

# Breast metastatic cARBOplatin and gemcitabine

ID: 1324 v.5 **Endorsed** Essential Medicine List

## ⚠ ADDIKD Carboplatin dosing:

For dosing carboplatin, ADDIKD recommends that:

- Directly measured glomerular filtration rate (mGFR) is the preferred kidney function value in the Calvert formula, especially where estimated kidney function may be unreliable for accurate therapeutic dosing.
- Where mGFR is unavailable, eGFR adjusted to an individual's body surface area (BSA-adjusted eGFR) is a suitable alternative for use in the Calvert formula.
- Kidney function should not be capped at 125 mL/min for use in the Calvert formula.
- Recalculation of carboplatin doses at each cycle is unnecessary, except when baseline kidney function (e.g., eGFR) alters by > 20% or when there is a change in the clinical status of the patient.

For further information refer the [eviQ Factsheet](#) around carboplatin dosing and the carboplatin drug monograph within the ADDIKD guideline. To assist with calculations, use the [eviQ Estimated Glomerular Filtration Rate \(eGFR\)](#) and [carboplatin dose calculators](#).

This protocol is based on limited evidence; refer to the evidence section of this protocol for more information.

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 (ADIKD)

2022

[Click here](#)



## Treatment schedule - Overview

### Cycle 1 and further cycles

Drug	Dose	Route	Day
Gemcitabine	1,000 mg/m <sup>2</sup>	IV infusion	1 and 8
cARBOplatin	5 AUC *	IV infusion	1

\*If estimated GFR is greater than 125 mL/min (i.e. 5 AUC dose greater than 750 mg), obtaining direct measurement rather than an estimated renal function and/or dose capping is strongly recommended

**Frequency:** 21 days

**Cycles:** Continuous until disease progression or unacceptable toxicity

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

**Cost:** ~ \$260 per cycle

## Treatment schedule - Detail

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

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

## Cycle 1 and further cycles

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	8 mg (PO)	60 minutes before chemotherapy
Gemcitabine	1,000 mg/m <sup>2</sup> (IV infusion)	in 100 mL to 500 mL sodium chloride 0.9% over 30 minutes
cARBOplatin	5 AUC (IV infusion)	in 500 mL glucose 5% over 30 to 60 minutes (Note: if estimated GFR is greater than 125 mL/min (i.e. 5 AUC dose greater than 750 mg), obtaining direct measurement rather than an estimated renal function and/or dose capping is strongly recommended)
Day 2 and 3		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food. Note: dexamethasone doses on day 2 and 3 may not be required and may be reduced or omitted at the clinicians discretion. *
Day 8		
Metoclopramide	10 mg (PO)	one tablet when necessary (maximum of 30 mg/24 hours, up to 5 days)
Gemcitabine	1,000 mg/m <sup>2</sup> (IV infusion)	in 100 mL to 500 mL sodium chloride 0.9% over 30 minutes

\* Link to [ID 7 Prevention of antineoplastic induced nausea and vomiting](#)

**Frequency:** 21 days

**Cycles:** Continuous until disease progression or unacceptable toxicity

## Indications and patient population

- Metastatic breast cancer after prior treatment with an anthracycline and taxane or in patients for whom there is a contraindication to an anthracycline and/or taxane.

## Clinical information

<b>Venous access required</b>	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about <a href="#">central venous access device line selection</a>
<b>Hypersensitivity/infusion related reaction</b>	High risk with carboplatin. Hypersensitivity risk increases with number of cycles of carboplatin.

<b>Emetogenicity MODERATE</b>	<p>Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy.</p> <p>Carboplatin AUC <math>\geq 4</math> is classified by MASCC/ESMO Antiemetic Guidelines 2016 and ASCO Antiemetic Guidelines 2017 as having moderate emetogenicity.</p> <p>However, a NK1 receptor antagonist and a 5HT<sub>3</sub> receptor antagonist in combination with dexamethasone are available on the PBS for primary prophylaxis of carboplatin induced nausea and vomiting.</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 <a href="#">preventing anti-cancer therapy induced nausea and vomiting</a></p>
<b>Pulmonary toxicity</b>	<p>Dyspnoea developing within hours of the infusion has been reported in about 10% of patients treated with gemcitabine.</p> <p>Read more about <a href="#">pulmonary toxicity associated with anti-cancer drugs</a>.</p>
<b>Blood tests</b>	<p>FBC, EUC and LFTs at baseline and prior to each cycle. Repeat FBC prior to each treatment. Calcium and magnesium at baseline and as clinically indicated. Recalculate carboplatin dose if significant change in weight and/or creatinine.</p>
<b>Hepatitis B screening and prophylaxis</b>	<p>Routine screening for HBsAg and anti-HBc is NOT usually recommended for patients receiving this treatment.</p> <p>Read more about <a href="#">hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy</a></p>
<b>Vaccinations</b>	<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 <a href="#">Australian Immunisation Handbook</a>.</p> <p>Read more about <a href="#">COVID-19 vaccines and cancer</a>.</p>
<b>Fertility, pregnancy and lactation</b>	<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 <a href="#">effect of cancer treatment on fertility</a></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.

For dosing carboplatin, ADDIKD recommends that:

- Directly measured glomerular filtration rate (mGFR) is the preferred kidney function value in the Calvert formula, especially where estimated kidney function may be unreliable for accurate therapeutic dosing.
- Where mGFR is unavailable, eGFR adjusted to an individual's body surface area (BSA-adjusted eGFR) is a suitable alternative for use in the Calvert formula.
- Kidney function should not be capped at 125 mL/min for use in the Calvert formula.
- Recalculation of carboplatin doses at each cycle is unnecessary, except when baseline kidney function (e.g., eGFR) alters by > 20% or when there is a change in the clinical status of the patient.

For further information refer the [eviQ Factsheet](#) around carboplatin dosing and the carboplatin drug monograph within the ADDIKD guideline. To assist with calculations, use the eviQ [Estimated Glomerular Filtration Rate \(eGFR\)](#) and [carboplatin dose calculators](#).

**Note:** all dose reductions are calculated as a percentage of the starting dose.

<b>Haematological toxicity</b>	
<b>ANC x 10<sup>9</sup>/L (pre-treatment blood test)</b>	
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 reduce carboplatin and gemcitabine by 25% for subsequent cycles
Febrile neutropenia or previous delay for myelosuppression	Delay treatment until recovery and reduce carboplatin and gemcitabine by 25% for subsequent cycles
Prolonged recovery greater than two weeks delay or 3 <sup>rd</sup> delay for myelosuppression	Delay treatment until recovery and reduce carboplatin and gemcitabine by 50% for subsequent cycles or cease
<b>Platelets x10<sup>9</sup>/L (pre-treatment blood test)</b>	
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 reduce carboplatin and gemcitabine by 25% for subsequent cycles

**Note:** If treatment cannot be delivered on Day 8, it should be omitted rather than delayed. Treatment for the next cycle should proceed on the date originally scheduled and should incorporate dose modifications as appropriate.

<b>Renal impairment</b>	
<b>Creatinine clearance (mL/min)</b>	
30 to 50	Reduce gemcitabine by 25% and recalculate carboplatin dose using Calvert formula
less than 30	Reduce gemcitabine by 50% and recalculate carboplatin dose using Calvert formula

<b>Hepatic impairment</b>	
<b>Hepatic dysfunction</b>	
Moderate	Reduce gemcitabine by 25%
Severe	No data for gemcitabine

<b>Mucositis and stomatitis</b>	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for

## Mucositis and stomatitis

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

## Cease gemcitabine if either of the following develop:

- Pulmonary toxicity
- Haemolytic uraemic syndrome (HUS)

## 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](#)

### Carboplatin

	Interaction	Clinical management
<b>Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, cisplatin, contrast dye, frusemide, NSAIDs)</b>	Additive nephrotoxicity	Avoid combination or monitor renal function closely
<b>Ototoxic drugs (e.g. aminoglycosides, frusemide, NSAIDs)</b>	Additive ototoxicity	Avoid combination or perform regular audiometric testing
<b>Paclitaxel</b>	Administration schedule may influence the development of myelosuppression	Minimise toxicity by administering paclitaxel first in regimens using the combination

### Gemcitabine

	Interaction	Clinical management
<b>Warfarin</b>	Increased anticoagulant effect/increased bleeding risk due to decreased hepatic metabolism of warfarin and decreased synthesis of clotting factors	Monitor INR regularly and adjust warfarin dosage as appropriate

NK-1 antagonist e.g. aprepitant, fosaprepitant, netupitant		
	Interaction	Clinical management
<b>Dexamethasone</b>	Increased effects/toxicity of dexamethasone due to inhibition of its metabolism via CYP3A4	Reduce dose of <b>antiemetic dexamethasone</b> by approximately 50% when adding a NK-1 antagonist. For protocols that already recommend a NK-1 antagonist, the dose reduction of <b>antiemetic dexamethasone</b> has already been taken into account.  If <b>dexamethasone is part of the chemotherapy protocol</b> , dose reduction as per the product information is not routinely recommended in clinical practice and no additional dexamethasone is required for antiemetic cover.
<b>Warfarin</b>	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
<b>Combined oral contraceptive</b>	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
<b>CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)</b>	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
<b>CYP3A4 inhibitors (e.g. azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)</b>	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)
<b>Drugs metabolised by CYP3A4 (e.g. etoposide, imatinib, irinotecan, midazolam, paclitaxel, vinblastine, vincristine etc.)</b>	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
<b>Warfarin</b>	Anti-cancer drugs may alter the anticoagulant effect of warfarin.	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant.
<b>Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran</b>	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.
<b>Digoxin</b>	Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin.	Monitor digoxin serum levels; adjust digoxin dosage as appropriate.
<b>Antiepileptics</b>	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.
<b>Antiplatelet agents and NSAIDs</b>	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.
<b>Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)</b>	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 <a href="#">TGA Medicines Safety Update</a>
<b>Vaccines</b>	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 <a href="#">Australian Immunisation Handbook</a>

## 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: 2 hours**

[Safe handling and waste management](#)

[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](#).

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Verify dexamethasone taken or administer as prescribed.

## 🕒 Chemotherapy - Time out

### Gemcitabine

**Administer gemcitabine (irritant):**

- via IV infusion over 30 minutes
  - if pain develops along the vein, verify the drug has not extravasated
  - further dilution (using a second saline line), warmth or temporarily slowing the infusion may help
- flush with ~ 100 mL of sodium chloride 0.9%
- prolonged infusion times have been shown to increase toxicity.

### Carboplatin

**Administer carboplatin (irritant):**

- via IV infusion over 30 to 60 minutes
- observe for hypersensitivity reactions
- flush with ~100 mL of sodium chloride 0.9%
- hypersensitivity risk increases with number of cycles administered.

**Stop infusion at first sign of reaction:**

- if symptoms are mild and resolve when infusion is stopped, consider recommencing infusion after review by medical officer at a slower rate
- for severe reactions seek medical assistance immediately and do not restart infusion.

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

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

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## Day 8

**Approximate treatment time: 60 minutes**

[Safe handling and waste management](#)

[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](#).

### Pre treatment medication

Verify antiemetics taken or administer as prescribed.

### ⦿ Chemotherapy - Time out

#### Gemcitabine

##### Administer gemcitabine (irritant):

- via IV infusion over 30 minutes
  - if pain develops along the vein, verify the drug has not extravasated
  - further dilution (using a second saline line), warmth or temporarily slowing the infusion may help
- flush with ~ 100 mL of sodium chloride 0.9%
- prolonged infusion times have been shown to increase toxicity.

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

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

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### Discharge information

#### 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)

<b>Hypersensitivity reaction</b>	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about <a href="#">hypersensitivity reaction</a>
<b>Nausea and vomiting</b>	Read more about <a href="#">prevention of treatment induced nausea and vomiting</a>
<b>Taste and smell alteration</b>	Read more about <a href="#">taste and smell changes</a>
<b>Flu-like symptoms</b>	

Early (onset days to weeks)	
<b>Neutropenia</b>	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 <a href="#">immediate management of neutropenic fever</a>
<b>Thrombocytopenia</b>	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding.  Read more about <a href="#">thrombocytopenia</a>
<b>Oral mucositis</b>	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 <a href="#">oral mucositis</a>
<b>Diarrhoea</b>	Read more about <a href="#">treatment induced diarrhoea</a>
<b>Fatigue</b>	Read more about <a href="#">fatigue</a>
<b>Skin rash</b>	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 <a href="#">skin rash</a>
<b>Fluid retention and oedema</b>	An excess amount of fluid around the cells, tissues or serous cavities of the body, leading to swelling.

Late (onset weeks to months)	
<b>Anaemia</b>	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about <a href="#">anaemia</a>
<b>Alopecia - partial</b>	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 <a href="#">alopecia</a>
<b>Pulmonary toxicity</b>	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about <a href="#">pulmonary toxicity associated with anti-cancer drugs</a>
<b>Haemolytic uraemic syndrome (HUS)</b>	A rare but serious acute syndrome characterised by haemolysis of red blood cells and renal failure. Read more about <a href="#">haemolytic uraemic syndrome (HUS)</a>

## Evidence

A search of the literature did not find strong evidence to support the use of carboplatin/gemcitabine in the treatment of breast cancer. The expert reference panel supported publication of the protocol on the basis of the information summarised below. The committee was most strongly influenced by the phase II study by Maisano et al.<sup>1</sup>

Source	Study & year published	Supports use	Is the dose and regimen consistent with the protocol?	Comments
<b>Phase II trials</b>	Yardley et al. 2018 <sup>2</sup>	No	No	Gemcitabine 1000 mg/m <sup>2</sup> and carboplatin AUC 2 on day 1 and 8 q21d (control arm)
	Maisano et al. 2011 <sup>1</sup>	Yes	Yes	
	Laessig et al. 2007 <sup>3</sup>	Yes	No	Gemcitabine 1000 mg/m <sup>2</sup> on day 1 and 8, and carboplatin AUC 4 on day 1 q21d
Guidelines	Date published/revised	Supports use	Is the dose and regimen consistent with	Comments

Source	Study & year published	Supports use	Is the dose and regimen consistent with the protocol? the protocol?	Comments
NCCN	V.6 2020	Yes	No	Gemcitabine 1000 mg/m <sup>2</sup> and carboplatin AUC 2 on day 1 and 8 q21d  Single agent therapy recommended, combination chemotherapy useful in certain circumstances
BCCA	September 2020	Yes	No	Available as a cisplatin/gemcitabine (750 mg/m <sup>2</sup> day 1 and 8) protocol with the option to substitute cisplatin with carboplatin
CCO	December 2018	Yes	No	Gemcitabine 800 mg/m <sup>2</sup> and carboplatin AUC 2 on day 1 and 8 q21d
ESMO	September 2020	Yes	N/A	Single agent therapy recommended, combination chemotherapy useful in certain circumstances

## Efficacy

A summary of the evidence supporting the effect of this protocol is below:

Outcome	Yardley et al <sup>2</sup>			Maisano et al <sup>1</sup>	Laessig et al <sup>3</sup>
	Gemcitabine/carboplatin (control arm) (n = 66)	nab-paclitaxel/carboplatin (n = 64)	nab-paclitaxel/gemcitabine (n = 61)	n = 31 (single arm study)	n = 39 (single arm study)
Overall survival (months)	12.6	16.8	12.1	11	13.2
Progression-free survival (months)	6.0	8.3	5.5	5.5	5.3
Overall response rate (%)	44	73	39	32	31
Stable disease ≥ 12 weeks (%)	-	-	-	16	-
Stable disease ≥ 16 weeks (%)	32	20	44	-	-
Stable disease (%)	-	-	-	-	31

## Toxicity

A summary of the toxicity associated with this protocol including the serious and/or common side effects are below:

Toxicity (n = 31) <sup>1</sup>	Incidence of grade 3/4 toxicity (%)
Neutropenia	56
Leukopenia	38
Thrombocytopenia	33
Alopecia*	22
AST	19

Toxicity (n = 31) <sup>1</sup>	Incidence of grade 3/4 toxicity (%)
ALT	16
Febrile neutropenia	13
Anaemia	13
Fatigue	10
Bilirubin	6
Alkaline phosphatase	3
Vomiting	0
Neuro-sensory toxicity	0

\*Grade 2 alopecia

## References

- 1 Maisano, R., M. Zavettieri, D. Azzarello, et al. 2011. "Carboplatin and gemcitabine combination in metastatic triple-negative anthracycline- and taxane-pretreated breast cancer patients: a phase II study." *J Chemother* 23(1):40-43.
- 2 Yardley, D. A., R. Coleman, P. Conte, et al. 2018. "nab-Paclitaxel plus carboplatin or gemcitabine versus gemcitabine plus carboplatin as first-line treatment of patients with triple-negative metastatic breast cancer: results from the tnAcity trial." *Ann Oncol* 29(8):1763-1770
- 3 Laessig, D., H. J. Stemmler, U. Vehling-Kaiser, et al. 2007. "Gemcitabine and carboplatin in intensively pretreated patients with metastatic breast cancer." *Oncology* 73(5-6):407-414.

## History

### Version 5

Date	Summary of changes
23/11/2020	Protocol reviewed electronically by Medical Oncology Reference Committee. Evidence tables updated and Yardley et al 2018 study added. Version increased to V.5. Next review in 5 years.

### Version 4

Date	Summary of changes
27/04/2012	New protocol taken to Medical Oncology Reference Committee meeting.
12/06/2012	Approved and published on eviQ.
30/06/2013	Protocol reviewed by committee via email survey. No changes and next review in 2 years.
09/03/2015	Carboplatin dosing - for estimated GFR > 125 mL/min, note about measuring GFR and/or dose capping added.
02/07/2015	Protocol reviewed electronically by Medical Oncology Reference Committee. No changes, review in 2 years.
18/02/2016	Discussion with Medical Oncology Reference Committee Chairs and protocol to be reviewed every 5 years. Next review due in 4 years.
31/05/2017	Transferred to new eviQ website. Version number changed to V.2.  Antiemetic change: A NK1 receptor antagonist and a 5HT <sub>3</sub> receptor antagonist in combination with dexamethasone has been added as available on the PBS for primary prophylaxis of carboplatin induced nausea and vomiting.  Hepatitis B screening changed to NOT recommended.

Date	Summary of changes
10/05/2018	Haematological dose modifications updated as per consensus of the expert clinician group. Version number changed to V.3.
17/01/2019	Carboplatin AUC $\geq 4$ changed from highly to moderately emetogenic as per MASCC/ESMO and ASCO guidelines and medical oncology reference committee consensus. Dexamethasone day 4 dose removed. NK1 receptor antagonist unchanged. Treatment detail and clinical information updated to reflect the change. Version number changed to V.4.

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](http://www.eviQ.org.au)

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07 Jun 2023

# Patient information - Breast cancer metastatic - Carboplatin and gemcitabine

Patient's name:

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## Your treatment

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


### Carboplatin and gemcitabine

This treatment cycle is repeated every 21 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	<b>Gemcitabine</b> ( <i>jem-sie-ta-been</i> ) <b>Carboplatin</b> ( <i>carb-o-PLAT-in</i> )	By a drip into a vein	About 2 hours
8	<b>Gemcitabine</b>	By a drip into a vein	About 1 hour

## 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><b>IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:</b></p>	<b>Emergency contact details</b> Ask your doctor or nurse from your treating team who to contact if you have a problem
<ul style="list-style-type: none"><li>• a temperature of 38°C or higher</li><li>• chills, sweats, shivers or shakes</li><li>• shortness of breath</li><li>• uncontrolled vomiting or diarrhoea</li><li>• pain, tingling or discomfort in your chest or arms</li><li>• you become unwell.</li></ul>	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. Tell your doctor if you are on an anticoagulant (medication used to treat or prevent blood clots) e.g. warfarin. You may need to have additional 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.

## **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)

<b>Allergic reaction</b>	<ul style="list-style-type: none"><li>• Allergic reactions are uncommon but can be life threatening.</li><li>• <b>If you feel unwell during the infusion or shortly after it, or:</b><ul style="list-style-type: none"><li>◦ <b>get a fever, shivers or shakes</b></li><li>◦ <b>feel dizzy, faint, confused or anxious</b></li><li>◦ <b>start wheezing or have difficulty breathing</b></li><li>◦ <b>have a rash, itch or redness of the face</b></li></ul></li></ul> <p><b><u>While you are in hospital:</u> Tell your doctor or nurse immediately.</b></p> <p><b><u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.</b></p>
<b>Nausea and vomiting</b>	<ul style="list-style-type: none"><li>• You may feel sick (nausea) or be sick (vomit).</li><li>• Take your anti-sickness medication as directed even if you don't feel sick.</li><li>• Drink plenty of fluids (unless you are fluid restricted).</li><li>• Eat small meals more frequently.</li><li>• Try food that does not require much preparation.</li><li>• Try bland foods like dry biscuits or toast.</li><li>• Gentle exercise may help with nausea.</li><li>• Ask your doctor or nurse for eviQ patient information - <a href="#">Nausea and vomiting during cancer treatment</a>.</li><li>• <b>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.</b></li></ul>
<b>Taste and smell changes</b>	<ul style="list-style-type: none"><li>• You may find that food loses its taste or tastes different.</li><li>• These changes are likely to go away with time.</li><li>• Do your mouth care regularly.</li><li>• Chew on sugar-free gum or eat sugar-free mints.</li><li>• Add flavour to your food with sauces and herbs.</li><li>• Ask your doctor or nurse for eviQ patient information - <a href="#">Taste and smell changes during cancer treatment</a>.</li></ul>
<b>Flu-like symptoms</b>	<ul style="list-style-type: none"><li>• You may get:<ul style="list-style-type: none"><li>◦ a fever</li><li>◦ chills or sweats</li><li>◦ muscle and joint pain</li><li>◦ a cough</li><li>◦ headaches.</li></ul></li><li>• The drug gemcitabine can cause a fever or flu-like illness within the first day or two of having the treatment.</li><li>• You can take paracetamol to help settle these symptoms.</li><li>• <b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if the symptoms do not settle or you become unwell.</b></li></ul>

## Early (onset days to weeks)



<p><b>Infection risk (neutropenia)</b></p>	<ul style="list-style-type: none"> <li>• 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.</li> <li>• Wash your hands often.</li> <li>• Keep a thermometer at home and take your temperature regularly, and if you feel unwell.</li> <li>• Do your mouth care regularly.</li> <li>• Inspect your central line site (if you have one) daily for any redness, pus or swelling.</li> <li>• Limit contact with people who are sick.</li> <li>• Learn how to recognise the signs of infection.</li> <li>• Ask your doctor or nurse for eviQ patient information - <a href="#">Infection during cancer treatment</a>.</li> <li>• <b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:</b> <ul style="list-style-type: none"> <li>◦ a temperature of 38°C or higher</li> <li>◦ chills, shivers, sweats or shakes</li> <li>◦ a sore throat or cough</li> <li>◦ uncontrolled diarrhoea</li> <li>◦ shortness of breath</li> <li>◦ a fast heartbeat</li> <li>◦ become unwell even without a temperature.</li> </ul> </li> </ul>
<p><b>Low platelets (thrombocytopenia)</b></p>	<ul style="list-style-type: none"> <li>• 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.</li> <li>• Try not to bruise or cut yourself.</li> <li>• Avoid contact sport or vigorous exercise.</li> <li>• Clear your nose by blowing gently.</li> <li>• Avoid constipation.</li> <li>• Brush your teeth with a soft toothbrush.</li> <li>• Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to.</li> <li>• Tell your doctor or nurse if you have any bruising or bleeding.</li> <li>• <b>Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.</b></li> </ul>
<p><b>Mouth pain and soreness (mucositis)</b></p>	<ul style="list-style-type: none"> <li>• You may have: <ul style="list-style-type: none"> <li>◦ bleeding gums</li> <li>◦ mouth ulcers</li> <li>◦ a white coating on your tongue</li> <li>◦ pain in the mouth or throat</li> <li>◦ difficulty eating or swallowing.</li> </ul> </li> <li>• Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks.</li> <li>• Try bland and soft foods.</li> <li>• Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so.</li> <li>• Rinse your mouth after you eat and brush your teeth, using either: <ul style="list-style-type: none"> <li>◦ 1/4 teaspoon of salt in 1 cup of warm water, or</li> <li>◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water</li> </ul> </li> <li>• Ask your doctor or nurse for eviQ patient information - <a href="#">Mouth problems during cancer treatment</a>.</li> <li>• <b>Tell your doctor or nurse if you get any of the symptoms listed above.</b></li> </ul>

<b>Diarrhoea</b>	<ul style="list-style-type: none"> <li>• You may get bowel motions (stools, poo) that are more frequent or more liquid.</li> <li>• You may also get bloating, cramping or pain.</li> <li>• Take your antidiarrhoeal medication as directed by your doctor.</li> <li>• Drink plenty of fluids (unless you are fluid restricted).</li> <li>• Eat and drink small amounts more often.</li> <li>• Avoid spicy foods, dairy products, high fibre foods, and coffee.</li> <li>• Ask your doctor or nurse for eviQ patient information - <a href="#">Diarrhoea during cancer treatment</a>.</li> <li>• <b>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.</b></li> </ul>
<b>Tiredness and lack of energy (fatigue)</b>	<ul style="list-style-type: none"> <li>• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy.</li> <li>• Do not drive or operate machinery if you are feeling tired.</li> <li>• Nap for short periods (only 1 hour at a time)</li> <li>• Prioritise your tasks to ensure the best use of your energy.</li> <li>• Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted).</li> <li>• Try some gentle exercise daily.</li> <li>• Allow your friends and family to help.</li> <li>• <b>Tell your doctor or nurse if you get any of the symptoms listed above.</b></li> </ul>
<b>Skin rash</b>	<ul style="list-style-type: none"> <li>• You may get a red, bumpy rash and dry, itchy skin.</li> <li>• Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream.</li> <li>• Do not scratch your skin.</li> <li>• Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher.</li> <li>• <b>Talk to your doctor or nurse about other ways to manage your skin rash.</b></li> </ul>
<b>Extra fluid in the body (fluid retention)</b>	<ul style="list-style-type: none"> <li>• You may gain weight over a short amount of time.</li> <li>• Your hands and feet may become swollen, appear red or feel hot and uncomfortable.</li> <li>• Wear loose clothing and shoes that are not too tight.</li> <li>• Try not to stand up or walk around too much at one time.</li> <li>• If your ankles or legs get swollen, try raising them.</li> <li>• Make sure that any cuts or areas of broken skin are treated as soon as possible.</li> <li>• <b>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.</b></li> <li>• <b>Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you become short of breath.</b></li> </ul>

Late (onset weeks to months)	
<b>Low red blood cells (anaemia)</b>	<ul style="list-style-type: none"> <li>You may feel dizzy, light-headed, tired and appear more pale than usual.</li> <li>Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion.</li> <li><b>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.</b></li> </ul>
<b>Hair thinning</b>	<ul style="list-style-type: none"> <li>Your hair may become dry and may break easily.</li> <li>You may lose some of your hair.</li> <li>Use a gentle shampoo and a soft hairbrush.</li> <li>Take care with hair products like hairspray, hair dye, bleaches and perms.</li> <li>Protect your scalp from the cold with a hat or scarf.</li> <li>Protect your scalp from the sun with a hat and sunscreen of SPF 50 or higher.</li> <li>Ask your doctor or nurse about the <a href="http://www.lgfb.org.au">Look Good Feel Better</a> program (www.lgfb.org.au)</li> </ul>
<b>Lung problems</b>	<ul style="list-style-type: none"> <li>Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment.</li> <li>You may get: <ul style="list-style-type: none"> <li>shortness of breath</li> <li>fever</li> <li>dry cough</li> <li>wheezing</li> <li>fast heartbeat</li> <li>chest pain.</li> </ul> </li> <li>Your doctor will monitor how well your lungs are working during your treatment.</li> <li><b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.</b></li> </ul>
<b>Red blood cell and kidney damage (haemolytic uraemic syndrome)</b>	<ul style="list-style-type: none"> <li>This side effect is rare, but can be very serious.</li> <li><b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if it has been longer than 12 hours since you have emptied your bladder or if you have any of the following signs or symptoms:</b> <ul style="list-style-type: none"> <li><b>black, tarry bowel motions (stools, poo)</b></li> <li><b>blood in your urine or are not urinating as often</b></li> <li><b>pinpoint red spots on your skin</b></li> <li><b>major bruising</b></li> <li><b>a fever</b></li> <li><b>shortness of breath</b></li> <li><b>a severe headache</b></li> <li><b>confusion.</b></li> </ul> </li> </ul>

## 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.
- 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.
- 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.

### 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



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](http://www.eviq.org.au)

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