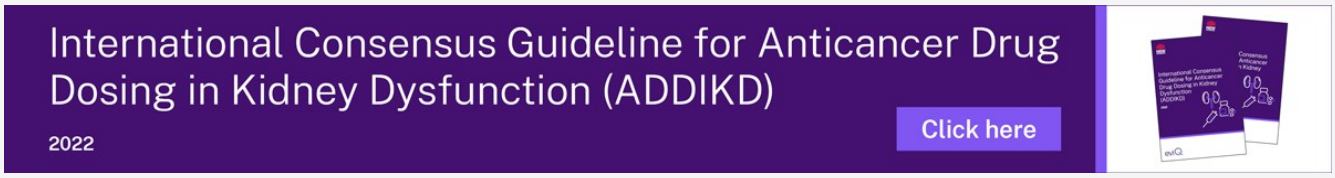
Breast metastatic everolimus and exemestane

ID: 1590 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.



Treatment schedule - Overview

Drug	Dose	Route
Everolimus	10 mg ONCE a day	PO
Exemestane	25 mg ONCE a day	PO

Continuous until disease progression or unacceptable toxicity

Notes:
This is a potentially toxic treatment and requires close monitoring of side effects.

Drug status: Exemestane is a PBS restricted benefit

Everolimus is PBS authority

Everolimus is available as **5 mg** and **10 mg** tablets and exemestane as **25 mg** tablets.

Cost: ~ $1,680 per month

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.*

Continuous treatment		
Everolimus	10 mg (PO)	ONCE a day with or without food
Exemestane	25 mg (PO)	ONCE a day with or after food

Continuous until disease progression or unacceptable toxicity

Indications and patient population

Indication:

- hormone-receptor positive, HER-2 negative advanced breast cancer in post-menopausal women after failure of treatment with letrozole or anastrozole

Exclusion:

- history of hepatitis B or C, or human immunodeficiency virus (HIV) infection.

Clinical information

Caution with oral anti-cancer drugs	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the COSA guidelines and oral anti-cancer therapy
Emetogenicity minimal or low	No routine prophylaxis required. If patients experience nausea and/or vomiting, consider using the low emetogenic risk regimen. Read more about preventing anti-cancer therapy induced nausea and vomiting
Oral mucositis	Oral mucositis is a common side effect with this treatment and may manifest as mouth and tongue ulceration. Early intervention may help to avoid dose alteration or interruption. Topical treatments (alcohol free) are recommended. Pre-emptive use of a steroid-based mouthwash has been shown to reduce the incidence and severity of oral mucositis in patients receiving everolimus.[1, 2] Read more about oral mucositis and stomatitis
Infections	Patients may be immunosuppressed and should be carefully observed for the occurrence of infections, including opportunistic infections.
Pneumonitis	There have been cases of non-specific interstitial pneumonitis, including rare fatal reports, occurring in patients who have received this treatment. Read more about pulmonary toxicity associated with anti-cancer drugs.
Wound healing	This treatment may impair wound healing and temporary interruption of treatment is recommended in patients undergoing major surgical procedures. Resume treatment based on clinical judgement of adequate wound healing.
Hyperglycaemia	Hyperglycaemia has been observed with this treatment. Close monitoring of blood sugar levels is recommended. Initiation of antidiabetic therapy may be required. In patients with pre-existing diabetes, dose adjustment of oral antidiabetic medications or insulin may be required.
Hyperlipidaemia	Hyperlipidaemia is a common adverse event. Dose adjustment or initiation of lipid-lowering agents may be required.
Blood tests	FBC, EUC, LFTs, calcium, magnesium, phosphate and BSL at baseline and repeat monthly or as clinically indicated. Lipid studies every 6 to 8 weeks.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is NOT usually recommended for patients receiving this treatment. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
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 .

The dose recommendations in kidney dysfunction (i.e.renal impairment) displayed may not reflect those in the ADDIKD guideline and have been included for historical reference only. Recommendations will be updated once the individual protocol has been evaluated by the reference committee, with this version of the protocol then being archived. Clinicians are expected to refer to the ADDIKD guideline prior to prescribing in kidney dysfunction.
International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD).

Note: treatment was discontinued permanently in patients who required more than two dose reductions and in those who had treatment interruptions lasting more than 4 weeks.[3]

Mucositis and stomatitis	
• Pre-emptive use of a steroid-based mouthwash may help the patient avoid dose alteration or interruption • Manage with topical analgesic mouth treatments (e.g. benzocaine, lignocaine etc.) with or without topical corticosteroids (i.e. triamcinolone oral paste) • Avoid using agents containing alcohol, hydrogen peroxide, iodine and thyme derivatives	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce everolimus to 5 mg once a day 3rd occurrence: Reduce everolimus to 5 mg on alternate days 4th occurrence: Discontinue everolimus
Grade 3	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: Reduce everolimus to 5 mg once a day 2nd occurrence: Discontinue everolimus
Grade 4	Discontinue everolimus

Haematological toxicity	
ANC x 10^9/L (pre-treatment blood test)	
1.0 to less than 1.5	Refer to local institutional guidelines; it is the view of the expert clinicians that treatment should continue if patient is clinically well.
0.5 to less than 1.0	Delay treatment until recovery
less than 0.5	Delay treatment until recovery and consider reducing everolimus to 5 mg once a day for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and consider reducing everolimus to 5 mg once a day for subsequent cycles
Platelets x 10^9/L (pre-treatment blood test)	
75 to less than 100	The general recommendation is to delay, however if the patient is clinically well it may be appropriate to continue treatment; refer to treating team and/or local institutional guidelines.

Haematological toxicity	
50 to less than 75	Delay treatment until recovery
25 to less than 50	Delay treatment until recovery and consider reducing everolimus to 5 mg once a day for subsequent cycles
less than 25	Omit everolimus

Renal impairment
No dose modifications necessary

Hepatic impairment	
Hepatic dysfunction	
Mild	No dose modifications necessary
Moderate	Reduce everolimus to 5 mg once a day
Severe	Omit everolimus

Diarrhoea	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce everolimus to 5 mg once a day 3rd occurrence: Reduce everolimus to 5 mg on alternate days 4th occurrence: Discontinue everolimus
Grade 3	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: Reduce everolimus to 5 mg once a day 2nd occurrence: Discontinue everolimus
Grade 4	Discontinue everolimus

Pneumonitis (non-infectious)	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: Reduce everolimus to 5 mg once a day 2nd occurrence: Discontinue everolimus
Grade 3 or Grade 4	Discontinue everolimus

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*

Everolimus		
	Interaction	**Clinical management**
CYP3A4 and P-gp inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin, grapefruit juice etc.)	Increased toxicity of everolimus possible due to reduced clearance	Avoid combination or monitor for everolimus toxicity. If concomitant use cannot be avoided, consider reducing everolimus dose based on careful monitoring of tolerability.
CYP3A4 and P-gp inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort, dexamethasone etc.)	Reduced efficacy of everolimus possible due to increased clearance	Avoid combination or monitor for decreased clinical response to everolimus. If concomitant use cannot be avoided, consider increasing everolimus dose based on careful monitoring of tolerability.
Potassium lowering drugs (e.g. thiazide diuretics, amphotericin)	Additive risk of hypokalaemia with everolimus	Avoid combination or monitor potassium level and for signs of hypokalaemia.

Exemestane		
	Interaction	**Clinical management**
Oestrogen containing therapies	Negate the pharmacological action of exemestane	Combination contraindicated (minimal use of topical oestrogen therapy for vulvo-vaginal complaints may be considered)
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of exemestane possible due to increased clearance	Caution advised if combination used - monitor for decreased clinical response to exemestane

General		
	Interaction	**Clinical management**
Antiplatelet agents and NSAIDs	Increased risk of bleeding due to treatment related thrombocytopenia.	Avoid or minimise combination. If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding.
Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)	Increased risk of serotonin syndrome with concurrent use of 5-HT3 receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	Avoid combination. If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia). For more information link to TGA Medicines Safety Update.
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines	Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy. For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook

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

This is a continuous oral treatment

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each treatment.

Any toxicity grade 2 or greater may require dose reduction, delay or omission of treatment and review by medical officer before recommencing treatment.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Everolimus

- administer orally ONCE a day, at the same time every day (preferably in the morning)
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with food or without food (advise to take consistently with regard to food)
- if difficulty is experienced swallowing the tablet advise patient to:
  - place tablet in a glass with approx 30 mL water
  - stir or shake gently, the tablet will disperse in about 7 minutes
  - drink straight away
  - rinse glass with 30 mL and drink remaining residual drug.

Note: missed doses may be taken up to 6 hours after regularly scheduled time; if more than 6 hours, resume at next regularly scheduled time.

Exemestane

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken with or immediately after food
- if nausea develops, take after food at night

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

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

Discharge information

Everolimus and exemestane tablets

- Everolimus and exemestane tablets with written instructions on how to take them.

Antiemetics

- Antiemetics as prescribed.

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)	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Headache	

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Oral mucositis	Erythematous and ulcerative lesions of the gastrointestinal tract (GIT). It commonly develops following chemotherapy, radiation therapy to the head, neck or oesophagus, and high dose chemotherapy followed by a blood and marrow transplant (BMT). Pre-emptive use of a steroid-based mouth wash has been shown to reduce the incidence and severity of oral mucositis and may help to avoid dose alteration or interruption in patients receiving this treatment. Read more about oral mucositis
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Hot flushes	
Hyperglycaemia	High blood sugar, an excess of glucose in the blood stream.
Hyperlipidaemia and hypercholesterolaemia	Abnormally elevated levels of lipids and cholesterol in the blood.
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash
Fluid retention and oedema	An excess amount of fluid around the cells, tissues or serous cavities of the body, leading to swelling.
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs
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.
Nephrotoxicity	Renal dysfunction resulting from damage to the glomeruli, tubules or renal vasculature.

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
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
Periorbital oedema	Accumulation of fluid in the tissue surrounding the eye sockets (orbits).
Mood changes	

Evidence

The evidence supporting this protocol is provided by BOLERO-2, a phase III, double-blind, placebo-controlled, multicentre international randomised trial (2:1 ratio) involving 724 patients comparing everolimus (10 mg/day) and exemestane (25 mg/day) with exemestane alone in patients with hormone-receptor-positive advanced breast cancer who had recurrence or progression while receiving previous therapy with a nonsteroidal aromatase inhibitor in the adjuvant setting or to treat advanced disease.[4]

The primary end point was progression-free survival. Secondary end points were overall survival, overall response rate, and safety.

Everolimus combined with exemestane improved progression-free survival in patients with hormone-receptor-positive advanced breast cancer previously treated with nonsteroidal aromatase inhibitors. Response rates were also superior in patients treated with combination therapy. Overall survival results were immature at the time of interim analysis.[4,5]

Efficacy

Final progression-free survival analysis by central assessment revealed a PFS benefit of 6.9 months with combination therapy (11.0 months for everolimus in combination with exemestane versus 4.1 months for exemestane alone; HR 0.38 (95%CI 0.31-0.48); log-rank $p < 0.0001$). Everolimus and exemestane treatment substantially extended PFS benefits compared with exemestane alone regardless of baseline disease or prior therapy characteristics.[5] At the time of analysis, fewer deaths were reported with combination therapy than in patients treated with exemestane alone (25.4% vs 32.2%). A final analysis of overall survival is planned after 398 events. Improvements were also observed in overall response, objective response rate and clinical benefit rate.[5]

Kaplan-Meier estimates progression-free survival [5]

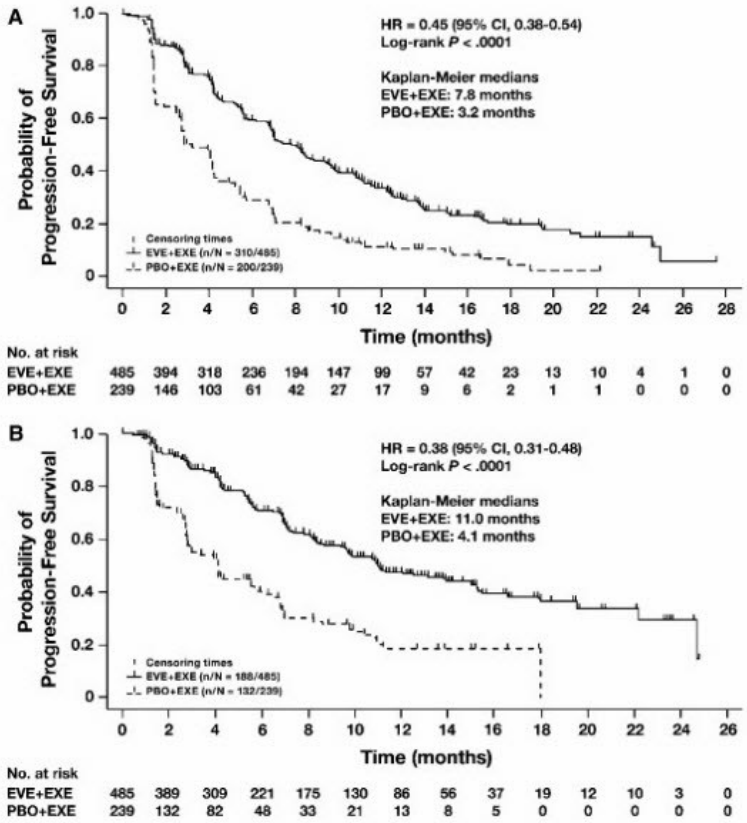


Fig. 1 Kaplan–Meier estimates of progression-free survival of patients treated with everolimus plus exemestane versus exemestane alone based on assessment by a local investigator or **b** central review. *CI* confidence interval, *HR* hazard ratio, *EVE* everolimus, *EXE* exemestane, *PBO* placebo

Overall survival and tumour response[5]

Table 2 Between-arm differences in overall survival over time

	PFS interim (7-month follow-up)	PFS update (12-month follow-up)	PFS final (18-month follow-up)
Cutoff date	Feb 11, 2011	Jul 8, 2011	Dec 15, 2011
OS events, *n*	83	137	200
EVE vs PBO, % of events	10.6 vs 13.0	17.3 vs 22.7	25.4 vs 32.2
Δ OS events, % of events	2.4	5.4	6.8

EVE everolimus, *OS* overall survival, *PBO* placebo, *PFS* progression-free survival, Δ change

Table 3 Summary of tumor response

Response	Local assessment		Central assessment	
	EVE+EXE (*n* = 485)	PBO+EXE (*n* = 239)	EVE+EXE (*n* = 485)	PBO+EXE (*n* = 239)
Best overall response (%)				
Complete response (CR)	0.6	0	0	0
Partial response (PR)	12.0	1.7	12.6	2.1
Stable disease (SD)	71.3	59.0	73.4	62.8
Progressive disease	10.1	32.6	5.8	23.4
Unknown	6.0	6.7	8.2	11.7
ORR (CR or PR), %	12.6*	1.7	12.6	2.1
95% CI for ORR	9.8–15.9	0.5–4.2	9.8–15.9	0.7–4.8
CBR (CR+PR+SD ≥ 24 weeks), %	51.3*	26.4	49.9	22.2
95% CI for CBR	46.8–55.9	20.9–32.4	45.4–54.4	17.1–28.0

CI confidence interval, *CBR* clinical benefit rate, *EVE* everolimus, *EXE* exemestane, *ORR* objective response rate, *PBO* placebo

* Statistically significant difference, $P < 0.0001$

Toxicity

Adverse events [4]

Table 2. Adverse Events Irrespective of Relationship to Study Treatment (with at Least 10% Incidence in the Everolimus–Exemestane Group).

Adverse Event	Everolimus and Exemestane (N=482)			Placebo and Exemestane (N=238)		
	Any Event	Grade 3 Event	Grade 4 Event	Any Event	Grade 3 Event	Grade 4 Event
	percent					
Stomatitis	56	8	0	11	1	0
Rash	36	1	0	6	0	0
Fatigue	33	3	<1	26	1	0
Diarrhea	30	2	<1	16	1	0
Decreased appetite	29	1	0	10	0	0
Nausea	27	<1	<1	27	1	0
Cough	22	1	0	11	0	0
Dysgeusia	21	<1	0	5	0	0
Headache	19	<1	0	13	0	0
Decreased weight	19	1	0	5	0	0
Dyspnea	18	4	0	9	1	<1
Arthralgia	16	1	0	16	0	0
Anemia	16	5	1	4	<1	<1
Epistaxis	15	0	0	1	0	0
Vomiting	14	<1	<1	11	<1	0
Peripheral edema	14	1	0	6	<1	0
Pyrexia	14	<1	0	6	<1	0
Aspartate aminotransferase level increased	13	3	<1	6	1	0
Constipation	13	<1	0	11	<1	0
Hyperglycemia	13	4	<1	2	<1	0
Pneumonitis	12	3	0	0	0	0
Thrombocytopenia	12	2	1	<1	0	<1
Asthenia	12	2	0	3	0	0
Alanine aminotransferase level increased	11	3	<1	3	2	0
Pruritus	11	<1	0	3	0	0
Insomnia	11	<1	0	8	0	0
Back pain	11	0	0	8	1	0

References

1 Peterson, D., C. Boers-Doets, R. Bensadoun, et al. 2015. "Management of oral and gastrointestinal mucosal injury: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up". Annals of Onc 26 (Supp 5): v139-v151.

2 Rugo, H. S., L. Seneviratne, J. T. Beck, et al. 2017. "Prevention of everolimus-related stomatitis in women with hormone receptor-positive, HER2-negative metastatic breast cancer using dexamethasone mouthwash (SWISH): a single-arm, phase 2 trial." Lancet Oncol 18(5):654-662.

3 Rugo, H. S., K. I. Pritchard, M. Gnant, et al. 2014. "Incidence and time course of everolimus-related adverse events in postmenopausal women with hormone receptor-positive advanced breast cancer: insights from BOLERO-2." Ann Oncol 25(4):808-815.

4 Baselga, J., M. Campone, M. Piccart, et al. 2012. "Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer." N Engl J Med 366(6):520-529.

5 Yardley, D. A., S. Noguchi, K. I. Pritchard, et al. 2013. "Everolimus plus exemestane in postmenopausal patients with HR(+) breast cancer: BOLERO-2 final progression-free survival analysis." Adv Ther 30(10):870-884.

History

Version 4

Date	Summary of changes
21/12/2021	Changed antiemetic clinical information block to minimal or low, to align with new categories. See ID 7 Prevention of anti-cancer therapy induced nausea and vomiting (AINV) v5. Metoclopramide removed from treatment schedule. Version number changed to V.4.

Version 3

Date	Summary of changes
09/05/2014	New protocol taken to Medical Oncology Reference Committee meeting.
16/06/2014	Approved and published on eviQ.
22/06/2015	Protocol reviewed electronically by Medical Oncology Reference committee. No changes and next review in 2 years.
31/05/2017	Transferred to new eviQ website. Protocol version number changed to V.2. Hepatitis B screening changed to NOT recommended.
03/11/2017	Protocol reviewed at Medical Oncology Reference Committee meeting. Clinical information and side effects updated - pre-emptive use of steroid-based mouthwash added to mucositis information. Review protocol in 2 years.
10/05/2018	Haematological dose modifications updated as per consensus of the expert clinician group. Version number changed to V.3.
23/09/2019	Protocol reviewed at Medical Oncology Reference Committee meeting on 30/08/2019. No changes. Next review in 2 years.
13/08/2021	Protocol reviewed electronically by Medical Oncology Reference Committee. Nil changes. Review in 2 years.

First approved: 16 June 2014
Last reviewed: 13 August 2021
Review due: 31 December 2023

The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/p/1590
07 Jun 2023

Patient information - Breast cancer metastatic - Everolimus and exemestane

Patient's name:

Your treatment

The treatment schedule below explains how the drugs for this treatment are given.

Everolimus and exemestane		
This treatment is continuous. Your doctor will advise you how long to take this treatment for. Do not stop taking everolimus or exemestane tablets without telling your doctor.		
Day	**Treatment**	**How it is given**
Continuous	**Everolimus** *(e-ver-OH-li-mus)*	Take orally ONCE a day at the same time each day. It can be taken with or without food, but it is best to take it the same way each time. Swallow whole with a glass of water, do not break, crush or chew. If you are unable to swallow the tablets whole they may be dissolved in water and the solution swallowed (see directions in *Other information about your treatment)*.
	Exemestane *(EX-e-MES-tane)*	Take orally ONCE a day, at the same time each day, after food. Swallow tablets whole with a glass of water, do not break, crush or chew.

Missed doses

Everolimus: if you forget to take a tablet, and if it is less than 6 hours late, take it as soon as you remember. If it is more than 6 hours late, skip that dose and take your normal dose the next time it is due. Do not take an extra dose.

Exemestane: if you forget to take a tablet or vomit a tablet, take your normal dose the next time it is due. Do not take an extra dose.

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 become unwell.

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	**Emergency contact details** Ask your doctor or nurse from your treating team who to contact if you have a problem
• a temperature of 38°C or higher • chills, sweats, shivers or shakes • shortness of breath • uncontrolled vomiting or diarrhoea • pain, tingling or discomfort in your chest or arms • you become unwell.	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

Anti-cancer drugs can reduce the number of blood cells in your body. You will need to have regular blood tests to check that your blood cell count has returned to normal. If your blood count is low, your treatment may be delayed until it has returned to normal. Your doctor or nurse will tell you when to have these blood tests.

Surgery and wound healing

This treatment may affect wound healing. Tell your doctor if you are planning to have surgery or have a wound that has not healed.

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.

Instructions for dissolving everolimus tablets:

- Everolimus tablets should not be crushed, cut or chewed. For patients with swallowing difficulties everolimus tablets can be dissolved.
- You (or whoever is dissolving the tablets) should wear disposable gloves and try to minimise touching the tablets.
- Place the everolimus tablet(s) in a glass with approximately 30 mL of plain drinking water. No other liquids should be used.
- Gently stir the contents until the tablet breaks up into very small particles. This may take up to 7 minutes.
- Drink the liquid straight away.
- Rinse the empty glass with approximately 30 mL of water and drink it.

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)	
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)	

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening.
	• Wash your hands often.
	• Keep a thermometer at home and take your temperature regularly, and if you feel unwell.
	• Do your mouth care regularly.
	• Inspect your central line site (if you have one) daily for any redness, pus or swelling.
	• Limit contact with people who are sick.
	• Learn how to recognise the signs of infection.
	• Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment.
	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:**
	  ◦ **a temperature of 38°C or higher**
	  ◦ **chills, shivers, sweats or shakes**
	  ◦ **a sore throat or cough**
	  ◦ **uncontrolled diarrhoea**
	  ◦ **shortness of breath**
	  ◦ **a fast heartbeat**
	  ◦ **become unwell even without a temperature.**

Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**

Mouth pain and soreness (mucositis)	• You may have:
	  ◦ bleeding gums
	  ◦ mouth ulcers
	  ◦ a white coating on your tongue
	  ◦ pain in the mouth or throat
	  ◦ difficulty eating or swallowing.
	• Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks.
	• Try bland and soft foods.
	• Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so.
	• Rinse your mouth after you eat and brush your teeth, using either:
	  ◦ 1/4 teaspoon of salt in 1 cup of warm water, or
	  ◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water
	• Your doctor may prescribe a steroid mouthwash to help prevent the mouth ulcers from occurring.
	• Ask your doctor or nurse for eviQ patient information - Mouth problems during cancer treatment.
	• **Tell your doctor or nurse if you get any of the symptoms listed above.**

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.
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.**
Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
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.
High blood sugar level (hyperglycaemia)	• You may feel thirsty and need to urinate more often than normal. • You may get repeated infections, especially thrush. • If you are a diabetic you will need to have your blood sugar levels checked more often. You may also need to have your diabetes medication increased. • **Tell your doctor or nurse if you get any of the signs or symptoms listed above.**

High blood cholesterol levels	• This treatment may increase your blood cholesterol levels. This is not a side effect you will notice. • Your cholesterol levels will be checked during your treatment.
Skin rash	• You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • **Talk to your doctor or nurse about other ways to manage your skin rash.**
Extra fluid in the body (fluid retention)	• You may gain weight over a short amount of time. • Your hands and feet may become swollen, appear red or feel hot and uncomfortable. • Wear loose clothing and shoes that are not too tight. • Try not to stand up or walk around too much at one time. • If your ankles or legs get swollen, try raising them. • Make sure that any cuts or areas of broken skin are treated as soon as possible. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above or gain 1 to 2 kg in a week.** • **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you become short of breath.**
Lung problems	• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment. • You may get: ◦ shortness of breath ◦ fever ◦ dry cough ◦ wheezing ◦ fast heartbeat ◦ chest pain. • Your doctor will monitor how well your lungs are working during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**
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.**
Kidney damage	• This treatment can cause changes to how your kidneys work. • You will have blood tests to make sure your kidneys are working properly. • You may need to drink more fluids while you are having treatment. Your doctor or nurse will tell you if you need to do this. • **Tell your doctor or nurse as soon as possible if you notice that your urine changes colour or you don't need to empty your bladder as often.**

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
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.
Swelling around the eyes	• You may get: ◦ swelling or heaviness around your eyes ◦ irritated eyes ◦ eye discharge ◦ changes to your vision. • **Tell your doctor or nurse if you get any of these symptoms.**
Changes in your mood	• You may become tearful, angry or more emotional than usual. • Tell your doctor or nurse if you get any of these symptoms.

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.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

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.
- Grapefruit and grapefruit juice can interact with your medication and should be avoided while you are on this treatment.
- 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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The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/pi/1590
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