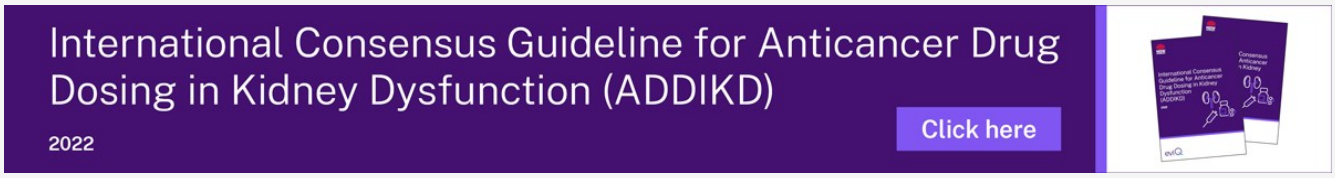
Breast metastatic fulvestrant

ID: 1305 v.4 **Endorsed**

Check for clinical trials in this patient group. Link to Australian Clinical Trials website

The anticancer drug(s) in this protocol may have been included in the ADDIKD guideline. Dose recommendations in kidney dysfunction have yet to be updated to align with the ADDIKD guideline. Recommendations will be updated once the individual protocol has been evaluated by the reference committee. For further information refer to the ADDIKD guideline. To assist with calculations, use the eviQ Estimated Glomerular Filtration Rate (eGFR) calculator.



Related pages:

- Breast metastatic abemaciclib
- Breast metastatic palbociclib
- Breast metastatic ribociclib

Treatment schedule - Overview

Cycle 1

Drug	Dose	Route	Day
Fulvestrant	500 mg	IM	1 and 15

Cycle 2 and further cycles

Drug	Dose	Route	Day
Fulvestrant	500 mg	IM	1

Frequency: 28 days

Cycles: Continuous until disease progression or unacceptable toxicity

Drug status: Fulvestrant is PBS authority

Fulvestrant is available as 250 mg/5 mL pre-filled syringes.

Cost: ~ $260 per cycle

Treatment schedule - Detail

The supportive therapies (e.g. antiemetics, premedications, etc.), infusion times, diluents, volumes and routes of administration, if included, are listed as defaults. They may vary between institutions and can be substituted to reflect individual institutional policy.

*Antiemetics if included in the treatment schedule are based upon recommendations from national and international guidelines. These are **defaults only** and may be substituted to reflect individual institutional policy. Select here for recommended doses of alternative antiemetics.*

Cycle 1

Day 1 and 15		
Fulvestrant	500 mg (IM)	administered intramuscularly as two 5 mL injections, one in each buttock

Cycle 2 and further cycles

Day 1		
Fulvestrant	500 mg (IM)	administered intramuscularly as two 5 mL injections, one in each buttock

Frequency: 28 days

Cycles: Continuous until disease progression or unacceptable toxicity

Indications and patient population

- Hormone-receptor positive, locally advanced or metastatic breast cancer in post-menopausal women.
  - Fulvestrant may be used in combination with abemaciclib, palbociclib or ribociclib.

Clinical information

Injection site reactions	This treatment has been associated with a high rate of injection site reactions (pain, erythema, swelling etc.) These reactions occurred more frequently with the starting dose and were transient and mostly mild to moderate.
Blood tests	LFTs at baseline and repeat as clinically indicated.
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.

Dose modifications

Evidence for dose modifications is limited, and the recommendations made on eviQ are intended as a guide only. They are generally conservative with an emphasis on safety. Any dose modification should be based on clinical judgement, and the individual patient's situation including but not limited to treatment intent (curative vs palliative), the anti-cancer regimen (single versus combination therapy versus chemotherapy versus immunotherapy), biology of the cancer (site, size, mutations, metastases), other treatment related side effects, additional co-morbidities, performance status and patient preferences.Suggested dose modifications are based on clinical trial findings, product information, published guidelines and reference committee consensus . The dose reduction applies to each individual dose and not to the total number of days or duration of treatment cycle unless stated otherwise. Non-haematological gradings are based on Common Terminology Criteria for Adverse Events (CTCAE) unless otherwise specified. Renal and hepatic dose modifications have been standardised where possible. For more information see dosing considerations & disclaimer .

Renal impairment
No dose modifications necessary

Hepatic impairment	
Hepatic dysfunction	
Mild	No dose modifications necessary
Moderate and Severe	Use with caution as the clearance of fulvestrant may be reduced

Interactions

Drug interactions in eviQ protocols are under review and being updated to align with current literature. Further site-wide updates and changes will occur in due course. References & Disclaimer

The drug interactions shown below are not an exhaustive list. For a more comprehensive list and for detailed information on specific drug interactions and clinical management, please refer to the specific drug product information and the following key resources:

- *MIMS - interactions tab (includes link to a CYP-450 table) (login required)*
- *Australian Medicines Handbook (AMH) – interactions tab (login required)*
- *Micromedex Drug Interactions (login required)*
- *Cancer Drug Interactions*
- *Cytochrome P450 Drug Interactions*

Fulvestrant		
	Interaction	**Clinical management**
Oestrogen containing therapies	Negate the pharmacological action of fulvestrant	Combination contraindicated (minimal use of topical oestrogen therapy for vulvo-vaginal complaints may be considered)

Administration

eviQ provides safe and effective instructions on how to administer cancer treatments. However, eviQ does not provide every treatment delivery option, and is unable to provide a comprehensive list of cancer treatment agents and their required IV line giving set/filter. There may be alternative methods of treatment administration, and alternative supportive treatments that are also appropriate. Please refer to the individual product information monographs via the TGA website for further information.

Administration

Intramuscular injection

Safe handling and waste management (reproductive risk only)

Safe administration

Treatment - Time out

Fulvestrant

- administer via intramuscular injection (1 to 2 minutes per injection)
- as two 5 mL injections
- one in each buttock.

Continue safe handling precautions (reproductive risk only) for 7 days after completion of drug(s).

Discharge information

Patient information

- Ensure patient receives patient information sheet.

Side effects

The side effects listed below are not a complete list of all possible side effects for this treatment. Side effects are categorised into the approximate onset of presentation and should only be used as a guide.

Immediate (onset hours to days)	
Injection-site reactions	Inflammation of or damage to the tissue surrounding the area where a drug was injected.
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Headache	

Early (onset days to weeks)	
Diarrhoea	Read more about treatment induced diarrhoea
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Hot flushes	
Hepatotoxicity	Anti-cancer drugs administered either alone or in combination with other drugs and/or radiation may cause direct or indirect hepatotoxicity. Hepatic dysfunction can alter the metabolism of some drugs resulting in systemic toxicity.

Late (onset weeks to months)	
Arthralgia and myalgia	Generalised joint pain or and/or stiffness and muscle aches, often worse upon waking or after long periods of inactivity. Can improve with movement. May be mild or severe, intermittent or constant and accompanied by inflammation. Read more about arthralgia and myalgia

Evidence

The initial evidence for fulvestrant comes from two Phase III clinical trials (Trials 0020 and 0021) involving a total of 851 patients with locally advanced or metastatic hormone-receptor breast cancer who had progressed on prior endocrine therapy, primarily tamoxifen. The women were randomised to receive fulvestrant 250 mg IM monthly or anastrozole 1 mg PO daily. The primary endpoint was overall survival to determine non-inferiority for fulvestrant.[1]

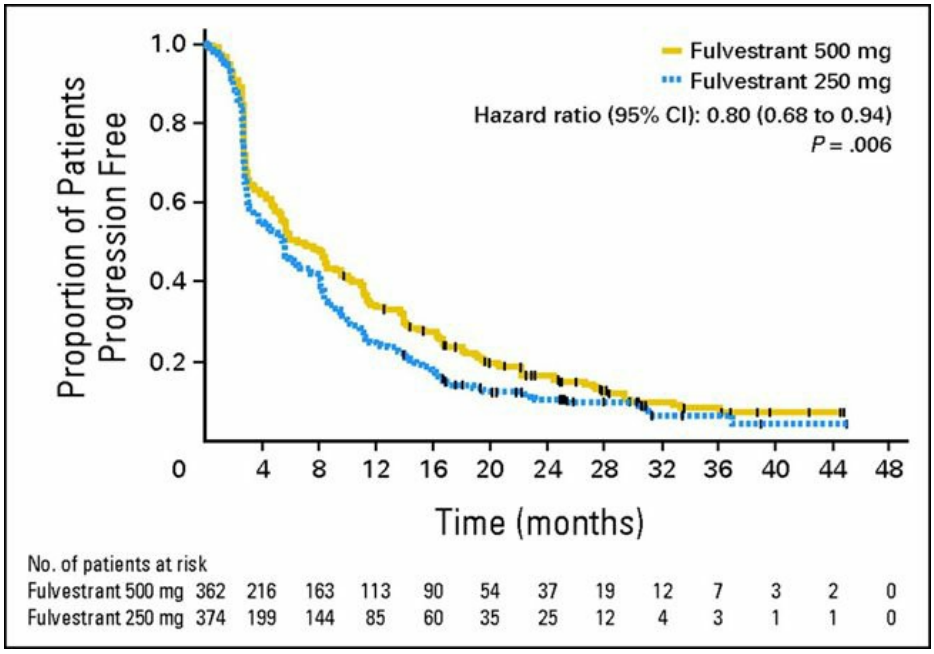
The EFECT Phase III trial compared the use of fulvestrant 250 mg IM given day 1, 14, 28 and every 28 days thereafter with exemestane 25 mg PO daily in post-menopausal women with locally advanced or metastatic breast cancer who had relapsed during or within 6 months of completion of adjuvant treatment or failed first line metastatic treatment with a non-steroidal aromatase inhibitor. A total of 639 women were accrued from August 2003 to November 2005. The primary endpoint of the study was time to disease progression.[2]

The CONFIRM Phase III trial involved 736 post-menopausal patients enrolled from February 2005 to August 2007 with locally advance or metastatic ER-positive breast cancer who had experienced a relapse on or within 1 year from completion of adjuvant endocrine therapy or who had failed first line endocrine treatment for metastatic disease. Patients were randomly assigned to fulvestrant 500 mg day 1, 14, 28 and every 28 days thereafter or fulvestrant 250 mg in the same schedule. The primary endpoint was progression free survival.[3]

Efficacy

In both the analysis of Trial 0020 and 0021 and the EFECT trial, fulvestrant 250 mg was shown to be at least as effective as anastrozole and exemestane respectively.[1,2] In the analysis of Trial 0020 and 0021, the overall survival was 27.4 months in the fulvestrant group compared with 27.7 in the anastrozole group.[2] In EFECT, the time to disease progression was 3.7 months in both groups.[2] Fulvestrant 500 mg was shown to lead to a significant prolongation of progression free survival over 250 mg in CONFIRM, 6.5 months vs 5.5 months (HR = 0.80; 95% CI, 0.68-0.94; *P* = 0.006). There was no difference in the groups in overall response and clinical benefit rates, however a greater number of patients in the 500 mg group had stable disease compared with the 250 mg group.[3]

Kaplan-Meier analysis of Progression-free survival[3]



Toxicity

In EFECT and Trials 0020 and 0021, fulvestrant was as tolerable as exemestane and anastrozole respectively.[1,2] Joint symptoms were slightly less in all studies in the fulvestrant groups. In CONFIRM, there was no substantial difference in the incidence and severity of side effects in the 500 mg fulvestrant group compared with the 250 mg group. Serious adverse events were uncommon in both groups, however 1 patient died in the 500 mg group due to interstitial lung disease and 1 in the 250 mg due to cardiac failure resulting from hypertension.[3]

Toxicity [2]	Fulvestrant % (n=351)	Exemestane % (n=340)
Injection-site pain	9	8
Hot flashes	9	12
Nausea	7	8
Fatigue	6	10
Myalgia	4	4
Arthralgia	4	6
Diarrhoea	3	3
Asthenia	3	2
Injection-site reaction	2	2
Alopecia	2	2
Headache	2	3
Anorexia	2	2
Dyspepsia	1	2
Pain in extremity	0	2

References

1 Howell, A., J. Pippen, R. M. Elledge, et al. 2005. "Fulvestrant versus anastrozole for the treatment of advanced breast carcinoma: a prospectively planned combined survival analysis of two multicenter trials." Cancer 104(2):236-239.

2 Chia, S., W. Gradishar, L. Mauriac, et al. 2008. "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 26(10):1664-1670.

3 Di Leo, A., G. Jerusalem, L. Petruzelka, et al. 2010. "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 28(30):4594-4600.

History

Version 4

Date	Summary of changes
01/04/2021	Indications and patient information updated to include combination with abemaciclib, and 'with progressive disease following tamoxifen therapy' removed. Drug status changed to PBS authority. Drug cost added. ID 3625 Breast metastatic abemaciclib added as a related page. Version number changed to V.4.
13/08/2021	Protocol reviewed electronically by Medical Oncology Reference Committee. Nil changes. Review in 2 years.

Version 3

Date	Summary of changes
27/04/2012	New protocol taken to Medical Oncology Reference Committee meeting.
14/06/2012	Approved and published on eviQ.
09/05/2014	Protocol reviewed by email survey. No change and next review in 2 years.
15/05/2015	Skin rash (Dryness, Erythema and Pruritus) side effect removed.
08/04/2016	Protocol reviewed at Medical Oncology Reference Committee meeting. No change and next review in 1 year.
31/05/2017	Transferred to new eviQ website. Version number change to V.2.
03/11/2017	Protocol reviewed at Medical Oncology Reference Committee meeting. No changes. Review protocol in 2 years
26/03/2018	Indication and patient information sheet updated to include combination with palbociclib. Added link to ID 3369 Breast metastatic palbociclib protocol.
23/09/2019	Protocol reviewed at Medical Oncology Reference Committee Meeting on 30/08/2019. Indications, related pages and patient information updated to include combination with ribociclib. Drug cost changed to not available. Version number change to V.3. Next review in 2 years.

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Last reviewed: 13 August 2021
Review due: 31 December 2023

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https://www.eviq.org.au/p/1305
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Patient information - Breast cancer metastatic - Fulvestrant

Patient's name:

Your treatment

The treatment schedule below explains how the drug for this treatment is given.

Fulvestrant			
This treatment cycle is repeated every 28 days. Your doctor will advise you how long you will have the treatment for.			
Day	**Treatment**	**How it is given**	**How long it takes**
1 and 15 (cycle 1 only), then day 1 only (all other cycles)	**Fulvestrant** (*ful-VES-trant*)	By injection into a muscle in each buttock. You may develop bruising around the site of the injection, this will fade over time.	About 5 minutes

- Fulvestrant injections may be used alone or in combination with another oral medication (called abemaciclib, palbociclib or ribociclib). Your doctor will discuss your treatment plan with you.

When to get help

Anticancer drugs (drugs used to treat cancer) can sometimes cause serious problems. It is important to get medical help immediately if you suddenly become unwell.

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you notice any pain or swelling in your legs or arms or if you develop any sudden shortness of breath or chest pain

Emergency contact details

Ask your doctor or nurse from your treating team who to contact if you have a problem

Daytime: .....

Night/weekend: .....

Other instructions: .....

.....

.....

.....

Other information about your treatment

Changes to your dose or treatment delays

Sometimes a treatment may be started at a lower dose or the dose needs to be changed during treatment. There may also be times when your treatment is delayed. This can happen if your doctor thinks you are likely to have severe side effects, if you get severe side effects, if your blood counts are affected and causing delays in treatment, or if you are finding it hard to cope with the treatment. This is called a dose reduction, dose change or treatment delay. Your doctor will explain if you need any changes or

delays to your treatment and the reason why.

Blood tests and monitoring

You may need to have blood tests while you are receiving this treatment. Your doctor or nurse will tell you when to have these blood tests.

Hormonal cancer treatment

Certain types of breast cancer need oestrogen to grow. Fulvestrant works by stopping the action of oestrogen in the body. This can help to stop the cancer cells from growing. You must not take any medications that contain oestrogen while you are having this treatment. This includes some oral contraceptives, hormone replacement therapy (HRT) and oestrogen creams. Ask your doctor or pharmacist for more information.

Side effects

Cancer treatments can cause damage to normal cells in your body, which can cause side effects. Everyone gets different side effects, and some people will have more problems than others.

The table below shows some of the side effects you may get with this treatment. You are unlikely to get all of those listed and you may also get some side effects that have not been listed.

Tell your doctor or nurse about any side effects that worry you. Follow the instructions below and those given to you by your doctor or nurse.

Immediate (onset hours to days)	
Injection-site reaction	• At the injection site you may get pain, redness, swelling or bruising. • These symptoms are usually not serious. • **Tell your doctor or nurse immediately if you notice any redness or pain during or after treatment.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**
Headache	• You can take paracetamol if you have a headache. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.**

Early (onset days to weeks)	
Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Appetite loss (anorexia)	• You may not feel like eating. • Try to avoid drinking fluids at meal times. • Try to eat small meals or snacks regularly throughout the day. • Try to eat food that is high in protein and calories. • If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.
Hot flushes	• You may get flushing of your face, sweating and sensations of heat. • Avoid alcohol, coffee, tea and spicy foods, as they can make hot flushes worse. • Wear lightweight clothes made from natural fibres; dress in layers. • Put a cold, wet towel against your neck during hot flushes. • Talk to your doctor or nurse about other ways to manage these symptoms.
Liver problems	• You may get: ◦ yellowing of your skin or eyes ◦ itchy skin ◦ pain or tenderness in your stomach ◦ nausea and vomiting ◦ loss of appetite • You will have regular blood tests to check how well your liver is working. • **Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes look yellow, or if you have stomach pain.**

Late (onset weeks to months)	
Joint and muscle pain and stiffness	• You may get muscle, joint or general body pain and stiffness. • Applying a heat pack to affected areas may help. • Talk to your doctor or nurse about other ways to manage these symptoms. You may need medication to help with any pain.

General advice for people having cancer treatment

Blood clot risk

- Cancer and anticancer drugs can increase the risk of a blood clot (thrombosis).
- Tell your doctor if you have a family history of blood clots.
- A blood clot can cause pain, redness, swelling in your arms or legs, shortness of breath or chest pain.
- If you have any of these symptoms go to your nearest hospital Emergency Department.

Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don’t stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Vaccinations such as flu and tetanus vaccines are safe to receive while you are having treatment. If you are unsure, check with your doctor before you have any vaccinations.

Other medical and dental treatment

- If you go to hospital or any other medical appointment (including dental appointments), always tell the person treating you that you are receiving anticancer drugs.
- Before you have any dental treatment, talk to your doctor.

Diet

- While you are receiving this treatment it is important that you try to maintain a healthy diet.
- Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.

Sex life and sexuality

- The desire to have sex may decrease as a result of this treatment or its side effects.
- Your emotions and the way you feel about yourself may also be affected by this treatment.
- It may help to discuss your concerns with your partner and doctor or nurse.

Quitting smoking

- It is never too late to quit smoking. Quitting smoking is one of the best things you can do to help your treatment work better.
- There are many effective tools to improve your chances of quitting.
- Talk to your treating team for more information and referral to a smoking cessation support service.

Staying active

- Research shows that exercise, no matter how small, has many benefits for people during and after cancer treatment.
- Talk to your doctor before starting an exercise program. Your doctor can advise whether you need a modified exercise program.

For more information about cancer treatment, side effects and side effect management see our Patient and carers section.

Where to get more information

Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support.

Breast cancer information

- Australasian Lymphology Association – lymphoedema.org.au
- Australasian Menopause Society – menopause.org.au
- Breast Cancer Network Australia – bcna.org.au
- National Breast Cancer Foundation – nbcf.org.au
- YWCA Encore breast cancer exercise program – ywcaencore.org.au

General cancer information and support

- Australian Rare Cancer (ARC) Portal – arcportal.org.au/
- Beyondblue – beyondblue.org.au
- Cancer Australia – canceraustralia.gov.au
- Cancer Council Australia – cancer.org.au
- Cancer Voices Australia – cancervoicesaustralia.org
- CanTeen – canteen.org.au
- Carers Australia – carersaustralia.com.au
- CHILL Cancer related hair loss – scalpcooling.org
- eviQ Cancer Treatments Online – eviQ.org.au
- LGBTQI+ People and Cancer - cancercouncil.com.au/cancer-information/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information – patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer – targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au

- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

Quit smoking information and support

Quitting smoking is helpful even after you have been diagnosed with cancer. The following resources provide useful information and support to help you quit smoking. Talk to your treating team about any other questions you may have.

- Call Quitline on 13 QUIT (13 78 48)
- iCanQuit – iCanQuit.com.au
- Patient Information – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/quitting-smoking
- Quitnow – quitnow.gov.au

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