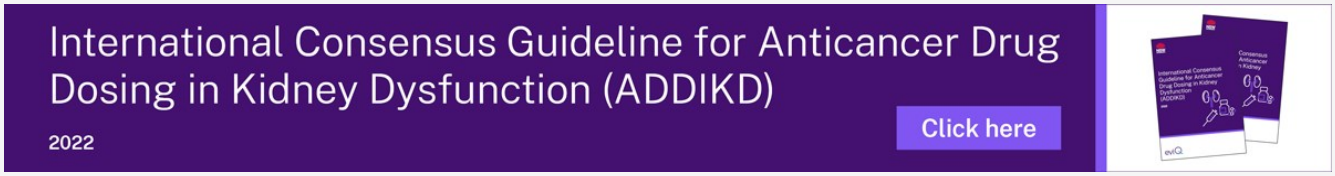
Breast metastatic pamidronate SUPERSEDED

ID: 307 v.3 **Superseded**

This protocol has been superseded because other alternatives (i.e. zoledronic acid or denosumab) are preferable in most circumstances

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 zoledronic acid
- Breast metastatic denosumab

Treatment schedule - Overview

Cycle 1 and further cycles

Drug	Dose	Route	Day
Pamidronate	90 mg	IV infusion	1

Frequency: 28 days

Cycles: Continuous (cycle length may be 21 to 28 days)

Drug status: Pamidronate is PBS authority

Cost: ~ $80 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 and further cycles

Day 1		
Calcium	500 mg (PO)	ONCE a day (daily oral supplement of at least calcium 500 mg is required)
Vitamin D	400 International Units (PO)	ONCE a day (daily oral supplement of at least vitamin D

Day 1		
		400 international units is required)
Pamidronate	90 mg (IV infusion)	in 250 mL to 500 mL sodium chloride 0.9% over 90 to 120 minutes

Day 2 to 28		
Calcium	500 mg (PO)	ONCE a day (daily oral supplement of at least calcium 500 mg is required)
Vitamin D	400 International Units (PO)	ONCE a day (daily oral supplement of at least vitamin D 400 international units is required)

Frequency: 28 days

Cycles: Continuous (cycle length may be 21 to 28 days)

Indications and patient population

Indications:

- Bone metastases from breast cancer where the following guidelines are met:
  - lytic bone metastases, with bony destruction proven on X-ray, CT or MRI.

Not recommended:

- for patients with significant multi-organ disease where bone-related disease is unlikely to be clinically significant.
- as adjuvant to radiation for control of bony pain where no systemic anticancer treatment is being employed.

Clinical information

Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Dental review	Dental review prior to treatment and 6 monthly dental review during treatment is recommended to minimise risk of osteonecrosis of the jaw. Read more about medication-related osteonecrosis of the jaw (MRONJ)
Electrolyte imbalances	If hypocalcaemia, hypophosphataemia or hypomagnesaemia occurs short term supplemental therapy may be necessary. Patients who have undergone thyroid surgery may be particularly susceptible to developing hypocalcaemia due to relative hypoparathyroidism. Severe electrolyte imbalances may require hospital admission and aggressive intravenous replacement. Daily oral supplements of at least calcium 500 mg and vitamin D 400 International Units is required (unless contraindicated) for the duration of the therapy.
Length of treatment	It is unclear whether continuing the drug is of benefit once a skeletal related event has occurred.
Blood tests	EUC, calcium, magnesium and phosphate at baseline and prior to each treatment.

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	
Baseline creatinine clearance (mL/min)	**Recommended dose**
30 to 90	Slow infusion of 90 mg over 4 hours *
less than 30	Not recommended
Baseline serum creatinine (micromol/L)	
265 or higher	Not recommended

** Treatment should be withheld for deterioration in renal function (increase of serum creatinine of more than 45 micromol/L in patients with normal baseline (i.e. less than 125 micromol/L), or increase of serum creatinine of more than 90 micromol/L in patients with abnormal baseline). Resumption of therapy may be considered when serum creatinine returns to within 10% of baseline.*

Hepatic impairment	
Hepatic dysfunction	**Recommended dose**
Mild/Moderate	Limited clinical data. Until further experience is gained, a maximum infusion rate of 20 mg/hour is recommended
Severe	No data in severe hepatic impairment therefore no specific recommendations

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*

Pamidronate		
	Interaction	**Clinical management**
Thalidomide	Increased risk of kidney dysfunction	Monitor kidney function
Anti-angiogenic drugs (e.g. sunitinib, bevacizumab)	Increased risk of osteonecrosis of the jaw	Monitor for development of osteonecrosis of the jaw if used in combination
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicty	Monitor kidney function
Drugs that may cause hypocalcaemia (e.g. other bisphosphonates, cinacalcet, phenytoin etc.)	Additive effect with pamidronate	Avoid combination or monitor calcium levels closely; ensure calcium and vitamin D supplementation is occurring (unless hypercalcaemic)

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.

Day 1

Approximate treatment time: 90 minutes

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

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

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Treatment - Time out

Pamidronate infusion

Prior to administration:

- ensure creatinine has been checked
- ensure patient is adequately hydrated

Administer pamidronate:

- via IV infusion over 1.5 to 2 hours
- flush with ~ 50 mL of sodium chloride 0.9%.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Discharge information

Supplements

- Daily oral supplements of calcium 500 mg and vitamin D 400 International Units are recommended.

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)	
Flu-like symptoms	
Headache	

Early (onset days to weeks)	
Fatigue	Read more about fatigue
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

Delayed (onset months to years)	
Osteonecrosis of the jaw (ONJ)	Exposed, necrotic bone in the maxillofacial region is associated with IV bisphosphonates and denosumab. It can persist for more than 8 weeks. Read more about medication-related osteonecrosis of the jaw

Evidence

Voluntary guidelines were updated by the American Society of Clinical Oncology in 2003. Evidence is based on studies showing a reduction at 12 months in the number of skeletal related events (SRE: pathological fracture, cord compression or requirement for radiation of bony metastases, or hypercalcaemia) in patients randomised to receive bisphosphonate (mainly pamidronate) versus placebo.[1] In two major studies,[2, 3] the SRE rate was reduced by 10-14%, from a baseline level of around 56%, with subsequent trials of zolendronic acid demonstrating equivalent efficacy but increased convenience over APD (15 v 90 minute administration time).[4]

There is minimal data regarding efficacy of less frequent administration, or the efficacy of continuing the drug once a skeletal related event has occurred.[5] There is significant data to demonstrate that bisphosphonates are frequently administered to patients not meeting the guideline criteria.[6] It has also been observed that the SRE rate in clinical practice is lower than that reported in the large clinical trials, perhaps due to less frequent imaging.[7, 8]

References

1 Pavlakis, N., R. Schmidt and M. Stockler. 2005. "Bisphosphonates for breast cancer." Cochrane.Database.Syst.Rev. (3):CD003474

2 Theriault, R. L., A. Lipton, G. N. Hortobagyi, et al. 1999. "Pamidronate reduces skeletal morbidity in women with advanced breast cancer and lytic bone lesions: a randomized, placebo-controlled trial. Protocol 18 Aredia Breast Cancer Study Group." J.Clin Oncol 17(3):846-854.

3 Hortobagyi, G. N., R. L. Theriault, L. Porter, et al. 1996. "Efficacy of pamidronate in reducing skeletal complications in patients with breast cancer and lytic bone metastases. Protocol 19 Aredia Breast Cancer Study Group." N.Engl.J.Med. 335(24):1785-1791.

4 Rosen, L. S., D. H. Gordon, W. Dugan, Jr., et al. 2004. "Zoledronic acid is superior to pamidronate for the treatment of bone metastases in breast carcinoma patients with at least one osteolytic lesion." Cancer 100(1):36-43.

5 Hillner, B. E., J. N. Ingle, R. T. Chlebowski, et al. 2003. "American Society of Clinical Oncology 2003 update on the role of bisphosphonates and bone health issues in women with breast cancer." J.Clin Oncol. 21(21):4042-4057.

6 Clemons, Mark, Katherine Enright, Annemarie Cesta, et al. 2004. "Do physicians follow systemic treatment and funding policy guidelines?" Canadian Journal of Clinical Pharmacology/Journal Canadien de Pharmacologie Clinique 11(1):e168-178.

7 Gainford, M. C., G. Dranitsaris and M. Clemons. 2005. "Recent developments in bisphosphonates for patients with metastatic breast cancer." BMJ. 330(7494):769-773.

8 Liauw, W., E. Segelov, A. Lih, et al. 2005. "Off-trial evaluation of bisphosphonates in patients with metastatic breast cancer." BMC cancer 5(1):89.

History

Version 3

Date	Summary of changes
08/09/2009	Reviewed and transferred to eviQ.
02/07/2010	Calculator removed.
17/01/2011	New format to allow for export of protocol information. Protocol version number changed to *V.2.* Antiemetics and premedications added to the treatment schedule. Additional Clinical Information, Key Prescribing table and Key Administration table combined into new section titled Clinical Considerations. Drug specific information placed behind the drug name link.
03/04/2012	Patient information updated to include ONJ.
27/04/2012	Protocol reviewed at Medical Oncology Reference Committee meeting. Decision to supersede protocol as other alternatives are preferable in most circumstances. Next review in 2 years.
23/05/2012	Calcium and vitamin D added to the treatment schedule.
09/05/2014	Protocol reviewed by email survey. No change and next review in 2 years. PHC view removed.
08/04/2016	Protocol reviewed at Medical Oncology Reference Committee meeting. No changes and next review in 2 years.
31/05/2017	Transferred to new eviQ website. Protocol version number changed to V.3
03/11/2017	Reviewed by Medical Oncology Reference Committee. No changes. Review in 2 years.
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: 1 July 2005
Last reviewed: 13 August 2021
Review due: 31 December 2023
Superseded: 27 April 2012

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https://www.eviq.org.au/p/307
03 Jul 2023

Patient information - Breast cancer metastatic - Pamidronate

Patient's name:

Your treatment

Pamidronate is **not** chemotherapy. It is used to slow down the spread of cancer in the bones and help to prevent changes to the bones that can make them weak

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

Pamidronate

This treatment cycle is repeated every 21 or every 28 days. Your doctor will advise you of the number of treatments you will have.

Day	Treatment	How it is given	How long it takes
1	**Pamidronate** (*pa-mi-DROE-nate*)	By a drip into a vein	About 2 hours

When to get help

Emergency contact details

Ask your doctor or nurse from your treating team when you should get help and who to contact if you have a problem

Daytime: .....

Night/weekend: .....

Other instructions: .....

.....

.....

.....

During your treatment immediately tell the doctor or nurse looking after you if you get any of the following problems:

- pain, stinging, swelling or redness around the injection site
- a skin rash, itching, feeling short of breath, wheezing, fever, shivers, or feeling dizzy or unwell in any way (allergic reaction).

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.

Other medications given during this treatment

- **Calcium and vitamin D supplements:** you may be given some calcium and vitamin D tablets. Your doctor or nurse will tell you how and when to take these.

Superseded treatments

This treatment is superseded meaning that better treatments have taken its place. Uncommonly superseded treatments are still used. Your doctor will explain why this treatment has been selected for you.

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)	
Flu-like symptoms	• You may get: ◦ a fever ◦ chills or sweats ◦ muscle and joint pain ◦ a cough ◦ headaches. • Tell your doctor or nurse if you get any of the symptoms listed above. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have a temperature of 38°C or higher.**
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)	
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.**
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.

Delayed (onset months to years)	
Jaw problems (osteonecrosis of the jaw)	• You may get the following signs or symptoms during treatment, or after you have stopped treatment: ◦ pain, swelling or infection in the gums ◦ loosening of teeth ◦ numbness or heaviness in the jaw ◦ poor healing of gums and sockets, especially after dental treatment • Do your mouth care regularly. • See a dentist before you begin treatment and then for 6 monthly check ups. • Make sure you tell your dentist that you are starting treatment with a bisphosphonate or denosumab. • If you need a tooth removed, talk to your doctor first, as you will need to stop treatment 6 to 8 weeks before the dental work. Only start treatment again when the tooth socket has healed. • **Tell your doctor or dentist immediately if you get any of the symptoms listed above.**

General advice for patients 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.

Pregnancy and breastfeeding

- Some cancer treatments can be dangerous to unborn babies. Talk to your doctor or nurse if you think there is any chance that you could be pregnant.
- Do not try to get pregnant or father a child during this treatment. Contraception should be used during treatment and after stopping treatment. Ask your doctor or nurse about what type of contraception you should use.
- If you are planning pregnancy/fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.
- Do not breastfeed if you are on this treatment, as anti-cancer medications can also pass into breast milk.

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

Additional notes:

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