

Mesothelioma ciSPlatin and pemetrexed

ID: 229 v.5 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](#).

International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD)

2022

[Click here](#)



Related pages:

- [Mesothelioma cARBOplatin and pemetrexed](#)
- [Mesothelioma ciSPlatin pemetrexed and beVACizumab](#)

Treatment schedule - Overview

Cycle 1 to 6

Drug	Dose	Route	Day
Pemetrexed	500 mg/m ²	IV infusion	1
ciSPlatin	75 mg/m ²	IV infusion	1

Frequency: 21 days

Cycles: 6 unless otherwise indicated

Notes:

Cisplatin may be substituted with carboplatin as they have been shown to have similar efficacy from phase II trials.¹

Drug status: All drugs in this protocol are on the [PBS general schedule](#)

Cost: ~ \$200 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 to 6

Day before chemotherapy

Day before chemotherapy		
Dexamethasone	4 mg (PO)	TWICE a day with or after food*
Day 1		
Netupitant	300 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with palonosetron)
Palonosetron	0.5 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with netupitant)
Dexamethasone	4 mg (PO)	TWICE a day with or after food*
Pemetrexed	500 mg/m ² (IV infusion)	in 100 mL sodium chloride 0.9% over 10 minutes given 30 minutes prior to cisplatin
ciSPlatin	75 mg/m ² (IV infusion)	in 1000 mL sodium chloride 0.9% over 60 minutes
Day 2		
Dexamethasone	4 mg (PO)	TWICE a day with or after food*
Day 3 and 4		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food

* Dexamethasone alternative dosing is 8 mg ONCE a day from day 1 as per reference committee consensus

Frequency: 21 days

Cycles: 6 unless otherwise indicated

Indications and patient population

Indications:

- Mesothelioma

Cautions/Exclusions:

- pre existing neuropathies [Grade 2](#) or greater
- moderate/severe renal impairment (creatinine clearance less than 60 mL/min.)
- significant hearing impairment/tinnitus.

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
Premedication	Original pemetrexed trials included hydroxocobalamin and folic acid to commence 5 to 7 days prior to the first cycle of chemotherapy, however the PEMVITASTART (Singh et al 2019) trial has demonstrated that concurrent administration does not lead to increased haematological toxicity. It is the opinion of the reference committee that hydroxocobalamin and folic acid may be administered 5 to 7 days prior to, or simultaneously with, cycle 1 of pemetrexed based chemotherapy. Hydroxocobalamin (Vit B12) 1000 micrograms intramuscularly and repeat once every 3 cycles; Folic acid 500 micrograms PO once daily continuously until 21 days after the last dose of pemetrexed. Read more about PEMVITASTART Singh et al 2019

Emetogenicity HIGH	<p>Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy.</p> <p>A steroid has been included both as an antiemetic and premedication for hypersensitivity in this protocol.</p> <p>Ensure that patients also have sufficient antiemetics for breakthrough emesis:</p> <p>Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR</p> <p>Prochlorperazine 10 mg PO every 6 hours when necessary.</p> <p>Read more about preventing anti-cancer therapy induced nausea and vomiting</p>
Hydration	<p>Hydration helps to prevent cisplatin-induced nephrotoxicity.</p> <p>The default regimen is appropriate for patients with normal electrolytes, kidney function, fluid status etc. and should be adjusted according to individual requirements.</p> <p>Read more about cisplatin hydration regimens</p>
Ototoxicity	<p>Ototoxicity may occur with platinum-based therapy; patients should be monitored for signs and symptoms. Platinum compounds should be used with caution in patients with pre-existing conditions or risk factors.</p> <p>Ototoxicity may become more severe in patients being treated with other drugs with nephrotoxic potential e.g. aminoglycosides.</p> <p>An audiometry test should be performed if symptoms develop.</p> <p>Read more about ototoxicity - tinnitus and hearing loss</p>
Peripheral neuropathy	<p>Assess prior to each treatment. If a patient experiences grade 2 or greater peripheral neuropathy, a dose reduction, delay, or omission of treatment may be required; review by medical officer before commencing treatment.</p> <p>Read more about peripheral neuropathy</p> <p>Link to chemotherapy-induced peripheral neuropathy screening tool</p>
Blood tests	<p>FBC, EUC, eGFR, LFTs, calcium, magnesium and phosphate at baseline and prior to each treatment.</p>
Hepatitis B screening and prophylaxis	<p>Routine screening for HBsAg and anti-HBc is NOT usually recommended for patients receiving this treatment.</p> <p>Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy</p>
Vaccinations	<p>Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease.</p> <p>Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook.</p> <p>Read more about COVID-19 vaccines and cancer.</p>
Fertility, pregnancy and lactation	<p>Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients.</p> <p>Read more about the effect of cancer treatment on fertility</p>

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: All dose reductions are calculated as a percentage of the starting dose

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 pemetrexed and cisplatin by 25% for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and consider reducing pemetrexed and cisplatin by 25% 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.
50 to less than 75	Delay treatment until recovery
less than 50	Delay treatment until recovery and consider reducing pemetrexed and cisplatin by 25% for subsequent cycles
less than 50 with bleeding	Delay treatment until recovery and consider reducing pemetrexed and cisplatin by 50% for subsequent cycles

Renal impairment	
eGFR (CKI-EPI or MDRD) or eCrCl (Cockcroft Gault) (mL/min)*	
greater than or equal to 70	No dose modifications necessary
50 to less than 70	Reduce cisplatin by 25%
30 to less than 50	Reduce pemetrexed and cisplatin by 50% or consider substituting carboplatin for cisplatin
less than 30	Withhold chemotherapy

* Each method has its limitations; refer to [Nephrotoxicity associated with cisplatin](#) for more information.

Hepatic impairment	
No dose modifications necessary	

Peripheral neuropathy	
Grade 2 which is present at the start of the next cycle	Reduce cisplatin by 25%; if persistent, reduce cisplatin by 50%

Peripheral neuropathy

Grade 3 or Grade 4	Omit cisplatin
--------------------	----------------

Mucositis and stomatitis

Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1 st occurrence: No dose reduction 2 nd occurrence: Reduce pemetrexed by 25% 3 rd occurrence: Reduce pemetrexed by 50% 4 th occurrence: Omit pemetrexed
---------	--

Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1 st occurrence: Reduce pemetrexed by 50% 2 nd occurrence: Omit pemetrexed
--------------------	---

Diarrhoea

Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce doses for subsequent cycles as follows: 1 st occurrence: No dose reduction 2 nd occurrence: Reduce pemetrexed and cisplatin 25% 3 rd occurrence: Reduce pemetrexed and cisplatin by 50% 4 th occurrence: Omit pemetrexed and cisplatin
---------	--

Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce doses for subsequent cycles as follows: 1 st occurrence: Reduce pemetrexed and cisplatin by 50% 2 nd occurrence: Omit pemetrexed and cisplatin
--------------------	--

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](#)

Cisplatin		
	Interaction	Clinical management
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Ototoxic drugs (e.g. aminoglycosides, frusemide, NSAIDs)	Additive ototoxicity	Avoid combination or perform regular audiometric testing
Neurotoxic drugs (e.g. vincristine, paclitaxel)	Additive neurotoxicity	Monitor closely for neuropathy if combination used
Paclitaxel	Administration schedule may influence the development of myelosuppression	Minimise toxicity by administering paclitaxel first in regimens using the combination
Carbamazepine, phenytoin, valproate	Decreased antiepileptic plasma levels	Monitor antiepileptic serum levels and seizure frequency for efficacy; adjust dosage as appropriate or select alternative antiepileptic (e.g. clonazepam, diazepam, lorazepam)

Pemetrexed		
	Interaction	Clinical management
NSAIDs (short acting e.g. ibuprofen, long acting e.g. piroxicam) and Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs) and Drugs secreted by the renal tubules (e.g. probenecid, penicillins etc.)	Increased toxicity of pemetrexed possible due to reduced clearance	Avoid combination or monitor for increased pemetrexed toxicity (esp. myelosuppression, renal and gastrointestinal toxicities) Patients with mild to moderate kidney dysfunction should avoid short and long acting NSAIDs from 2 and 5 days respectively prior, until 2 days after, pemetrexed administration.

NK-1 antagonist e.g. aprepitant, fosaprepitant, netupitant		
	Interaction	Clinical management
Dexamethasone	Increased effects/toxicity of dexamethasone due to inhibition of its metabolism via CYP3A4	Reduce dose of antiemetic dexamethasone by approximately 50% when adding a NK-1 antagonist. For protocols that already recommend a NK-1 antagonist, the dose reduction of antiemetic dexamethasone has already been taken into account. If dexamethasone is part of the chemotherapy protocol , dose reduction as per the product information is not routinely recommended in clinical practice and no additional dexamethasone is required for antiemetic cover.
Warfarin	Reduced anticoagulant efficacy of warfarin due to increased clearance (aprepitant induces CYP2C9). *Note interaction only applicable to aprepitant/ fosaprepitant	INR should be monitored in the 2 week period, particularly at 7 to 10 days following the administration of aprepitant/ fosaprepitant
Combined oral contraceptive	Reduced contraceptive efficacy due to increased clearance. *Note interaction only applicable to aprepitant/ fosaprepitant	Alternative non-hormonal methods should be used during and for 1 month after stopping aprepitant/ fosaprepitant
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of NK-1 antagonist possible due to increased clearance	Avoid combination or monitor for decreased antiemetic effect. Consider using an alternative antiemetic regimen
CYP3A4 inhibitors (e.g. azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of NK-1 antagonist possible due to reduced clearance	Avoid combination or monitor for increased adverse effects of NK-1 antagonist (e.g. headache, hiccups, constipation)
Drugs metabolised by CYP3A4 (e.g. etoposide, imatinib, irinotecan, midazolam, paclitaxel, vinblastine, vincristine etc.)	Increased effects/toxicity of these drugs possible due to inhibition of CYP3A4 by NK-1 antagonist	Avoid combination or monitor for increased toxicity especially with orally administered drugs

General		
	Interaction	Clinical management
Warfarin	Anti-cancer drugs may alter the anticoagulant effect of warfarin.	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant.
Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran	Interaction with both CYP3A4 and P-gp inhibitors /inducers. DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).	Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers. Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. Dabigatran: avoid combination with strong P-gp inducers and inhibitors. If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.
Digoxin	Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin.	Monitor digoxin serum levels; adjust digoxin dosage as appropriate.
Antiepileptics	Both altered antiepileptic and anti-cancer drug levels may occur, possibly leading to loss of efficacy or toxicity.	Where concurrent use of an enzyme-inducing antiepileptic cannot be avoided, monitor antiepileptic serum levels for toxicity, as well as seizure frequency for efficacy; adjust dosage as appropriate. Also monitor closely for efficacy of the anti-cancer therapy.
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

Day 1

Approximate treatment time: 4 hours

[Safe handling and waste management](#)

[Safe administration](#)

[General patient assessment](#) prior to each day of treatment.

[Peripheral neuropathy assessment tool](#)

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](#).

Pre treatment medication

Verify premedication taken or administer as prescribed.

Verify antiemetics taken or administer as prescribed.

⌚ Chemotherapy - Time out

Pemetrexed

- administer pemetrexed 30 minutes prior to cisplatin infusion
- via IV infusion over 10 minutes
- may be administered concurrently with prehydration
- flush with ~ 50 mL of sodium chloride 0.9%
- continue with pre hydration fluids until administration of cisplatin.

Cisplatin

Commence prehydration for cisplatin:

- administer 10 mmol magnesium sulphate (MgSO₄) in 1000 mL sodium chloride 0.9% over 60 minutes
- ensure patient has passed urine prior to cisplatin administration as per institutional policy.

Administer cisplatin (irritant):

- via IV infusion over 60 minutes
- flush with 100 mL of sodium chloride 0.9%.

Post hydration:

- 1000 mL sodium chloride 0.9% over 60 minutes.

20/11/23 Mannitol information removed to align with updated [ID 184 Prevention and management of cisplatin induced nephrotoxicity](#).

Remove IV cannula and/or deaccess [TIVAD](#) or [CVAD](#).

Continue [safe handling](#) precautions until 7 days after completion of drug(s)

Discharge information

Antiemetics

- Antiemetics as prescribed.

Pemetrexed premedication

- Premedications as prescribed and written instructions on how to take them:
 - folic acid

- ◊ hydroxocobalamin (vitamin B12)
- ◊ dexamethasone

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
Taste and smell alteration	Read more about taste and smell changes

Early (onset days to weeks)

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). Read more about oral mucositis
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
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
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
Peripheral neuropathy	Typically symmetrical sensory neuropathy, affecting the fingers and toes, sometimes progressing to the hands and feet. It is associated with several classes of anti-cancer drugs. These include taxanes, platinum-based compounds, vinca alkaloids and some drugs used to treat multiple myeloma. Read more about peripheral neuropathy
Nephrotoxicity	Renal dysfunction resulting from damage to the glomeruli, tubules or renal vasculature.
Hypomagnesaemia, hypokalaemia, hypocalcaemia	Abnormally low levels of magnesium, potassium and calcium in the blood.
Ototoxicity	Tinnitus and hearing loss may occur due to damage in the inner ear. Tinnitus is usually reversible, while hearing loss is generally irreversible. Hearing loss is dose-related, cumulative and may be worse in those with pre-existing hearing problems. Read more about ototoxicity - tinnitus and hearing loss

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia - partial	Hair thinning and/or patchy hair loss. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling

Evidence

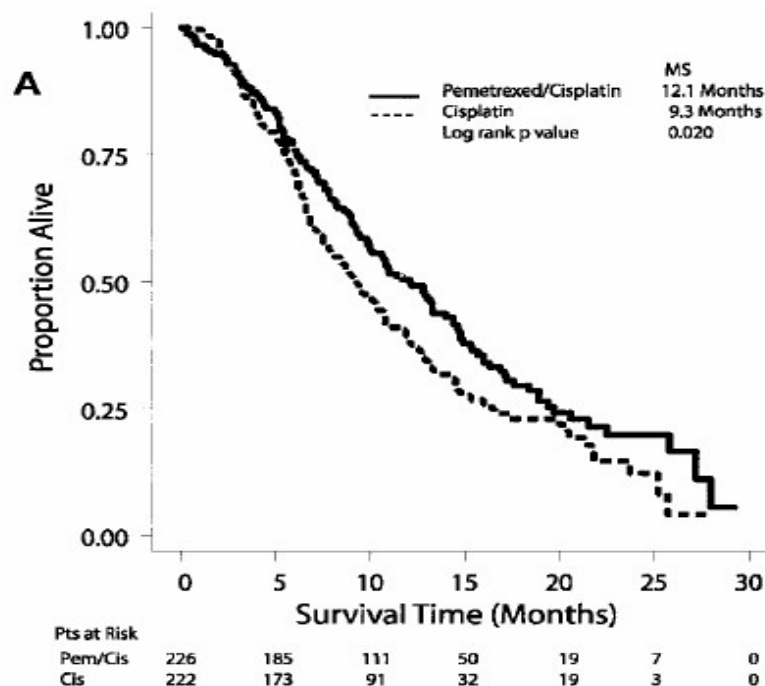
As of June 2005, there has only been one published completed randomised controlled trial (RCT) evaluating chemotherapy for malignant pleural mesothelioma (MPM), the study by Vogelzang et al. Prior to this study, any evidence for the use of chemotherapy was from Phase II studies, indicating modest response rates (usually < 20%) with uncertain quality of life and survival benefits. Combination chemotherapy (e.g. cisplatin/gemcitabine) is associated with higher response rates but uncertain benefit in survival (Nowak et al). The pivotal Vogelzang study compared the efficacy of pemetrexed and cisplatin compared with cisplatin alone, and incorporated formal quality of life assessment using the LCSS tool (Gralla et al).² Statistically superior overall survival, time to progression, response rate and patient rated quality of life was observed in favour of the pemetrexed and cisplatin combination. Serious haematologic and gastro-intestinal toxicity with the combination was substantially reduced with the addition of folic acid and B12 supplementation, without loss of efficacy, making the combination tolerable in appropriately selected patients. This study provides the best evidence to date for the use of chemotherapy as palliative treatment of patients with advanced MPM. Other randomised studies are in progress evaluating other chemotherapy regimens in the first and second-line setting.³

Efficacy

The 1 year survival was 50.3% (HR=0.77; p=0.20) and 38% (HR=0.77; p=0.20).³

Vogelzang ³	Pemetrexed, Cisplatin	Cisplatin	p-value
Response rate	41.3%	16.7%	
Time to progression	5.7 months	3.9 months	0.001
Median survival	12.1 months	9.3 months	0.020

Overall survival of patients³



© J Clin Oncol 2003

Comparative Quality of Life (QoL) effects:³

Analysis of QoL data from the Vogelzang study using the AUC method was reported by Gralla et al at ASCO in 2003, using the validated LCSS tool.² All comparisons are reported for cisplatin/pemetrexed compared with cisplatin alone. A p value < 0.05

indicates QoL score in favour of the cisplatin/pemetrexed arm compared with cisplatin alone arm. This report has not yet been published in full, however it does indicate a QoL benefit in favour of cisplatin/pemetrexed).³

Parameter	% Pts with symptom baseline		P-values For b/w arm comparisons	
		Week 12	Week 15	Week 18
Global QoL		0.167	0.025	0.012
Pain	53	0.008	<0.001	<0.001
Dyspnoea	65	0.012	<0.001	<0.001
Fatigue	72	0.149	0.027	0.010
Anorexia	58	0.516	0.062	0.017
Cough	35	0.014	<0.001	<0.001

Toxicity

Toxicities of pemetrexed with cisplatin comparing with and without vitamin supplementation.³

Adverse event ³	Pemetrexed/Cisplatin with vitamin supplements Grade 3-4 (n =168) (%)	Pemetrexed/Cisplatin No vitamin supplements Grade 3-4 (n = 32) (%)	p-value
Anaemia	4	9	0.192
Leucopenia	15	34	0.12
Neutropenia	23	38	0.205
Thrombocytopenia	5	9	0.403
Nausea	12	31	0.12
Fatigue	10	16	0.338
Vomiting	11	31	0.003
Diarrhoea	4	9	0.154
Dehydration	4	6	0.619
Stomatitis	3	3	0.999
Anorexia	1	6	0.148
Febrile neutropenia	1	9	0.009
Infection with neutropenia	0	6	0.053
Rash	1	0	0.999

References

- 1 Ceresoli, G. L., P. A. Zucali, A. G. Favaretto, et al. 2006. "Phase II study of pemetrexed plus carboplatin in malignant pleural mesothelioma." *J Clin Oncol* 24(9):1443-1448.
- 2 Hollen, P. J., R. J. Gralla, A. M. Liepa, et al. 2004. "Adapting the Lung Cancer Symptom Scale (LCSS) to mesothelioma: using the LCSS-Meso conceptual model for validation." *Cancer* 101(3):587-595.
- 3 Vogelzang, N. J., J. J. Rusthoven, J. Symanowski, et al. 2003. "Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma." *J.Clin Oncol.* 21(14):2636-2644.

Version 5

Date	Summary of changes
09/06/2022	<p>Pemetrexed containing protocols reviewed by Medical Oncology Reference Committee. The following changes were made to mesothelioma protocols containing pemetrexed.</p> <p>Treatment schedule:</p> <ul style="list-style-type: none"> • number of cycles updated to 6 • alternative dexamethasone premedication dosing notes in treatment schedule detail <p>Clinical information:</p> <ul style="list-style-type: none"> • pemetrexed premedication updated based on the PEMVITASTART study (Singh et al 2019) <p>Patient information:</p> <ul style="list-style-type: none"> • number of cycles updated to 6 • pemetrexed premedication updated to align with clinical information <p>Version number changed to V.5.</p>

Version 4

Date	Summary of changes
4/5/2007	Patient information updated.
8/12/2008	PBS indications updated.
25/8/2009	Review, new dose modifications and transferred to eviQ.
2/7/2010	Haematological dose modifications updated (20% changed to 25% dose reduction).
20/01/2011	<p>New format to allow for export of protocol information.</p> <p>Protocol version number changed to V.2.</p> <p>Antiemetics and premedications added to the treatment schedule.</p> <p>Additional Clinical Information, Key Prescribing table and Key Administration table combined into new section titled Clinical Considerations.</p> <p>Drug specific information placed behind the drug name link.</p>
10/03/2011	Ototoxicity added to clinical consideration table.
30/11/2012	<p>Protocol reviewed at Medical Oncology Reference Committee meeting.</p> <p>No change and next review in 2 years.</p>
18/3/2013	Dexamethasone premedication timing clarified.
10/7/2013	Dose modifications for cisplatin updated.
04/09/2014	PHC view removed.
12/09/2014	Protocol reviewed by Medical Oncology Reference Committee. No change. Review in 2 years.
18/02/2016	Discussed with Medical Oncology Reference Committee Chairs, for review every 5 years. Next review due 3 years.
09/12/2016	NSW dust diseases board information removed as per reference committee chair.
31/05/2017	<p>Transferred to new eviQ website. Version number changed to V.3.</p> <p>Antiemetic change: Netupitant/palonosetron combination has replaced aprepitant and a 5HT₃ receptor antagonist in combination with dexamethasone for all highly emetogenic regimens.</p> <p>Hepatitis B screening changed to NOT recommended.</p>
10/05/2018	Haematological dose modifications updated as per consensus of the expert clinician group. Version number changed to V.4.
01/07/2019	Drug status updated and note removed as pemetrexed is now on the PBS general schedule.
08/05/2020	Protocol reviewed electronically by Medical Oncology Reference Committee. No change next review 4 years.

The information contained in this protocol is based on the highest level of available evidence and consensus of the eviQ reference committee regarding their views of currently accepted approaches to treatment. Any clinician (medical oncologist, haematologist, radiation oncologist, medical physicist, radiation therapist, pharmacist or nurse) seeking to apply or consult this protocol is expected to use independent clinical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. While eviQ endeavours to link to reliable sources that provide accurate information, eviQ and the Cancer Institute NSW do not endorse or accept responsibility for the accuracy, currency, reliability or correctness of the content of linked external information sources. Use is subject to eviQ's disclaimer available at www.eviq.org.au

First approved: 30 November 2012

Last reviewed: 8 May 2020

Review due: 30 June 2024

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/229>

04 Dec 2023

Patient information - Mesothelioma - Cisplatin and pemetrexed

Patient's name:

Your treatment

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


Cisplatin and pemetrexed

This treatment cycle is repeated every 21 days. You will have 6 cycles.

Day	Treatment	How it is given	How long it takes
1	Pemetrexed (<i>PEM-e-TREX-ed</i>) Cisplatin (<i>siss-PLAT-in</i>)	By a drip into a vein	About 4 hours

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.

 <p>IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:</p>	Emergency contact details <p>Ask your doctor or nurse from your treating team who to contact if you have a problem</p>
<ul style="list-style-type: none">• 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:.....

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

- leaking from the area where the drugs are being given
- pain, stinging, swelling or redness in the area where the drugs are being given or at any injection sites
- 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

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.

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.
- **Pemetrexed premedication:** you will need to have some medications to help reduce the side effects of this treatment. You will be given more information about this from your doctor. The premedication consists of the following tablets and an injection

Medication	Dose	When to take
Vitamin B12	1000 micrograms	As an injection before the first chemotherapy treatment then every 3 cycles and stops with the last cycle of chemotherapy
Folic acid	500 micrograms	Start before the first treatment and take one tablet daily until 3 weeks after the last chemotherapy treatment
Dexamethasone	4 mg	Your doctor will tell you how and when to take these tablets

Tell your doctor or nurse if you have not started your premedication or if you forget to take the dexamethasone tablets before your treatment.

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	<ul style="list-style-type: none"> • 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.
Taste and smell changes	<ul style="list-style-type: none"> • You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.

Early (onset days to weeks)	
Mouth pain and soreness (mucositis)	<ul style="list-style-type: none"> • You may have: <ul style="list-style-type: none"> ◦ 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: <ul style="list-style-type: none"> ◦ 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 • 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.
Infection risk (neutropenia)	<ul style="list-style-type: none"> • 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: <ul style="list-style-type: none"> ◦ 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)	<ul style="list-style-type: none"> • 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.

Appetite loss (anorexia)	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your anti-diarrhoeal 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)	<ul style="list-style-type: none"> • 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.
Skin rash	<ul style="list-style-type: none"> • 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.
Nerve damage (peripheral neuropathy)	<ul style="list-style-type: none"> • You may notice a change in the sensations in your hands and feet, including: <ul style="list-style-type: none"> ◦ tingling or pins and needles ◦ numbness or loss of feeling ◦ pain. • You may find it difficult to do everyday activities, such as doing up buttons or picking up small objects. • Test water temperature with your elbow when bathing to avoid burns. • Use rubber gloves, pot holders and oven mitts in the kitchen. • Wear rubber shoes or boots when working in the garden or garage. • Keep rooms well lit and uncluttered. • Ask your doctor or nurse for eviQ patient information – Nerve problems during cancer treatment. • Tell your doctor or nurse if you get any of the symptoms listed above.
Kidney damage	<ul style="list-style-type: none"> • 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.

Low blood magnesium, potassium and calcium levels (hypomagnesaemia, hypokalaemia, hypocalcaemia)	<ul style="list-style-type: none"> • This may be found from your routine blood tests and treated by your doctor. • If it is severe you may get: <ul style="list-style-type: none"> ◦ muscle cramps or twitches ◦ numbness or tingling in your fingers, toes or around your mouth ◦ constipation ◦ an irregular heartbeat ◦ sleepy, drowsy or confused • Tell your doctor or nurse as soon as possible if you get any of the signs or symptoms listed above.
Hearing changes (ototoxicity)	<ul style="list-style-type: none"> • You may get ringing in your ears or loss of hearing. • You may have your hearing tested before and during your treatment. • Tell your doctor or nurse as soon as possible if you notice any changes to your hearing.

Late (onset weeks to months)	
Low red blood cells (anaemia)	<ul style="list-style-type: none"> • 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.
Hair thinning	<ul style="list-style-type: none"> • Your hair may become dry and may break easily. • You may lose some of your hair. • Use a gentle shampoo and a soft hairbrush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat or scarf. • Protect your scalp from the sun with a hat and sunscreen of SPF 50 or higher. • Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au)

General advice for people having cancer treatment

Chemotherapy safety

- Learn how to keep you and your family safe while you are having anticancer drugs.
- See our patient information sheet - [Chemotherapy safety at home](#).

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.
- Some anti-inflammatory medicines known as NSAIDs (e.g. ibuprofen, diclofenac) may interact with your treatment. They should be stopped at least five days before each treatment and not restarted until two days after each treatment. Speak to your doctor if you are taking these medicines. However, do not stop taking any prescribed medicines (including low dose aspirin) without first speaking to your doctor
- Paracetamol is safe to take if you have a headache or other mild aches and pains.
- 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.
- 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.

Fertility

- Some cancer treatments can reduce your fertility. This can make it difficult or impossible to get pregnant or father a child.
- Talk to your doctor or nurse before you start any treatment. Depending on your situation there may be fertility sparing options available to you and/or your partner, discuss these with your doctor or nurse.

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.

Risk of developing a second cancer

- Some anticancer treatments can increase your chance of developing a second cancer, this is rare. Your doctor will discuss with you the specific risks of your treatment.

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
- Call the Lung Foundation Australia on 1800 654 301

Mesothelioma information

- Asbestos Diseases Foundation of Australia Inc. (ADFA) – adfa.org.au
- Lung Foundation Australia – lungfoundation.com.au
- Lungevity – lungevity.org

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
- Carer Help - carerhelp.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:

This document is a guide only and cannot cover every possible situation. The health professionals caring for you should always consider your individual situation when making decisions about your care. Contact your cancer clinic staff or doctor if you have any questions or concerns about your treatment, or you are having problems coping with side effects. While eviQ endeavours to link to reliable sources that provide accurate information, eviQ and the Cancer Institute NSW do not endorse or accept responsibility for the accuracy, currency, reliability or correctness of the content of linked external information sources. Use of this document is subject to eviQ's disclaimer available at www.eviq.org.au

First approved: 30 November 2012

Last reviewed: 8 May 2020

Review due: 30 June 2024

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/229>

04 Dec 2023