CARBOPLATIN HYPERSENSITIVITY GUIDELINES AND DESENSITISATION REGIMEN

The risk of developing a carboplatin hypersensitivity reaction (HSR) is related to increased exposure to the drug, with a peak incidence observed during cycle 2 of a patient's second course of carboplatin-based treatment[1].

To minimise the incidence and severity of a HSR, it has been decided to standardise practice such that all carboplatin doses are infused over a minimum of 1 hour.

Grading of Hypersensitivity Reactions (HSRs)

	Grade 1 MILD	Grade 2 MODERATE	Grade 3 SEVERE	Grade 4 Life-threatening	Grade 5
Symptoms of Allergic Reaction (any of)	Transient flushing or rash, temp < 38^{o}	Flushing; rash or urticaria; dyspnoea; asymptomatic bronchospasm; temp > 38^{o}.	Symptomatic bronchospasm; allergy-related oedema / angio-oedema; hypotension OR prolonged unresolving moderate symptoms.	Anaphylaxis	Death
	+ Back pain is a common symptom - if it presents as the only symptom, treat as Grade 1				

Grade 1-2 HSR to carboplatin: following a mild to moderate HSR, re-challenge should be carried out as follows:

a) Patients who **recover within 30 minutes** of receiving IV hydrocortisone and IV chlorphenamine;
- the infusion may be re-started on the same day at 50% rate for 30 minutes, then increased up to 100% rate again.
- For subsequent treatment cycles, use increased oral and IV HSR prophylaxis as below, along with a standard carboplatin bag for infusion, given over 2 – 4 hours.

b) Patients whose **symptoms do not resolve** 30 minutes post IV hydrocortisone and IV chlorphenamine;
- re-book patient to return one week later (if < 20% dose given before HSR) and supply oral prophylaxis as below to start the day before administration.
- Also prescribe IV prophylaxis as below, along with a standard carboplatin bag, given over 2 – 4 hours.
- If there is any further Grade 1 – 3 reaction, the desensitisation regimen should be considered for any further doses.

HSR Prophylaxis to be used before carboplatin re-challenge:

Starting 24 hours before carboplatin i.e. Day -1:

Cetirizine	10mg	po om x 2 doses	}
Ranitidine	150mg	po bd x 3 doses	} last dose on the morning of carboplatin administration
Dexamethasone	8mg	po bd x 3 doses	}

PLUS, 30 minutes before carboplatin:

Chlorphenamine	10mg	IV
Ranitidine	50mg	IV
Dexamethasone	8mg	IV

Grade 3 HSR to carboplatin: see overleaf

Grade 4 HSR to carboplatin: for any life-threatening Grade 4 reaction, the patient should **not** be re-challenged with carboplatin, and substitution with cisplatin should be considered.

Reason for Update: reviewed dosing so possible to go on Aria; reviewed duration of oral pre-meds	Approved by Consultant: Dr S Essapen
Version: 3	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 2	Date: 19.3.15
Prepared by: S Taylor	Checked by: C Tucker

CARBOPLATIN DESENSITISATION REGIMEN

For all subsequent cycles after a Grade 3 (severe) reaction to carboplatin, depending on an assessment of the patient and a detailed discussion with the patient regarding the risks and benefits.

Note: For patients on 3-weekly paclitaxel and carboplatin, the paclitaxel should be given one Day 1 and the carboplatin desensitisation on Day 2

Drugs/Dosage/ Administration:

Starting 24 hours before carboplatin i.e. Day -1:

Cetirizine	10mg	po om x 2 doses	}
Ranitidine	150mg	po bd x 3 doses	} last dose on the morning of carboplatin
Dexamethasone	8mg	po bd x 3 doses	} administration

PLUS, 30 minutes before Carboplatin:

Chlorphenamine	10mg	IV
Ranitidine	50mg	IV
Dexamethasone	8mg	IV

Carboplatin IV infusion:

Calculate total dose in mg, then divide dose between Bags 1, 2 and 3 as follows:

Bag 1: Carboplatin **1% of total dose** (to nearest mg) in 250 ml glucose 5%
Infuse 25 ml over 30 minutes
then
infuse 225 ml over 30 minutes

Bag 2: Carboplatin **10% of total dose** (to nearest mg) in 100 ml glucose 5%
Infuse 100 ml over 30 minutes

Bag 3: Carboplatin **89% of total dose** in 500 ml glucose 5%
Infuse 500 ml over 1 hour

Patient must be monitored at least every 15 minutes throughout, and there must be adequate nursing and medical staff available during the whole desensitisation period.
If a reaction occurs at any step, stop the infusion and administer chlorphenamine 10mg IV and hydrocortisone 100mg IV. Start appropriate monitoring and supportive care.

For any Grade 1 – 2 reaction: observe for 30 minutes:
If symptoms resolve completely after 30 minutes, re-start the infusion at 50% of the pre-reaction rate and complete the remaining steps at 50% rate also i.e. each dose level over 1 hour and the final dose level over 2 hours. **Follow this slower schedule for subsequent cycles.**
If symptoms do not resolve after 30 minutes, or if they recur, do not re-start infusion. Consider a switch to cisplatin, or an alternative regimen.

For any Grade 3 – 4 reaction: do not re-start the infusion and consider a switch to cisplatin, or an alternative regimen.

References:

Adapted from RMH Management Protocol for adult Hypersensitivity Reactions associated with systemic anti-cancer therapy.
[1]Makrilia et al; Hypersensitivity Reactions Associated with Platinum Antineoplastic Agents: A Systematic Review; Metal Based Drugs 2010: 207084
ICON 8 trial, Clinical management Guidance, May 2011

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