Non-Hodgkin lymphoma DHAC (dexamethasone cytarabine cARBOplatin)



ID: 373 v.4 Endorsed Essential Medicine List

A 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 <u>eviQ Factsheet</u> 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.

Patients with lymphoma should be considered for inclusion into clinical trials. Link to ALLG website, ANZCTR website and Lymphoma Australia website.

The anticancer drug(s) in this protocol <u>may</u> 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 <u>eviQ Estimated Glomerular Filtration Rate (eGFR) calculator</u>.

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

Click here



Treatment schedule - Overview

Cycle 1 and 2

2022

Drug	Dose	Route	Day
Dexamethasone	40 mg ONCE a day	IV/P0	1 to 4
cARBOplatin	5 AUC (Cap dose at 800 mg)	IV infusion	1
Cytarabine (Ara-C)	2,000 mg/m ²	IV infusion	1 and 2

Frequency: 21 days

Cycles: 2 to 6 cycles depending on response

Notes:

- There is very little published evidence for the DHAC protocol; this is a local adaptation of the Velasquez et al (1988) DHAP protocol, per the eviQ Reference Committee.
- · Carboplatin has been substituted for cisplatin in an attempt to reduce cisplatin-related toxicities.
- A carboplatin dose of AUC 5 over 60 minutes has been included per the eviQ Reference Committee.
- There are no specific references for capping of carboplatin dose in the DHAC protocol, but capping the dose at 800 mg as in the ICE and RICE protocols has been adopted for uniformity per consensus of the eviQ Reference Committee.

- Rituximab may be added to this protocol for patients with CD 20 +ve relapsed/refractory B-cell lymphoma.
- The administration schedule for cytarabine has also been modified to allow for outpatient administration of this regimen (changed from a twice daily dose on Day 2 to one dose on Day 1 and one dose on Day 2).
- Velasquez et al (1988)¹ modified the cytarabine dose for patients aged older than 70 years to 1 g/m².

Drug status: All drugs in this protocol are on the PBS general schedule

Cost: ~ \$1,040 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 2

Day 1		
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food OR by IV infusion on days 1 to 4.
cARBOplatin	5 AUC (IV infusion) (Cap dose at 800 mg)	in 500 mL glucose 5% over 30 to 60 minutes
Cytarabine (Ara-C)	2,000 mg/m ² (IV infusion)	in 500 mL sodium chloride 0.9% over 2 to 3 hours

Day 2		
Dexamethasone	40 mg (IV/P0)	ONCE a day orally in the morning with food OR by IV infusion on days 1 to 4.
Cytarabine (Ara-C)	2,000 mg/m ² (IV infusion)	in 500 mL sodium chloride 0.9% over 2 to 3 hours

Day 3 and 4		
Dexamethasone	40 mg (IV/PO)	ONCE a day orally in the morning with food OR by IV infusion on days 1 to 4.

Frequency: 21 days

Cycles: 2 to 6 cycles depending on response

Indications and patient population

· Relapsed or refractory non-Hodgkin lymphoma

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
Hypersensitivity/infusion related reaction	High risk with carboplatin. Hypersensitivity risk increases with number of cycles of carboplatin. Rechallenge with carboplatin after hypersensitivity carries a high risk of anaphylaxis, and where clinically indicated, should be undertaken with a desensitisation protocol with appropriate supports in place. Refer to local institutional policy. Read more about Hypersensitivity reaction

Antiemetics for multi-day protocols	Patients being treated with multi-day anticancer protocols should receive antiemetics tailored to the emetogenic risk of the drugs administered each day during treatment and for two days after completion of the anticancer protocol. No standard antiemetic regimen exists for multi-day anticancer protocols, and as such, no antiemetics have been added to the treatment schedule, despite the availability of a PBS approved combination of an NK1 receptor antagonist, 5HT3, and a steroid for preventing nausea and vomiting associated with moderate to highly emetogenic anti-cancer therapies. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary.
	Read more about preventing anti-cancer therapy induced nausea and vomiting
Cytarabine-induced neurotoxicity	This may occur in patients treated with high-dose cytarabine. Assess cerebellar function prior to each cytarabine dose. Note: an increased risk of cytarabine-induced neurotoxicity has been associated with kidney dysfunction. Read more about neurotoxicity associated with high-dose cytarabine and access the cytarabine cerebellar neurotoxicity assessment chart
Ocular toxicities	Administer corticosteroid eye drops to minimise corneal toxicity from high dose cytarabine. Commence on the day of first dose of cytarabine and continue for at least 72 hours after completion of final cytarabine dose. Read more about ocular toxicities associated with high dose cytarabine
Cytarabine syndrome	Treatment with cytarabine may cause a "cytarabine syndrome" characterised by flu-like symptoms, skin rash and occasionally chest pain.
Corticosteroids	Diabetic patients should monitor their blood glucose levels closely. To minimise gastric irritation, advise patient to take immediately after food. Consider the use of a H2 antagonist or proton pump inhibitor if appropriate. Read more about acute short term effects from corticosteroids
Central nervous system (CNS) prophylaxis	Consider CNS relapse assessment in patients with high grade lymphoma. Read more about CNS prophylaxis in diffuse large cell lymphoma
Tumour lysis risk	Patients are at high risk of developing tumour lysis syndrome, prophylaxis is recommended. Read more about the prevention and management of tumour lysis syndrome.
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients
Antiviral prophylaxis	Read more about antiviral prophylaxis drugs and doses
Antifungal prophylaxis	Read more about antifungal prophylaxis drugs and doses.
Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website
Blood tests	FBC at baseline and repeat prior to each cycle. EUCs, eGFR, LFTs, LDH and BSL at baseline and regularly throughout treatment as clinically indicated.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy

Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	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. Read more about the effect of cancer treatment on fertility

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).

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.

Haematological toxicity

Dose reductions for haematological toxicity not usually recommended. Discuss with Haematologist. Consider adding G-CSF

Renal impairment

Recalculate carboplatin dose using Calvert formula

No specific dose modifications recommended for cytarabine in renal impairment, but please note an increased risk of neurotoxicity has been associated with high dose cytarabine with creatinine clearance less than 60 mL/min.

Hepatic impairment

Elevations in liver function tests occur with both standard and high dose cytarabine. Significant liver function abnormalities may require discontinuation or a dose reduction.

Interactions

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

For more information see References & Disclaimer.

Carboplatin		
	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
Paclitaxel	Administration schedule may influence the development of myelosuppression	Minimise toxicity by administering paclitaxel first in regimens using the combination

Cytarabine		
	Interaction	Clinical management
Cytidine deaminase (CDA) inhibitors (e.g. cedazuridine)	Potential increased effect/toxicity of cytarabine due to reduced clearance	Avoid combination or monitor for increased cytarabine effect/toxicity

Dexamethasone		
	Interaction	Clinical management
CYP3A4 interactions	Dexamethasone is a substrate of CYP3A4 and a weak to moderate inducer of CYP3A4. The clinical relevance of CYP3A4 induction by dexamethasone is unknown as the mechanism has yet to be established	The effects of the concomitant use of dexamethasone with other CYP3A4 inducers, inhibitors or substrates is variable. If used concomitantly, monitor patients closely for adverse drug reactions
Warfarin	Concurrent use may result in increased risk of bleeding or diminished effects of warfarin	Monitor prothrombin time / INR (especially during initiation or discontinuation) and for signs of drug toxicity during concomitant use; adjust warfarin dose as required
Oral hypoglycaemics	Corticosteroids may cause hyperglycaemia and worsen diabetes control	Monitor blood glucose levels and adjust oral hypoglycaemic dose as required

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: 5 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 delay of treatment and review by medical officer before commencing treatment.

· weigh patient on each visit

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Commence corticosteroid eye drops 24 hours before starting cytarabine. Continue for 72 hours after completion of the last dose of cytarabine.

Dexamethasone

- · administer orally ONCE a day in the morning with food OR
- · via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%
- patients may receive dexamethasone on day 3 and 4 orally as an outpatient or administered via IV infusion if still an inpatient

Note: if a dose is forgotten or vomited, contact treating team.

Ochemotherapy - Time out

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.

Cytarabine

Prior to administration:

Ensure corticosteroid eye drops have been administered before starting cytarabine.

Verify that cytarabine neurological assessment has been performed prior to administration of cytarabine:

- if the patient scores 0 then administer cytarabine as charted
- if the patient scores 1 or above, do not administer the cytarabine and immediately notify medical officer.

Administer cytarabine:

• via IV infusion over 2 to 3 hours:

flush with ~50 mL of sodium chloride 0.9%.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Day 2

Approximate treatment time: 4 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 delay of treatment and review by medical officer before commencing treatment.

· weigh patient on each visit

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Hydration if prescribed

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Continue corticosteroid eye drops until 72 hours after completion of the last dose of cytarabine.

Dexamethasone

- · administer orally ONCE a day in the morning with food OR
- · via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%
- patients may receive dexamethasone on day 3 and 4 orally as an outpatient or administered via IV infusion if still an inpatient

Note: if a dose is forgotten or vomited, contact treating team.

Ochemotherapy - Time out

Cytarabine

Prior to administration:

Ensure corticosteroid eye drops have been administered before starting cytarabine.

Verify that cytarabine neurological assessment has been performed prior to administration of cytarabine:

- if the patient scores 0 then administer cytarabine as charted
- if the patient scores 1 or above, do not administer the cytarabine and immediately notify medical officer.

Administer cytarabine:

- via IV infusion over 2 to 3 hours:
- flush with ~50 mL of sodium chloride 0.9%.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Days 3 and 4

General patient assessment prior to each day of treatment.

Continue corticosteroid eye drops until 72 hours after completion of the last dose of cytarabine.

Dexamethasone

- · administer orally ONCE a day in the morning with food OR
- via IV infusion over 15 minutes
- flush with ~ 50mL sodium chloride 0.9%
- patients may receive dexamethasone on day 3 and 4 orally as an outpatient or administered via IV infusion if still an inpatient

Note: if a dose is forgotten or vomited, contact treating team.

Discharge information

Dexamethasone tablets

• Dexamethasone tablets with written instructions on how to take them.

Antiemetics

· Antiemetics as prescribed.

Corticosteroid eye drops

• Continue corticosteroid eye drops for at least 72 hours after completion of final cytarabine dose.

Growth factor support

· Arrangements for administration if prescribed.

Prophylaxis medications

• Prophylaxis medications (if prescribed) i.e. tumour lysis prophylaxis, PJP prophylaxis, antifungals, antivirals.

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 day	rs)
Ocular toxicities	Reversible corneal toxicity (keratitis), haemorrhagic conjunctivitis, vision loss and other ocular side effects can occur with high dose cytarabine. Corticosteroid eye drops must be administered concurrently with treatment. Read more about ocular toxicities associated with cytarabine
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Cytarabine (Ara-C) syndrome	Flu-like symptoms including fever, myalgia and malaise can occur 6 to 12 hours after cytarabine administration. Symptoms generally resolve within 24 hours of completing therapy.
Taste and smell alteration	Read more about taste and smell changes
Neurotoxicity	High dose cytarabine has been associated with acute cerebellar syndrome and diffuse cerebral dysfunction. Read more about neurotoxicity associated with high dose cytarabine

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Side effects of corticosteroids	Insomnia, oedema, increased risk of infection e.g. oral thrush, gastric irritation, worsening of peptic ulcer disease, increased blood sugar levels, loss of diabetic control, mood and behavioural changes - including anxiety, euphoria, depression, mood swings, increased appetite and weight gain, osteoporosis and fractures (long term use), bruising and skin fragility are associated with corticosteroid use.
Nephrotoxicity	Renal dysfunction resulting from damage to the glomeruli, tubules or renal vasculature.
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
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue

Late (onset weeks to months)		
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia	
Alopecia	Hair loss may occur from all parts of the body. 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	
Cognitive changes (chemo fog)	Changes in cognition characterised by memory loss, forgetfulness and feeling vague. This is also referred to as 'chemo brain' or 'chemo fog'. Read more about cognitive changes (chemo fog)	

Evidence

Although DHAP was the salvage regimen used in the Philips et al (1995)² study which first demonstrated the survival benefit of autologous transplantation vs salvage chemotherapy it is used much less frequently now compared with the mid to late 1990s. It has been replaced by salvage regimens which can be administered on an outpatient basis and which are effective at mobilising stem cells.

Philips et al (1995)² showed 5 year overall survival of 32% in DHAP compared to 53% in the transplant group and confirmed the benefit of autologous transplantation in NHL. Several other publications have not reported the OS rate seen in this study. OS of patients with relapsed DLBC NHL without transplantation is generally considered at <10% over 5 years with a median response duration of 6 months only.

Efficacy

The following response rates are for DHAP as there is no data on survival for DHAC.

5 year follow up of 112 patients with recurrent refractory lymphoma treated with DHAP from 1989-1995:3

- complete remission 10%
- partial remission 28%
- stable disease 15%
- median response duration was 6 months
- actuarial overall survival at 5 years was 6.5%

Deaths during study:

- 78 died from progressive disease
- · 5 died from DHAP toxicity
- · 26 died from unrelated causes

Toxicity

Carboplatin is included in this protocol instead of cisplatin as in the original regimen, in an attempt to reduce the toxicities associated with cisplatin. Carboplatin response rates have been shown to be similar to cisplatin in other regimens.

Myelosuppression incidence is likely to be higher with carboplatin compared with cisplatin. Anaemia is more common with carbolpatin compared with cisplatin.

References

- 1 Velasquez, W. S., F. Cabanillas, P. Salvador, et al. 1988. "Effective salvage therapy for lymphoma with cisplatin in combination with high-dose Ara-C and dexamethasone (DHAP)." Blood. 71(1):117-122.
- 2 Philip, T., C. Guglielmi, A. Hagenbeek, et al. 1995. "Autologous bone marrow transplantation as compared with salvage chemotherapy in relapses of chemotherapy-sensitive non-Hodgkin's lymphoma." N.Engl.J Med. 333(23):1540-1545.
- 3 Walewski, JA, J Romejko-Jarosinska and J Zwolinski. 2001. "DHAP chemotherapy for recurrent/refractory lymphoma–five year follow-up of 112 patients." Proc Am Soc Clin Oncol 20: 2001 (abstr 1161)

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Cruz R, Czuczman S, Hernandez F et al (2006). Dexamethasone (D), High Dose Ara-C (HA) and Carboplatin (DHAC) with or without Rituximab (R) Is an Effective Salvage Regimen for Patients with Relapsed/Refractory B-Cell Lymphoma in Preparation for Autologous Stem Cell Transplantation. Blood (ASH Annual Meeting Abstracts), Nov 2006; 108: 4730.

Tessoulin, B., P. Thomare, E. Delande, et al. 2017. "Carboplatin instead of cisplatin in combination with dexamethasone, high-dose cytarabine with or without rituximab (DHAC+/-R) is an effective treatment with low toxicity in Hodgkin's and non-Hodgkin's lymphomas." Ann Hematol 96(6):943-950.

History

Version 4

Date	Summary of changes
28/06/2007	Reformatting and minor editing.
10/10/2008	Addition of extra information including side effects, updated references and special clinical instructions. Updating of patient education sheet.
03/03/2010	Reviewed and transferred to eviQ.
17/03/2011	New format to allow for export of protocol information. Protocol version number changed to <i>V.2</i> . Antiemetics and premedications added to the treatment schedule. Additional Clinical Information, Key Prescribing table and Key Administration table combined into new section titled Clinical Considerations. Drug specific information placed behind the drug name link.
19/08/2011	Full protocol review at Haematology Reference Committee meeting: - inclusion of statement in notes section: 'There is very little published evidence on the DHAC protocol, this is

Date	Summary of changes
	a local adaptation of the protocol as per the eviQ RC'.
	- statement removed regarding association with DHAP and poorer stem cell mobilisation
	- addition of statement regarding use of rituximab
	- carboplatin dose to be capped at 800 mg for consistency with ICE and RICE protocols
	- peripheral neuropathy side effect removed from protocol as this side effect was considered to to be rare with this treatment at the given dose
	- removal of reference Padmanabhan et al 2007 as this abstract represents the same series of patients as in the Cruz et al 2006 abstract
09/09/2011	Infusion fluid for carboplatin changed from sodium chloride 0.9% to glucose 5% because of longer stability.
13/12/2011	PHC role permission created.
01/08/2013	Reviewed at categorisation meeting, not for review, review in 2 years. PHC view removed.
13/08/2014	Added link to ALLG, ANZCTR and Lymphoma Australia website with statement 'Patients with NHL should be considered for inclusion into clinical trials'.
11/09/2015	Reviewed at RCM, no changes, review in 2 years, updated drug costs.
31/05/2017	Transferred to new eviQ website. Version number change to V.4.
25/05/2018	Reviewed by Haematology Reference Committee with no significant changes, review in 2 years
13/09/2019	Reviewed by Haematology Reference Committee, no changes made. Review in 5 years.
10/10/2019	Clinical information updated with PBS expanded indications for GCSF.
27/03/2020	Reviewed by Haematology Reference Committee with no significant changes, review in 4 years.
20/01/2022	Interactions updated.

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

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https://www.eviq.org.au/p/373

01 Mar 2024



Patient information - Non-Hodgkin lymphoma (NHL) - DHAC (dexamethasone, cytarabine, carboplatin)

Patient's name:

Your treatment

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

DHAC (dexamethasone, cytarabine, carboplatin)			
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 to 4	Dexamethasone (dex a METH a sone)	By a drip into a vein OR take orally ONCE a day in the morning with food on days 1 to 4 only. If you forget to take your tablets or vomit your tablets, contact your treating team.	About 15 minutes if given by a drip
1	Carboplatin (carb-o-PLAT-in)	By a drip into a vein	About 1 hour
1 and 2	Cytarabine (sye-TARE-a-been)	By a drip into a vein	About 3 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.

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

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.

Central venous access devices (CVADs)

This treatment may involve having chemotherapy through a central venous access device (CVAD). Your doctor or nurse will explain this to you. For more information, see the eviQ patient information sheets on CVADs.

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.
- **Eye drops:** you will be given eye drops to help prevent sore eyes. You will start using the eye drops before you have your first dose of cytarabine and continue to use the eye drops until 72 hours after your last dose of cytarabine.
- **Prophylaxis medication:** you may need to take some medications to prevent infection and to help prevent or reduce some of the side effects of the chemotherapy. Your doctor or nurse will tell you how and when to take these medications.
- **G-CSF**: you may be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover. Your doctor will decide if you need this medication. Follow this link to read more information on how to give this injection.

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)

Eye problems from cytarabine

- You may get:
 - eye pain or irritation
 - blurred vision
 - o watery or gritty eyes
 - o sensitivity to light.
- You will be given eye drops to help prevent and control these symptoms. It is important to use these eye drops as directed.
- Protect your eyes from the weather (sun and wind) by wearing sunglasses, especially if you
 have lost your eyelashes.
- Tell your doctor or nurse if you get any of the symptoms listed above.

Allergic reaction	Allergic reactions are uncommon but can be life threatening.		
	If you feel unwell during the infusion or shortly after it, or: The following the infusion or shortly after it, or:		
	o get a fever, shivers or shakes		
	o feel dizzy, faint, confused or anxious		
	o start wheezing or have difficulty breathing		
	have a rash, itch or redness of the face		
	While you are in hospital: Tell your doctor or nurse immediately.		
	After you leave: Contact your doctor or nurse immediately, or go to the nearest hospital		
	Emergency Department.		
Nausea and vomiting	You may feel sick (nausea) or be sick (vomit).		
	Take your anti-sickness medication as directed even if you don't feel sick.		
	Drink plenty of fluids (unless you are fluid restricted).		
	Eat small meals more frequently.		
	Try food that does not require much preparation.		
	Try bland foods like dry biscuits or toast.		
	Gentle exercise may help with nausea.		
	Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment.		
	Tell your doctor or nurse immediately, or go to the nearest hospital Emergency		
	Department if you have uncontrolled vomiting or feel dizzy or light-headed.		
Flu-like symptoms from	You may get a fever, skin rash, aches and pains or increased sweating.		
cytarabine	These symptoms are caused by the drug cytarabine.		
	Symptoms usually happen 6 to 12 hours after your dose, and may last until 24 hours after your treatment has finished.		
	To reduce any pain or fever, take paracetamol, if needed.		
	 Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. 		
	Tell your doctor or nurse if these symptoms do not get better after 24 hours.		
Taste and smell changes	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.		
Nervous system changes	High doses of cytarabine can affect the nervous system.		
from cytarabine	Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Population of the following symptoms during or soon of the your treatment:		
	Department if you get any of the following symptoms during or soon after your treatment: o dizziness, drowsiness or double vision		
	∘ agitation		
	o difficulty walking in a straight line		
	o difficulty writing with a pen or pencil		
	o jerky movements		
	○ slow, slurred speech.		

Early (onset days to weeks)

Infection risk (neutropenia)

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

Low platelets (thrombocytopenia)

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

Side effects from steroid medication

- Steroid medication may cause:
 - mood swings and behaviour changes
 - o an increased appetite
 - o weight gain
 - o swelling in your hands and feet
 - o stomach upsets
 - trouble sleeping
 - fragile skin and bruising
 - o an increase in your blood sugar level
 - weak and brittle bones (osteoporosis)
- · Take your steroid medication with food to reduce stomach upset
- You may need to monitor your blood sugar levels closely while you are taking steroids
- If you have diabetes, your blood sugar levels may be tested more often and your diabetic medication may need to be adjusted because of the effects of steroids. Talk to your diabetes advisor if you have any concerns
- Tell your doctor or nurse if you get any of the symptoms listed above.

Kidney damage

- This treatment can cause changes to how your kidneys work.
- You will have blood tests to make sure your kidneys are working properly.
- You may need to drink more fluids while you are having treatment. Your doctor or nurse will tell you if you need to do this.
- Tell your doctor or nurse as soon as possible if you notice that your urine changes colour or you don't need to empty your bladder as often.

· You may have: Mouth pain and soreness o bleeding gums (mucositis) mouth ulcers a white coating on your tongue o pain in the mouth or throat o 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: o 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. • You may get bowel motions (stools, poo) that are more frequent or more liquid. Diarrhoea • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed. • You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or Tiredness and lack of energy things you enjoy. (fatigue) • 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.

Late (onset weeks to months)	
Low red blood cells (anaemia)	 You may feel dizzy, light-headed, tired and appear more pale than usual. Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.
Hair loss (alopecia)	 Your hair may start to fall out from your head and body. Hair loss usually starts 2 to 3 weeks after your first treatment. You may become completely bald and your scalp might feel tender. Use a gentle shampoo and a soft brush. Take care with hair products like hairspray, hair dye, bleaches and perms. Protect your scalp from the cold with a hat, scarf or wig. Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher. Moisturise your scalp to prevent itching. Ask your doctor or nurse about the Look Good Feel Better program
Chemo brain (chemotherapy-related cognitive impairment)	 You may notice that you are unable to concentrate, feel unusually disorganised or tired (lethargic) and have trouble with your memory. These symptoms usually improve once treatment is completed. Ask your doctor or nurse for eviQ patient information – Memory changes and chemotherapy (chemo brain). Tell your doctor or nurse if you get any of the symptoms listed above.

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 and food safety

- · While you are receiving this treatment, it is important that you try to maintain a healthy diet.
- Grapefruit and grapefruit juice can interact with your medication and should be avoided while you are on this treatment.

- · Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.
- There are some foods that may cause infection in high risk individuals and should be avoided. For further information on foods to avoid and food hygiene please ask for a copy of the Listeria and food brochure.

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
- Call the Leukaemia Foundation on 1800 620 420 (Mon to Fri 9am 5pm)
- Call the Lymphoma Nurse Support Line on 1800 953 081 (Mon to Fri 9am 5pm)
- Call the Myeloma Australia Support Line on 1800 693 566 (Mon to Fri 9am 5pm)

Haematology, transplant and cellular therapy information

- Arrow bone marrow transplant foundation arrow.org.au
- Australasian Menopause Society menopause.org.au
- Chris O'Brien Lifehouse Total Body Irradiation mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/
- Healthy Male Andrology Australia healthymale.org.au/
- International Myeloma Foundation myeloma.org
- Leukaemia Foundation leukaemia.org.au
- Lymphoma Australia lymphoma.org.au
- Myeloma Australia myeloma.org.au
- NSW Agency for Clinical Innovation, Blood & Marrow Transplant Network https://aci.health.nsw.gov.au/networks/bmtct
- NSW Agency for Clinical Innovation aci.health.nsw.gov.au/projects/immune-effector-cell-service
- NCCN Guidelines for Patients Immunotherapy Side Effects: CAR T-Cell Therapy nccn.org/patientresources/patient-

resources/quidelines-for-patients

• Talk Blood Cancer - cmlsupport.org.uk/organisation-type/social-media-groups

General cancer information and support

- Australian Rare Cancer (ARC) Portal arcportal.org.au/
- Beyond Blue 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
- eviQ Cancer Treatments Online eviQ.org.au
- Food Standards Australia New Zealand: Listeria & Food Safety https://www.foodstandards.gov.au/publications/listeriabrochuretext
- 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

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