CBR) and overall survival (OS). Efficacy results for the CONFIRM study are summarized in Table 2.

Table 2 Summary of results of the primary efficacy endpoint (PFS) and key secondary efficacy endpoints in the CONFIRM study

Variable	Type of treatment comparison	Faslodex 500 mg (N=362)	Faslodex 250 mg (N=374)	Comparison between groups estimate; (Faslodex 500 mg/Faslodex 250 mg) Hazard ratio	95% CI	p-value
PFS	**K-M median in months; hazard ratio**					
All Patients		6.5	5.5	0.80	0.68, 0.94	0.006
-AE subgroup (n=423)		8.6	5.8	0.76	0.62, 0.94	0.013
-AI subgroup (n=313)[a]		5.4	4.1	0.85	0.67, 1.08	0.195
OS[b]	**K-M median in months; hazard ratio**					
All Patients		26.4	22.3	0.81	0.69, 0.96	0.016[c]
-AE subgroup (n=423)		30.6	23.9	0.79	0.63, 0.99	0.038[c]
-AI subgroup (n=313)[a]		24.1	20.8	0.86	0.67, 1.11	0.241[c]
Variable	**Type of treatment comparison**	**Faslodex 500 mg (N=362)**	**Faslodex 250 mg (N=374)**	**Comparison between groups estimate; (Faslodex 500 mg/Faslodex 250 mg) Absolute difference in %**	**95% CI**	
ORR[d]	**% of patients with OR; absolute difference in %**					
All Patients		13.8	14.6	-0.8	-5.8, 6.3	
-AE subgroup (n=296)		18.1	19.1	-1.0	-8.2, 9.3	

-AI subgroup (n=205)[a]	7.3	8.3	-1.0	-5.5, 9.8
CBR[e] % of patients with CB; absolute difference in %				
All Patients	45.6	39.6	6.0	-1.1, 13.3
-AE subgroup (n=423)	52.4	45.1	7.3	-2.2, 16.6
-AI subgroup (n=313)[a]	36.2	32.3	3.9	-6.1, 15.2

[a] Faslodex is indicated in patients whose disease had recurred or progressed on an antiestrogen therapy. The results in the AI subgroup are inconclusive.

[b] OS is presented for the final survival analyses at 75% maturity.

[c] Nominal p-value with no adjustments made for multiplicity between the initial overall survival analyses at 50% maturity and the updated survival analyses at 75% maturity.

[d] ORR was assessed in patients who were evaluable for response at baseline (i.e. those with measurable disease at baseline: 240 patients in the Faslodex 500 mg group and 261 patients in the Faslodex 250 mg group).

[e] Patients with a best objective response of complete response, partial response or stable disease ≥24 weeks.

PFS:Progression-free survival; ORR:Objective response rate; OR:Objective response; CBR:Clinical benefit rate; CB:Clinical benefit; OS:Overall survival; K-M:Kaplan-Meier; CI:Confidence interval; AI:Aromatase inhibitor; AE:Antiestrogen.

A Phase 3, randomised, double-blind, double-dummy, multicentre study of Faslodex 500 mg versus anastrozole 1 mg was conducted in postmenopausal women with ER-positive and/or PgR-positive locally advanced or metastatic breast cancer who had not previously been treated with any hormonal therapy. A total of 462 patients were randomised 1:1 sequentially to receive either fulvestrant 500 mg or anastrozole 1 mg.

Randomisation was stratified by disease setting (locally advanced or metastatic), prior chemotherapy for advanced disease, and measurable disease.

The primary efficacy endpoint of the study was investigator assessed progression-free survival (PFS) evaluated according to RECIST 1.1 (Response Evaluation Criteria in Solid Tumours). Key secondary efficacy endpoints included overall survival (OS) and objective response rate (ORR).

Patients enrolled in this study had a median age of 63 years (range 36-90). The majority of patients (87.0%) had metastatic disease at baseline. Fifty-five percent (55.0%) of patients had visceral metastasis at baseline. A total of 17.1% of patients received a prior chemotherapy regimen for advanced disease; 84.2% of patients had measurable disease.

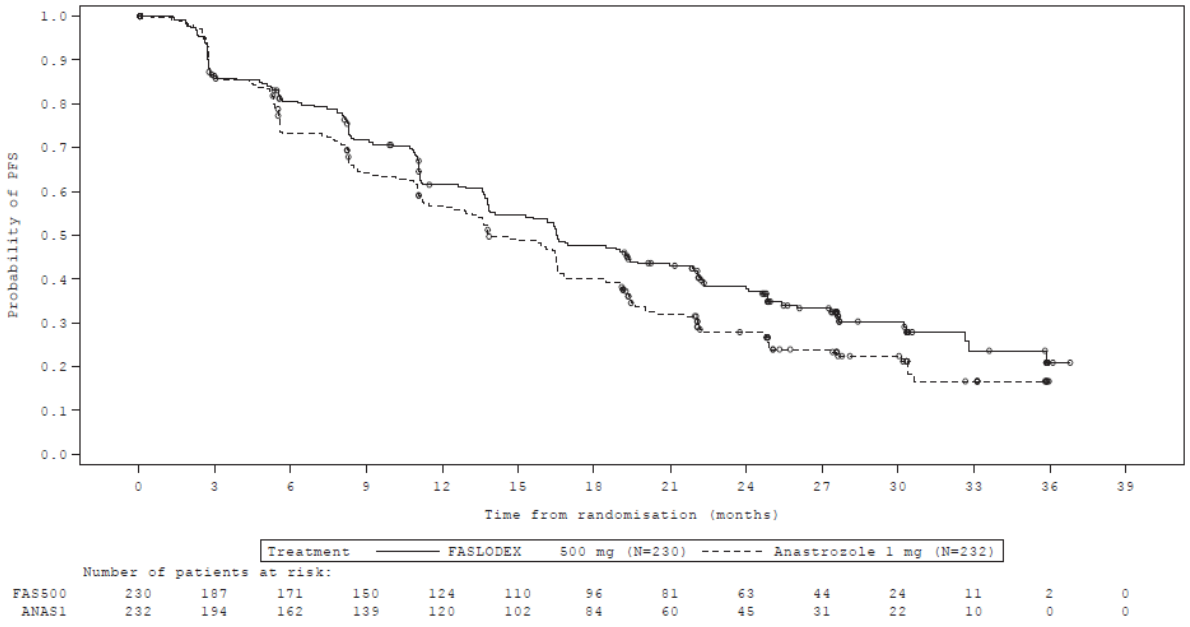
Consistent results were observed across the majority of pre-specified patient subgroups. For the subgroup of patients with disease limited to non-visceral metastasis (n=208), the HR was 0.592 (95% CI: 0.419, 0.837) for the Faslodex arm compared to the anastrozole arm. For the subgroup of patients with visceral metastasis (n=254), the HR was 0.993 (95% CI: 0.740, 1.331) for the Faslodex arm compared to the anastrozole arm. The efficacy results of the FALCON study are presented in Table 3 and Figure 1.

Table 3 Summary of results of the primary efficacy endpoint (PFS) and key secondary efficacy endpoints (Investigator Assessment, Intent-To-Treat Population) ─ FALCON study

	Faslodex 500 mg (N=230)	Anastrozole 1 mg (N=232)
Progression-Free Survival		
Number of PFS Events (%)	143 (62.2%)	166 (71.6%)
PFS Hazard Ratio (95% CI) and p-value	HR 0.797 (0.637 - 0.999) p = 0.0486	
PFS Median [months (95% CI)]	16.6 (13.8, 21.0)	13.8 (12.0, 16.6)
Number of OS Events*	67 (29.1%)	75 (32.3%)
OS Hazard Ratio (95% CI) and p-value	HR 0.875 (0.629 – 1.217) p = 0.4277	
ORR**	89 (46.1%)	88 (44.9%)
ORR Odds Ratio (95% CI) and p-value	OR 1.074 (0.716 – 1.614) p = 0.7290	
Median DoR (months)	20.0	13.2
CBR	180 (78.3%)	172 (74.1%)
CBR Odds Ratio (95% CI) and p-value	OR 1.253 (0.815 – 1.932) p = 0.3045	

*(31% maturity)-not final OS analysis
**for patients with measurable disease

Figure 1 Kaplan-Meier Plot of Progression-Free Survival (Investigator Assessment, Intent-ToTreat Population) ─ FALCON Study



Two Phase 3 clinical studies were completed in a total of 851 postmenopausal women with advanced breast cancer who had disease recurrence on or after adjuvant endocrine therapy or progression following endocrine therapy for advanced disease. Seventy seven percent (77%) of the study

population had estrogen receptor positive breast cancer. These studies compared the safety and efficacy of monthly administration of Faslodex 250 mg versus the daily administration of 1 mg anastrozole (aromatase inhibitor). Overall, Faslodex at the 250 mg monthly dose was at least as effective as anastrozole in terms of progression-free survival, objective response, and time to death. There were no statistically significant differences in any of these endpoints between the two treatment groups. Progression-free survival was the primary endpoint. Combined analysis of both studies showed that 83% of patients who received Faslodex progressed, compared with 85% of patients who received anastrozole. Combined analysis of both studies showed the hazard ratio of Faslodex 250 mg to anastrozole for progression-free survival was 0.95 (95% CI 0.82 to 1.10). The objective response rate for Faslodex 250 mg was 19.2% compared with 16.5% for anastrozole. The median time to death was 27.4 months for patients treated with Faslodex and 27.6 months for patients treated with anastrozole. The hazard ratio of Faslodex 250 mg to anastrozole for time to death was 1.01 (95% CI 0.86 to 1.19).

Effects on the postmenopausal endometrium
Preclinical data do not suggest a stimulatory effect of fulvestrant on the postmenopausal endometrium (see section Preclinical safety data). A 2-week study in healthy postmenopausal volunteers treated with 20 µg per day ethinylestradiol showed that pretreatment with Faslodex 250 mg resulted in significantly reduced stimulation of the postmenopausal endometrium, compared to pre-treatment with placebo, as judged by ultrasound measurement of endometrium thickness.

Neoadjuvant treatment for up to 16 weeks in breast cancer patients treated with either Faslodex 500 mg or Faslodex 250 mg did not result in clinically significant changes in endometrial thickness, indicating a lack of agonist effect. There is no evidence of adverse endometrial effects in the breast cancer patients studied. No data are available regarding endometrial morphology.

In two short-term studies (1 and 12 weeks) in premenopausal patients with benign gynaecologic disease, no significant differences in endometrial thickness were observed by ultrasound measurement between fulvestrant and placebo groups.

Effects on bone
There are no long-term data on the effect of fulvestrant on bone. Neoadjuvant treatment for up to 16 weeks in breast cancer patients with either Faslodex 500 mg or Faslodex 250 mg did not result in clinically significant changes in serum bone-turnover markers.

Paediatric population
Faslodex is not indicated for use in children. The European Medicines Agency has waived the obligation to submit the results of studies with Faslodex in all subsets of the paediatric population in breast cancer (see section Posology and method of administration for information on paediatric use).

An open-label Phase 2 study investigated the safety, efficacy and pharmacokinetics of fulvestrant in 30 girls aged 1 to 8 years with Progressive Precocious Puberty associated with McCune Albright Syndrome (MAS). The paediatric patients received 4 mg/kg monthly intramuscular dose of fulvestrant. This 12-month study investigated a range of MAS endpoints and showed a reduction in the frequency of vaginal bleeding and a reduction in the rate of bone age advancement. The steady-state trough concentrations of fulvestrant in children in this study were consistent with that in adults (see section Pharmacokinetic properties). There were no new safety concerns arising from this small study, but 5-year data are yet not available.

Combination therapy with abemaciclib
MONARCH 2 was a randomized, placebo-controlled, multicenter study conducted in women with HR-positive, HER2-negative metastatic breast cancer with disease progression following endocrine therapy treated with FASLODEX plus abemaciclib versus FASLODEX plus placebo. Randomization was

stratified by disease site (visceral, bone only, or other) and by sensitivity to prior endocrine therapy (primary or secondary resistance). A total of 669 patients received intramuscular injection of FASLODEX 500 mg on Days 1 and 15 of cycle 1 and then on Day 1 of cycle 2 and beyond (28-day cycles), plus abemaciclib or placebo orally twice daily. Pre/perimenopausal women were enrolled in the study and received the gonadotropin-releasing hormone agonist goserelin for at least 4 weeks prior to and for the duration of MONARCH 2. Patients remained on continuous treatment until development of progressive disease or unmanageable toxicity.

Patient median age was 60 years (range, 32-91 years), and 37% of patients were older than 65. The majority were White (56%), and 99% of patients had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Twenty percent (20%) of patients had *de novo* metastatic disease, 27% had bone only disease, and 56% had visceral disease. Twenty-five percent (25%) of patients had primary endocrine therapy resistance. Seventeen percent (17%) of patients were pre- or perimenopausal.

The efficacy results from the MONARCH 2 study are summarized in Table 4, Figure 2. PFS assessment based on a blinded independent radiologic review was consistent with the investigator assessment. Consistent results were observed across patient stratification subgroups of disease site and endocrine therapy resistance for PFS and OS.

Table 4 Efficacy Results in MONARCH 2 (Intent-to-Treat Population)

	FASLODEX plus Abemaciclib	**FASLODEX plus Placebo**
Progression-Free Survival (Investigator Assessment)	**N=446**	**N=223**
Number of patients with an event (n, %)	222 (49.8)	157 (70.4)
Median (months, 95% CI)	16.4 (14.4, 19.3)	9.3 (7.4, 12.7)
Hazard ratio (95% CI) [1]	0.553 (0.449, 0.681)	
p-value[1]	p<0.0001	
Overall Survival[2]		
Number of deaths (n, %)	211 (47.3)	127 (57.0)
Median OS in months (95% CI)	46.7 (39.2, 52.2)	37.3 (34.4, 43.2)
Hazard ratio (95% CI)[1]	0.757 (0.606, 0.945)	
p-value[1]	p=0.0137	
Objective Response for Patients with Measurable Disease	**N=318**	**N=164**
Objective response rate[3] (n, %)	153 (48.1)	35 (21.3)
95% CI	42.6, 53.6	15.1, 27.6

Abbreviations: CI=confidence interval, OS=overall survival.

[1] Stratified by disease site (visceral metastases vs. bone-only metastases vs. other) and endocrine therapy resistance (primary resistance vs. secondary resistance)

[2] Data from a pre-specified interim analysis (77% of the number of events needed for the planned final analysis) with the p-value compared with the allocated alpha of 0.021.

[3] Complete response + partial response.

Figure 2. Kaplan-Meier Curves of Progression-Free Survival: FASLODEX Plus Abemaciclib versus FASLODEX plus Placebo (MONARCH 2)

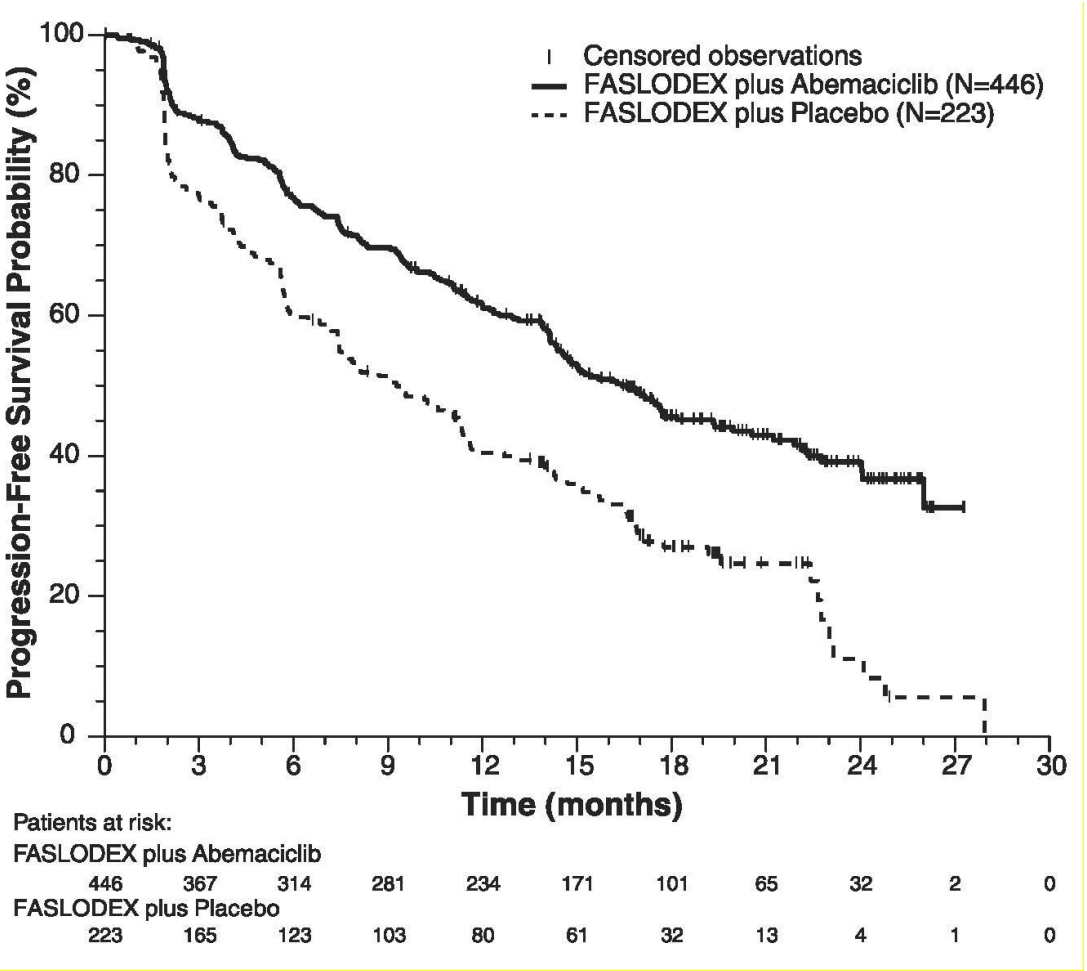
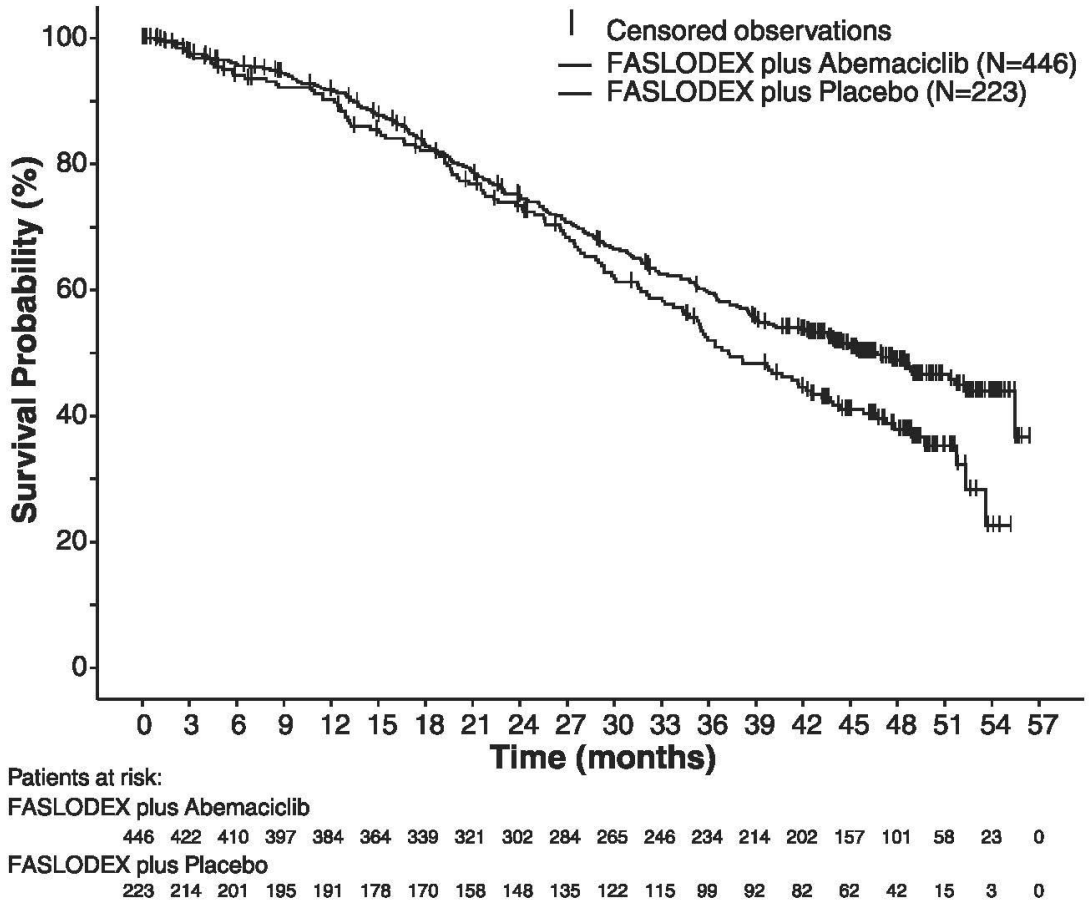

Censored observations
FASLODEX plus Abemaciclib (N=446)
FASLODEX plus Placebo (N=223)
Progression-Free Survival Probability (%)
100
80
60
40
20
0
0
3
6
9
12
15
18
21
24
27
30
Time (months)
Patients at risk:
FASLODEX plus Abemaciclib
446 367 314 281 234 171 101 65 32 2 0
FASLODEX plus Placebo
223 165 123 103 80 61 32 13 4 1 0

Figure 3. Kaplan-Meier Curves of Overall Survival: FASLODEX plus Abemaciclib versus FASLODEX plus Placebo (MONARCH 2)



Combination therapy with ribociclib

MONALEESA-3 was a randomized double-blind, placebo-controlled study of FASLODEX plus ribociclib versus FASLODEX plus placebo conducted in postmenopausal women with hormone receptor positive, HER2-negative, advanced breast cancer who have received no or only one line of prior endocrine treatment.

A total of 726 patients were randomized in a 2:1 ratio to receive FASLODEX plus ribociclib or FASLODEX plus placebo and stratified according to the presence of liver and/or lung metastases and prior endocrine therapy for advanced or metastatic disease. Fulvestrant 500 mg was administered intramuscularly on Days 1, 15, 29, and once monthly thereafter, with either ribociclib 600 mg or placebo given orally once daily for 21 consecutive days followed by 7 days off until disease progression or unacceptable toxicity. The major efficacy outcome measure for the study was investigator-assessed progression-free survival (PFS) using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.

Patients enrolled in this study had a median age of 63 years (range 31 to 89). Of the patients enrolled, 47% were 65 years and older, including 14% age 75 years and older. The patients enrolled were primarily Caucasian (85%), Asian (9%), and Black (0.7%). Nearly all patients (99.7%) had an ECOG performance status of 0 or 1. First and second line patients were enrolled in this study (of which 19% had *de novo* metastatic disease). Forty-three percent (43%) of patients had received chemotherapy in the adjuvant vs. 13% in the neoadjuvant setting and 59% had received endocrine therapy in the adjuvant vs. 1% in the neoadjuvant setting prior to study entry. Twenty-one percent (21%) of patients

had bone only disease and 61% had visceral disease. Demographics and baseline disease characteristics were balanced and comparable between study arms.

The efficacy results from MONALEESA-3 are summarized in Table 8 and Figure 5. Consistent results were observed in stratification factor subgroups of disease site and prior endocrine treatment for advanced disease.

Table 5 Efficacy Results – MONALEESA-3 (Investigator Assessment, Intent-to-Treat Population)

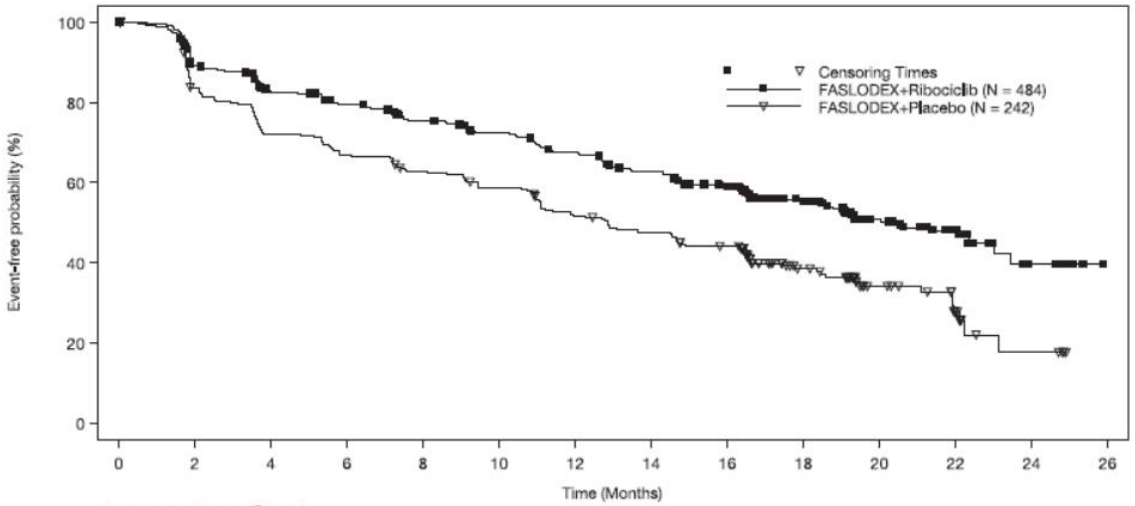
	FASLODEX plus Ribociclib	**FASLODEX plus Placebo**
Progression-free survival*	**N=484**	**N=242**
Events (n, %)	210 (43.4%)	151 (62.4%)
Median (months, 95% CI)	20.5 (18.5, 23.5)	12.8 (10.9, 16.3)
Hazard Ratio (95% CI)	0.593 (0.480 to 0.732)	
p-value[1]	<0.0001	
Overall Survival	**N=484**	**N=242**
Events (n, %)	167 (34.5%)	108 (44.6%)
Median (months, 95% CI)	NR (42.5, NR)	40.0 (37.0, NR)
Hazard Ratio (95% CI)	0.724 (0.568, 0.924)	
p-value[1]	0.00455	
Overall Response Rate[2]*	**N=379**	**N=181**
Patients with measurable disease (, 95% CI)	40.9 (35.9, 45.8)	28.7 (22.1, 35.3)

Abbreviation: NR, not reached

1. p-value is obtained from the one-sided log-rank
2. Based on confirmed responses

*Investigator Assessment

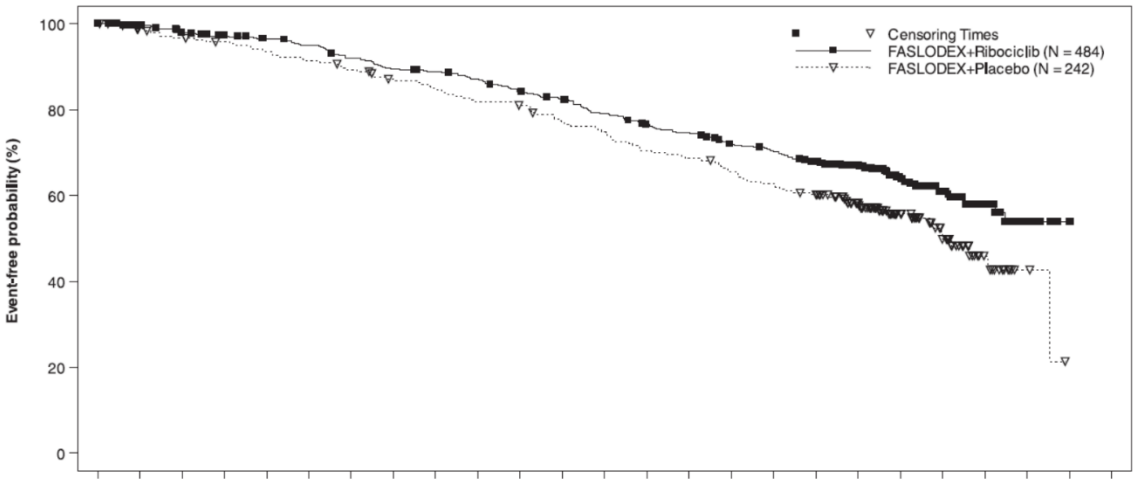
Figure 4. Kaplan-Meier Progression Free Survival Curves – MONALEESA-3 (Intent-To-Treat Population, Investigator assessment)]



Number of patients still at risk

Time (months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26
FASLODEX+Ribociclib	484	403	365	347	324	305	282	259	235	155	78	52	13	0
FASLODEX+Placebo	242	195	168	156	144	134	116	106	95	53	27	14	4	0

Figure 5. Kaplan-Meier plot of Overall Survival – MONALEESA-3 (Intent -to-Treat Population)



Number of patients still at risk

Time (Months)	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48
FASLODEX+Ribociclib	484	470	454	444	436	428	414	402	397	389	374	365	348	334	326	309	300	287	237	159	92	41	14	2	0
FASLODEX+Placebo	242	233	227	223	218	213	207	199	194	187	184	174	169	159	155	147	141	134	107	64	37	14	3	0	0

Pharmacokinetic properties

Absorption

After administration of Faslodex long-acting intramuscular injection, fulvestrant is slowly absorbed and maximum plasma concentrations (C_{max}) are reached after about 5 days. Administration of Faslodex 500 mg regimen achieves exposure levels at, or close to, steady state within the first month of dosing (mean [CV]: AUC 475 [33.4%] ng.days/ml, C_{max} 2Pharmacodynamic properties[35.3%] ng/ml, C_{min}

16.3 [25.9%] ng/ml, respectively). At steady state, fulvestrant plasma concentrations are maintained within a relatively narrow range with up to an approximately 3-fold difference between maximum and trough concentrations. After intramuscular administration, the exposure is approximately dose-proportional in the dose range 50 to 500 mg.

Distribution

Fulvestrant is subject to extensive and rapid distribution. The large apparent volume of distribution at steady state (Vd_{ss}) of approximately 3 to 5 l/kg suggests that distribution is largely extravascular. Fulvestrant is highly (99%) bound to plasma proteins. Very low density lipoprotein (VLDL), low density lipoprotein (LDL), and high density lipoprotein (HDL) fractions are the major binding components. No interaction studies were conducted on competitive protein binding. The role of sex hormone-binding globulin (SHBG) has not been determined.

Biotransformation

The metabolism of fulvestrant has not been fully evaluated, but involves combinations of a number of possible biotransformation pathways analogous to those of endogenous steroids. Identified metabolites (includes 17-ketone, sulphone, 3-sulphate, 3- and 17-glucuronide metabolites) are either less active or exhibit similar activity to fulvestrant in antiestrogen models. Studies using human liver preparations and recombinant human enzymes indicate that CYP3A4 is the only P450 isoenzyme involved in the oxidation of fulvestrant; however, non-P450 routes appear to be more predominant *in vivo*. *In vitro* data suggest that fulvestrant does not inhibit CYP450 isoenzymes.

Elimination

Fulvestrant is eliminated mainly in metabolised form. The major route of excretion is via the faeces, with less than 1% being excreted in the urine. Fulvestrant has a high clearance, 11±1.7 ml/min/kg, suggesting a high hepatic extraction ratio. The terminal half-life ($t_{1/2}$) after intramuscular administration is governed by the absorption rate and was estimated to be 50 days.

Special populations

In a population pharmacokinetic analysis of data from Phase 3 studies, no difference in fulvestrant's pharmacokinetic profile was detected with regard to age (range 33 to 89 years), weight (40-127 kg) or race.

Renal impairment

Mild to moderate impairment of renal function did not influence the pharmacokinetics of fulvestrant to any clinically relevant extent.

Hepatic impairment

The pharmacokinetics of fulvestrant has been evaluated in a single-dose clinical study conducted in women with mild to moderate hepatic impairment (Child-Pugh class A and B). A high dose of a shorter duration intramuscular injection formulation was used. There was up to about 2.5-fold increase in AUC in women with hepatic impairment compared to healthy subjects. In patients administered Faslodex, an increase in exposure of this magnitude is expected to be well tolerated. Women with severe hepatic impairment (Child-Pugh class C) were not evaluated.

Paediatric population

The pharmacokinetics of fulvestrant has been evaluated in a clinical study conducted in 30 girls with Progressive Precocious Puberty associated with McCune Albright Syndrome (see section 5.1). The paediatric patients were aged 1 to 8 years and received 4 mg/kg monthly intramuscular dose of fulvestrant. The geometric mean (standard deviation) steady state trough concentration ($C_{min,ss}$) and AUC_{ss} was Posology and method of administration (0.9) ng/mL and 3680 (1020) ng*hr/mL, respectively. Although the data collected were limited, the steady-state trough concentrations of fulvestrant in children appear to be consistent with those in adults.

Preclinical safety data

The acute toxicity of fulvestrant is low.

Faslodex and other formulations of fulvestrant were well tolerated in animal species used in multiple dose studies. Local reactions, including myositis and granulomata at the injection site were attributed to the vehicle but the severity of myositis in rabbits increased with fulvestrant, compared to the saline

control. In toxicity studies with multiple intramuscular doses of fulvestrant in rats and dogs, the antiestrogenic activity of fulvestrant was responsible for most of the effects seen, particularly in the female reproductive system, but also in other organs sensitive to hormones in both sexes. Arteritis involving a range of different tissues was seen in some dogs after chronic (12 months) dosing.

In dog studies following oral and intravenous administration, effects on the cardiovascular system (slight elevations of the S-T segment of the ECG [oral], and sinus arrest in one dog [intravenous]) were seen. These occurred at exposure levels higher than in patients (C_{max} >15 times) and are likely to be of limited significance for human safety at the clinical dose.
Fulvestrant showed no genotoxic potential.

Fulvestrant showed effects upon reproduction and embryo/foetal development consistent with its antiestrogenic activity, at doses similar to the clinical dose. In rats, a reversible reduction in female fertility and embryonic survival, dystocia and an increased incidence of foetal abnormalities including tarsal flexure were observed. Rabbits given fulvestrant failed to maintain pregnancy. Increases in placental weight and post-implantation loss of foetuses were seen. There was an increased incidence of foetal variations in rabbits (backwards displacement of the pelvic girdle and 27 pre-sacral vertebrae).

A two-year oncogenicity study in rats (intramuscular administration of Faslodex) showed increased incidence of ovarian benign granulosa cell tumours in female rats at the high dose, 10 mg/rat/15 days and an increased incidence of testicular Leydig cell tumours in males. In a two-year mouse oncogenicity study (daily oral administration) there was an increased incidence of ovarian sex cord stromal tumours (both benign and malignant) at doses of 150 and 500 mg/kg/day. At the no-effect level for these findings, systemic exposure levels (AUC) were, in rats, approximately 1.5–fold the expected human exposure levels in females and 0.8-fold in males, and in mice, approximately 0.8-fold the expected human exposure levels in both males and females. Induction of such tumours is consistent with pharmacology-related endocrine feedback alterations in gonadotropin levels caused by antiestrogens in cycling animals. Therefore these findings are not considered to be relevant to the use of fulvestrant in postmenopausal women with advanced breast cancer.

PHARMACEUTICAL PARTICULARS

List of excipients

Ethanol (96 per cent)
Benzyl alcohol
Benzyl benzoate
Castor oil

Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

Shelf life

4 years

Special precautions for storage

Store and transport in a refrigerator (2°C - 8°C).

Temperature excursions outside 2°C - 8°C should be limited. This includes avoiding storage at temperatures exceeding 30°C, and not exceeding a 28 day period where the average storage temperature for the product is below 25°C (but above 2°C - 8°C). After temperature excursions, the product should be returned immediately to the recommended storage conditions (store and transport in a refrigerator 2°C - 8°C). Temperature excursions have a cumulative effect on the product quality and the 28 day time period must not be exceeded over the duration of the 4-year shelf life of Faslodex (see

section Shelf life). Exposure to temperatures below 2°C will not damage the product providing it is not stored below – 20°C.

Store the pre-filled syringe in the original package in order to protect from light.

Special precautions for disposal and other handling

Instructions for administration

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 section Special warning and precautions for use).

Warning - Do not autoclave safety needle (BD SafetyGlide™ Shielding Hypodermic Needle) before use. Hands must remain behind the needle at all times during use and disposal.

For each syringe:

- Remove glass syringe barrel from tray and check that it is not damaged.
- Peel open the safety needle (SafetyGlide™) outer packaging.
- Parenteral solutions must be inspected visually for particulate matter and discolouration prior to administration. Hold the syringe upright on the ribbed part (C). With the other

hand, take hold of the cap (A) and carefully tilt back and forth until the cap disconnects and can be pulled off, do not twist (see Figure 1).

Figure 1

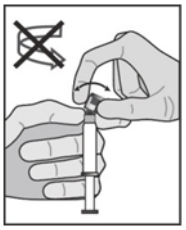
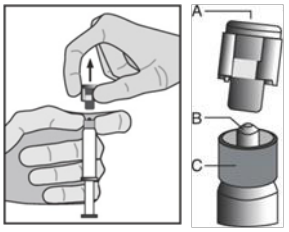


Figure 2



- Remove the cap (A) in a straight upward direction. To maintain sterility do not touch the syringe tip (B) (see Figure 2).

- Attach the safety needle to the syringe tip (Luer-Lok) and twist until firmly seated (see Figure 3).

- Check that the needle is locked to the Luer connector before moving out of the vertical plane.

- Pull shield straight off needle to avoid damaging needlepoint.

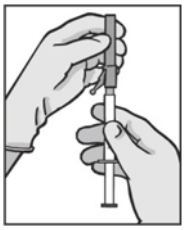
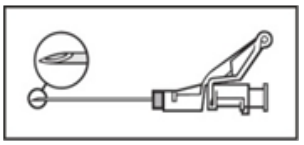


Figure 3

- Transport filled syringe to point of administration.
- Remove needle sheath.
- Expel excess gas from the syringe.

- Administer intramuscularly slowly (1-2 minutes/injection) into the buttock (gluteal area). For user convenience, the needle bevel-up position is oriented to the lever arm (see Figure 4).

Figure 4



- After injection, immediately apply a single-finger stroke to the activation assisted lever arm to activate the shielding mechanism (see Figure 5).

  NOTE: Activate away from self and others. Listen for click and visually confirm needle tip is fully covered.

Figure 5

Disposal

Pre-filled syringes are for single use **only**.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Pack Size

FASLODEX 500 mg, Box of 2 Pre-filled syringes @ 5 mL (DKI1759602343A1)

HARUS DENGAN RESEP DOKTER

Manufactured by

Vetter Pharma-Fertigung GmbH & Co. KG, Schützenstrasse 87, 88212 Ravensburg, Germany, release and secondary pack by AstraZeneca UK Limited, Macclesfield, Cheshire SK10 2NA, United Kingdom.

Imported by

PT AstraZeneca Indonesia

Cikarang, Bekasi – Indonesia

Date of revision of text

11 January 2024

ANGEL Doc ID : Doc ID-004917780

Proposed packaging material		
Code	FASLODEX 500 (2s) PFS-PI-01.03	
Submission	☐NDA ☐Renewal ☑Variation change detail no.: -	
Code of previous version	N/A	
Changes	Additional Indication – Combination with Abemaciclib and Ribociclib	
Reference	☐CDS version: ☑CPIL version: CPIL Faslodex V.3.0/ Doc ID-003518886	☐SmPC country/version/date: ☑GRL approval: 26 June 2022 and 10 January 2024
Name & Date	FTA – 19 July 2024	

Informasi untuk Pasien

Faslodex 500 mg Larutan untuk Injeksi
Fulvestrant

Bacalah seluruh isi leaflet ini dengan seksama sebelum Anda mulai menggunakan obat ini karena leaflet ini berisi hal-hal penting untuk Anda.

- Simpanlah leaflet ini. Anda mungkin perlu membacanya di kemudian hari
- Apabila Anda memiliki pertanyaan lebih lanjut, tanyakanlah dokter, apoteker, atau perawat Anda
- Obat ini telah diresepkan khusus untuk Anda. Dilarang memberikan obat ini untuk orang lain karena hal ini dapat membahayakan mereka, meskipun tanda dan gejala penyakit mereka sama dengan yang Anda alami.
- Apabila Anda mengalami efek samping, komunikasikanlah pada dokter atau apoteker Anda. Perhatikan pula kemungkinan efek samping yang tidak terdaftar dalam leaflet ini

Informasi yang terkandung dalam leaflet ini:

1. Faslodex dan kegunaannya

Faslodex mengandung zat aktif fulvestrant yang merupakan golongan obat penghambat estrogen. Estrogen adalah hormon seks pada wanita yang dalam beberapa kasus dapat berperan dalam pertumbuhan kanker payudara.

Faslodex digunakan untuk mengobati kanker payudara tahap lanjut atau kanker payudara yang telah metastase untuk pasien wanita pascamenopause dan untuk kanker payudara dengan metastase negatif pada wanita pascamenopause yang sebelumnya tidak diobati dengan terapi endokrin.

FASLODEX dapat diberikan dalam kombinasi dengan abemaciclib untuk mengobati kanker payudara tahap lanjut atau kanker payudara yang telah metastase. Pada pasien pre atau pasca yang siklus menstruasinya telah berhenti maka terapi endokrin harus dikombinasikan dengan agonis LHRH. Untuk perempuan berumur kurang dari 60 tahun maka perlu dilakukan pengukuran serum FSH dan estradiol. Penting untuk anda juga membaca informasi produk abemaciclib. Jika Anda memiliki pertanyaan terkait abemaciclib, silakan tanyakan kepada dokter Anda.

FASLODEX dapat diberikan dalam kombinasi dengan ribociclib untuk mengobati kanker payudara tahap lanjut atau kanker payudara yang telah metastase pada wanita yang siklus mentruasinya telah

berhenti. Penting bahwa Penting untuk anda juga membaca infromasi produk ribociclib. Jika Anda memiliki pertanyaan terkait ribociclib, silakan tanyakan kepada dokter Anda.

2. Hal yang perlu Anda ketahui sebelum menggunakan Faslodex

Jangan menggunakan Faslodex apabila

- Anda memiliki alergi terhadap Fulvestrant atau bahan-bahan lain yang terkandung dalam obat ini (diuraikan pada poin 6 'Kandungan Faslodex')
- Hamil atau menyusui
- Mempunyai gangguan hati

Peringatan dan pencegahan

Diskusikan dengan dokter, perawat, atau apoteker Anda sebelum mengkonsumsi Faslodex:

- Apabila Anda memiliki gangguan ginjal atau hati
- Apabila Anda memiliki jumlah keping darah/ platelet yang rendah (yang membantu dalam pembekuan darah) atau bila terjadi pendarahan.
- Pernah memiliki masalah pembekuan darah
- Memiliki masalah osteoporosis (kehilangan massa jenis tulang)
- Mengkonsumsi alkohol secara berlebihan (alkoholik)

Anak dan remaja

Faslodex tidak diindikasikan untuk anak dan remaja di bawah 18 tahun.

Obat lain dan Faslodex

Komunikasikan kepada dokter, perawat, atau apoteker Anda apabila Anda sedang menggunakan, akan menggunakan, atau telah menggunakan obat lain selain Faslodex.
Khususnya, Anda harus komunikasikan kepada dokter jika Anda mengkomsumsi obat antikoagulan (obat untuk mencegah pembekuan darah).

Kehamilan dan Menyusui

Anda tidak boleh menggunakan Faslodex jika Anda hamil. Apabila Anda memiliki rencana untuk hamil, Anda harus menggunakan alat kontrasepsi yang efektif selama diobati dengan Faslodex dan selama 2 tahun setelah dosis terakhir.

Anda tidak boleh menyusui saat menjalani pengobatan dengan Faslodex.

Mengendarai kendaraan bermotor dan menjalankan mesin

Faslodex tidak mempengaruhi kemampuan mengendarai kendaraan bermotor maupun menjalankan mesin. Jangan mengemudi, menggunakan alat ataupun mesin, apabila Anda merasa pusing setelah minum Faslodex.

Faslodex mengandung 10% w/v etanol (alkohol), yaitu hingga 500 mg per dosis.
Faslodex dapat berbahaya bagi mereka yang mengkonsumsi alkohol secara berlebihan (alkoholik)
Penggunaan Faslodex harus dipertimbangkan pada wanita hamil atau menyusui, anak-anak dan kelompok berisiko tinggi seperti pasien dengan penyakit hati, atau epilepsi

3. Cara Pemakaian Faslodex

Selalu gunakan obat ini sesuai dengan perintah dan saran dokter dan apoteker anda. Tanya dokter dan apoteker jika anda tidak yakin

Dosis yang direkomendasikan adalah 500 mg (dua syringe yang setiap syringenya mengandung 250 mg/ml) yang diberikan sekali dalam sebulan, dengan satu tambahan dosis 500 mg yang diberikan 2 minggu setelah dosis pertama.
Dokter ataupun perawat akan memberikan Faslodex melalui injeksi intramuscular secara perlahan, satu kali suntik pada kedua pantat.

4. Efek Samping yang Mungkin Terjadi

Sama seperti obat pada umumnya, obat ini dapat menimbulkan efek samping walaupun tidak semua orang akan mengalaminya.

Berhentilah mengkonsumsi Faslodex dan segera konsultasi ke dokter, apabila Anda mengalami efek samping berikut:

- Reaksi alergi (hipersensitivitas), termasuk pembengkakan pada wajah, bibir, lidah dan / atau tenggorokan
- Thromboembolisme (peningkatan resiko pembekuan darah)*
- Peradangan hati (hepatitis)
- Gagal hati

Hubungi dokter Anda segera apabila Anda mengalami efek samping dibawah ini:

Sangat sering (dialami oleh lebih dari 1 dari 10 orang)
- Reaksi pada tempat penyuntikan, seperti luka dan atau peradangan
- Jumlah enzim hati yang tidak biasa (pada hasil uji darah)*
- Mual (merasa sakit)
- Nyeri sendi dan otot
- Lemah dan lelah*

Efek Samping Lainnya:

Biasa terjadi (dialami oleh 1 dari 10 orang)
- Sakit kepala
- Kemerahan
- Muntah, diare, atau kehilangan nafsu makan *
- Ruam
- Infeksi saluran urin
- Nyeri tulang belakang*
- Peningkatan jumlah bilirubin (pigment empedu yang diproduksi hati)
- Thromboembolisme (peningkatan resiko pembekuan darah)*
- Reaksi alergi (hipersensitivitas), termasuk pembengkakan pada wajah, bibir, lidah dan / atau tenggorokan

Jarang (dialami oleh 1 dari 100 orang)
- Vagina mengalami pendarahan, terasa tebal, muncul debit keputihan dan kandidiasis (infeksi)
- Memar dan pendarahan di tempat suntikan
- Meningkatkan *gamma-GT*, enzim hati yang terlihat dalam tes darah
- Radang hati (hepatitis)
- Gagal hati

* Termasuk efek samping dari Faslodex yang tidak dapat dinilai karena penyakit yang mendasarinya.

Apabila Anda mengalami satu atau lebih efek samping diatas, hubungi dokter Anda segera. Hal yang sama berlaku untuk efek samping yang tidak terinci dalam leaflet ini.

5. Cara penyimpanan Faslodex

Disimpan dan didistribusikan di dalam pendingin (2°C - 8° C).

Paparan suhu selain 2 °C - 8 °C harus dibatasi, ini termasuk menghindari penyimpanan di atas 30 °C, dan tidak melebihi jangka waktu 28 hari pada suhu penyimpanan rata-rata di bawah 25 °C (tapi di atas 2 °C - 8 °C). Setelah suhu paparan, produk, harus dikembalikan segera ke kondisi penyimpanan yang direkomendasikan (toko dan transportasi di kulkas 2 °C - 8 °C). Paparan suhu memiliki efek kumulatif pada kualitas produk dan jangka waktu 28 hari tidak boleh melebihi masa kadaluarsa 4tahun Faslodex. Paparan suhu di bawah 2 °C tidak akan merusak produk asalkan tidak disimpan di bawah - 20 °C.

Simpan kembali *pre-filled syringe* ke dalam dus, untuk melindungi dari cahaya.

Jauhkan obat ini dari pandangan dan jangkauan anak-anak.

Jangan menggunakan obat ini setelah tanggal kadaluwarsa yang tertera pada karton atau label jarum suntik. Tanggal kadaluwarsa mengacu pada hari terakhir dari bulan itu.

Anda profesional perawatan kesehatan akan bertanggung jawab untuk penyimpanan yang benar, penggunaan dan pembuangan Faslodex.

6. Isi kemasan dan informasi lain

Faslodex mengandung
- Zat aktif berupa fulvestrant. Tiap *pre-filled syringe* (5 ml) mengandung 250 mg fulvestrant.
- Bahan – bahan lain berupa ethanol (96 %), benzyl alcohol, benzyl benzoate dan castor oil.

Bentuk sediaan dan isi kemasan
Faslodex berupa larutan kental bening, tidak berwarna sampai berwarna kekuning-kuningan dalam *pre-filled syringes* dilengkapi dengan penutup *tamper-evident*, mengandung 5 ml larutan untuk injeksi, dua syringe disuntikkan untuk menerima 250 mg dosis yang direkomendasikan setiap bulan.

Faslodex memiliki satu kemasan, yang berisi 2 *pre-filled syringes*.
Jarum Keselamatan (BD SafetyGlide ™) untuk koneksi ke setiap barel juga disediakan.

Tidak semua ukuran paket dapat dipasarkan.

HARUS DENGAN RESEP DOKTER

Pemegang Hak Pemasaran dan Produsen
Diproduksi oleh:

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