NHS
Kent and Medway
Cancer Collaborative

Systemic Anti-Cancer Therapy Care Pathway

Hypersensitivity Reactions and Anaphylaxis

Network Guidance Document

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1.0 AIMS

To ensure rapid and efficient action is taken in the event of anaphylaxis to minimise the effects for the patient and to maintain their well-being.

It is the responsibility of the individual trained nurse, skilled in the administration of systemic anti-cancer drugs to recognise when anaphylaxis has occurred and what action to take.

To ensure any designated systemic anti-cancer therapy in an acute area has an anaphylaxis kit and guidelines.

1.1 Introduction

The term anaphylaxis is derived from the Greek words ana, meaning again, and phulaxis, meaning guarding. The word, therefore aptly describes the condition where the individual affected has an increased, perhaps inappropriately so, guarding of the body from a substance originating from the external environment (Henderson 1998), resulting in the formation of antibodies (Allwood et al 2002).

For the purposes of this document the term anaphylaxis will be used for both anaphylactoid reactions, which are similar but do not depend on hypersensitivity and anaphylaxis which is the term commonly used for hypersensitivity reactions.

The degree of risk and type of reactions are variable (from mild to life threatening). The onset is more rapid and reactions are more often severe from the intravenous (I.V) route.

Progress may be rapid, slow, or biphasic (more rare – delayed by a few hours or persisting for more than 24 hours).

1.2 Content

1.2.1 Prevention

- A full history of previous allergic reactions is important as well as that of any recent incidents. In the event of hypersensitivity or anaphylaxis reaction, future planned treatments must be discussed with the patient's consultant. Prophylactic antihistamines may be required to prevent subsequent reactions.
- The nurse / doctor must be fully aware of drugs that may potentially cause an allergic reaction.
- All areas delivering systemic anti-cancer drugs must have easy access to an Anaphylaxis kit prepared and renewed by pharmacy, which should be easily accessible.
- Full consideration must be given to patients receiving high risk treatments such as antibodies and are on beta-blockers or ACE inhibitors, with regards their suitability for treatment.
- The availability and location of resuscitation equipment must be detailed in each location used for administration.

1.2.2 Clinical Features of Anaphylaxis

Clinical manifestations can occur within minutes of exposure to the antigen. Symptoms may include:

- **Cutaneous:** swelling, urticarial, erythema and pruritus, itching, flushing or paleness
- **Respiratory:** wheezing, dyspnoea, rhinitis, sneezing and angioedema (swelling of the lips, face, neck and tongue), laryngeal obstruction causing a husky voice, stridor and hypoxia
- **Cardiovascular:** hypotension, tachycardia and arrhythmia
- **Gastrointestinal:** nausea, diarrhoea, abdominal cramps and vomiting
- **Central Nervous System:** confusion, feeling of impending doom, apprehension, metallic taste, altered levels of consciousness, anxiety and unease
- **Sudden collapse**

Any anaphylactic reaction, irrespective of its severity, should be treated as a medical emergency requiring immediate intervention. Delay in recognition of the conditions or its treatment, especially in the delay of administering adrenaline can result in death, usually as a result of cardiovascular collapse or airway obstruction.

1.2.3 Hypersensitivity

Systemic anti-cancer drugs have the potential to cause immediate hypersensitivity reactions.

Among these are antibodies, taxanes and immunoglobulins, and platinum-based drugs.

It is the responsibility of the prescribing doctor and administering nurse to ensure they are fully aware of the potential to cause an anaphylactic reaction of the drug they are giving.

1.2.4 Management

- **Hypersensitivity reactions** – See Appendix 2 (slowly progressing peripheral oedema or changes restricted to the skin e.g. urticaria).
- **Anaphylaxis** with cardiovascular collapse – See Appendix 1 (common manifestation, vasodilatation and loss of plasma from blood compartment).

It is recommended that Appendix 1 and 2 are laminated and visible in all clinical areas.

Administer nebulised Salbutamol 2.5mg to 5mg as an adjunctive measure if bronchospasm is severe and does not respond rapidly to other treatment.

1.2.5 Cautions

- Beta blockers may increase the severity of an anaphylactic reaction and antagonise the response to adrenaline. Half the dose may be safer.

  Adrenaline may be given **IM** only to patients in anaphylaxis. The dilution should be 1:1000 (0.5 – 1ml administered). (See exception below for patients with life threatening profound shock).
- Patients taking tricyclic antidepressants or monoamine oxidase inhibitors should only receive 50% of the usual dose of adrenaline, as an interaction is potentially dangerous.
- Systemic anti-cancer therapy antibodies: Up to 80% of patients receiving systemic anti-cancer therapy antibodies may experience chills and/or fevers, rashes, hypotension and dyspnoea predominantly during the first infusion. All of the agents may produce a post infusion reaction starting 2-24 hours post dose. Severe allergic reactions are seen less commonly, in around 1-2% of patients.
- Taxanes: Taxanes are associated with acute hypersensitivity reactions. The incidence with paclitaxel is approximately 40% (2% severe) and the rate with docetaxel is 30% (7% severe). Clinical manifestations include skin changes (pruritus, erythema, rashes, urticarial), angioedema, dyspnoea (with or without bronchospasm), blood pressure changes (decrease or increase), but rarely cardiovascular collapse.
- Treating a patient with anaphylaxis in the community or on mobile chemotherapy units will not be the same as in an acute hospital. Out of hospital, an ambulance must be called immediately, whilst nurses carry out first line treatment, and the patient transported to an emergency department.

1.2.6 Recommencement of Treatment

Following an episode of anaphylaxis all patients should be reviewed by the Medical Team prior to continuing with their therapy.

2.0 APPENDIX 1: THE MANAGEMENT OF ANAPHYLAXIS

Action	Rationale
Diagnosis – sudden onset of airway and/or breathing and/or circulation problems	To identify need for intervention
Stop the infusion of drug immediately and take down any SACT that may be infusing	Prevent further exposure to allergen
Call for help (resus team), ensure resuscitation trolley in situ and commence CPR if required	To ensure medical team assistance in a timely manner
Explain all care to the patient and their family where possible	Help reduce anxiety and keep the patient fully informed
Lie patient flat	
Administer adrenaline 1:1000 (1mg/ml) IM Adult 500 micrograms IM (0.5 mL) (guidelines from resus council) **Repeat in 5 minutes if no clinical improvement Note IV Adrenaline only to be given by experienced clinicians only**	Alpha-receptor agonist, it reverses peripheral vasodilatation and reduces oedema. Its beta-receptor activity dilates the airways, increases the force of the myocardial contraction and suppresses histamine and leukotriene release.
Record vital signs and continue to monitor	To establish patient's overall condition and monitor any deterioration / improvement
Establish airway and give high flow oxygen	Increase cell perfusion
Ensure resuscitation trolley is in situ, and call the cardiac resuscitation team and commence C.P.R if required	
Administer adrenaline 1:1000 (1mg/ml) IM at the dose for an adult of 500 micrograms IM (0.5 mL) (guidelines from resus council) **Repeat in 5 minutes if no clinical improvement Note IV Adrenaline only to be given by experienced clinicians only**	Alpha-receptor agonist, it reverses peripheral vasodilatation and reduces oedema. Its beta-receptor activity dilates the airways, increases the force of the myocardial contraction and suppresses histamine and leukotriene release.
If shock persists, IV fluid bolus (colloid 500-1000ml)	Improve hypotension
If no improvement in breathing or circulation problems despite two doses of IM adrenaline, follow refractory anaphylaxis algorithm	
Obtain 10ml clotted blood 45-60 min after (no later than 6hrs) for specific IgE antibody and mast cell tryptase	Assess whether episode genuine anaphylactic reaction
Admit patient	Repeat episode can occur 1-72hrs after clinical recovery
Document fully the allergic reaction in the medical / nursing notes	Legal requirement
Complete an Incident Report Form	For a complete review and investigation of the clinical incident
Fill in yellow adverse drug reaction form if applicable	

In the absence of patient group directives all medication must be prescribed.	Legal requirement

Intravenous administration of adrenaline is hazardous. Intravenous injections of adrenaline must be reserved for patients with profound shock that is immediately life threatening and for special indications e.g. during anaesthesia. The use of adrenaline by the intravenous route should be reserved for medically qualified personnel who have experience of it, who know that it must be administered with extreme care, and who are aware of the hazards associated with its use. The dose administered should be in a dilution of 1:10000, never 1:1000.

3.0 APPENDIX 2: THE MANAGEMENT OF HYPERSENSITIVITY REACTIONS

Action	Rationale
Stop infusion of drug immediately	Prevent further exposure to allergen
Explain all care to the patient and their family	Help reduce anxiety and to ascertain whether patient experiencing panic attack / anaphylaxis
Evaluate patients' airway and breathing, circulation and level of consciousness	Ensure patient not developing anaphylaxis
Initiate frequent vital signs including oxygen saturation	Monitoring hypotension, tachycardia and respiratory status
Lay patient flat unless they are experiencing respiratory difficulties	Assist with hypotension
Ensure HCP remains with patient at all times	Risk of shock / severe reaction
Contact doctor F2 or above	Medical review if needed
Administer slow IV Chlorphenamine 10mgs diluted with 10ml N/Saline	Counter histamine mediated vasodilatation
Administer hydrocortisone IV 200mgs	Clinical experience shows that parenteral hydrocortisone is of value in hypersensitivity reactions
Administer bronchodilator if required	
Document allergic reaction in the medical / nursing notes	Legal requirement
Complete an Incident Report Form	For complete review and investigation of the clinical incident
Fill in yellow adverse drug reaction form if applicable	
Monitor for 8-24hrs	Risk of early recurrence

4.0 ANAPHYLAXIS KIT

Refer to local anaphylaxis kit as there may be variation by site.

Contents

- Anaphylaxis Policy
- Chloraprep
- 10ml syringe x 1
- 2ml syringe x 1
- 5ml syringe x 1
- Blue needle x 3 (check gauge)
- Chlorphenamine 10mgs/1ml x 2 vials
- Hydrocortisone 100mgs/2ml water for injection x 2 vials
- Minijet (adrenaline with epinephrine 1:1000)
- Salbutamol nebules 2.5mgs x 2 (nebuliser attachment)

To prevent the drugs being removed the anaphylaxis kit should be in a sealed container. After use it should be immediately returned to pharmacy and replaced. The kit should also be checked for expiry.

5.0 RESUSCITATION COUNCIL UK GUIDELINES: ANAPHYLAXIS

Resuscitation Council UK

GUIDELINES 2021

Anaphylaxis

Anaphylaxis?

A = Airway B = Breathing C = Circulation D = Disability E = Exposure

Diagnosis – look for:

- Sudden onset of Airway and/or Breathing and/or Circulation problems[1]
- And usually skin changes (e.g. itchy rash)

Call for HELP
Call resuscitation team or ambulance

- Remove trigger if possible (e.g. stop any infusion)
- Lie patient flat (with or without legs elevated)
  - A sitting position may make breathing easier
  - If pregnant, lie on left side

Give intramuscular (IM) adrenaline[2]

Inject at **anterolateral aspect** – middle third of the thigh

- Establish airway
- Give high flow oxygen
- Apply monitoring: pulse oximetry, ECG, blood pressure

If no response:

- Repeat IM adrenaline after 5 minutes
- IV fluid bolus[3]

If no improvement in Breathing or Circulation problems[1] despite TWO doses of IM adrenaline:

- Confirm resuscitation team or ambulance has been called
- Follow REFRACTORY ANAPHYLAXIS ALGORITHM

1. Life-threatening problems

Airway
Hoarse voice, stridor

Breathing
↑work of breathing, wheeze, fatigue, cyanosis, SpO_2 <94%

Circulation
Low blood pressure, signs of shock, confusion, reduced consciousness

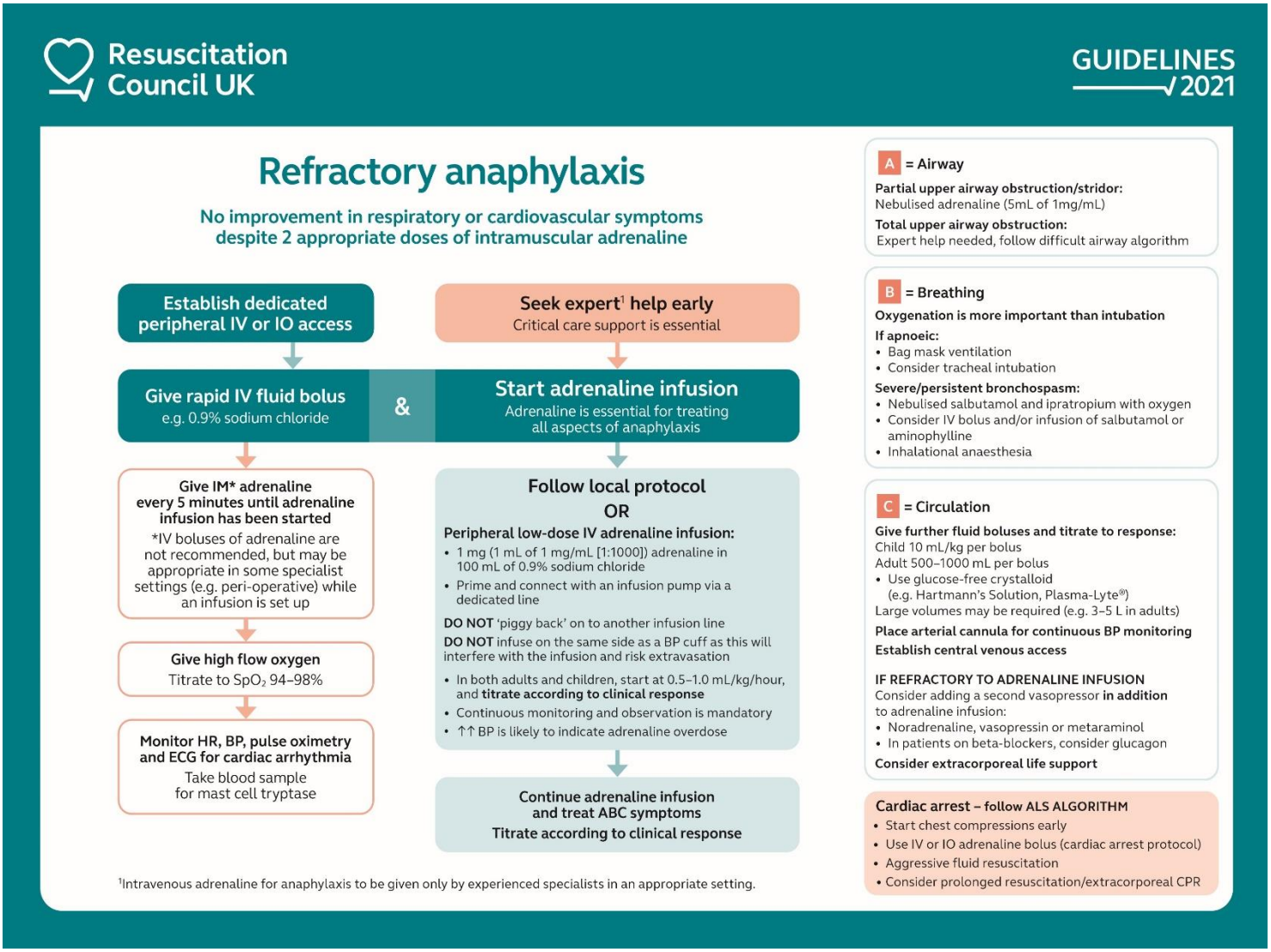
2. Intramuscular (IM) adrenaline
Use adrenaline at 1 mg/mL (1:1000) concentration

Adult and child >12 years:	500 micrograms IM (0.5 mL)
Child 6–12 years:	300 micrograms IM (0.3 mL)
Child 6 months to 6 years:	150 micrograms IM (0.15 mL)
Child <6 months:	100–150 micrograms IM (0.1–0.15 mL)

The above doses are for IM injection **only**.
Intravenous adrenaline for anaphylaxis to be given **only by experienced specialists** in an appropriate setting.

3. IV fluid challenge
Use crystalloid

Adults:	500–1000 mL
Children:	10 mL/kg



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7.0 GLOSSARY

BNF	British National Formulary
BOPA	British Oncology Pharmacist Association
CNB	Cancer Network Board
COSHH	Control of substances hazardous to health regulations.
CYP	Children & Young People (in relation to the IOG)
DCCAG	Diagnostic Cross Cutting Advisory Group
DOG	Disease Orientated Group (NSSG/TSSG/TWG)
DVH	Darent Valley Hospital
DGT	Dartford and Gravesham NHS Trust
EK	East Kent
EKHUFT	East Kent Hospitals University Foundation Trust
EPS	Electronic Prescribing System
FP10(HNC)	Prescriptions issued by hospital doctors for dispensing in the community
GP	General Practitioner
HoP	High Level Operational Policy
IOSC	Improving Outcomes: A Strategy for Cancer
IV	Intravenous
K&C	Kent & Canterbury Hospital, Canterbury, (EKHUFT)
KMCC	Kent & Medway Cancer Collaborative
KMCRN	Kent & Medway Cancer Research Network
KOMS	Kent Oncology Management System
LSESN	London & South East Sarcoma Network
MFT	Medway Foundation Trust
MTW	Maidstone & Tunbridge Wells NHS Trust
NHS	National Health Service
NMP	Non-medical prescriber
NPSA	National Patient Safety agency
NOG	Non Surgical Oncology Group *(Permanent oncologist sub group of the DOGs with a specific responsibility for chemo/rad pathways and advice to the DOG, Network and GEOGRAPHICAL LOCATIONs on new drugs)*
PoC	Pathway of Care *(Network agreed disease site specific clinical guidelines)*
QEQM	Queen Elizabeth the Queen Mother Hospital, Margate (EKHUFT)
QoL	Quality of life
QSIS	Quality service information system
QST	Quality Surveillance Team
RAT	Research and Trial Group *(Permanent sub-group of the DOGs with a specific responsibility for taking forward the clinical trials agenda)*
RMH	Royal Marsden Hospital
RNOH	Royal National Orthopaedic Hospital
SACT	Systemic Anti-Cancer therapy
SACT regimen	Systemic Anti-cancer prescription on the electronic prescribing system
SACT protocol	Systemic Anti-cancer protocol on KMCC website
TTO	Treatment to take home
QVH	Queen Victoria Foundation Trust Hospital East Grinstead

UCLH	University College Hospital London
WHH	William Harvey Hospital, Ashford (EKHUFT)
WK	West Kent

8.0 DOCUMENT ADMINISTRATION

The document is located on the Kent & Medway Cancer Collaborative website at www.kmcc.nhs.uk	
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Revision History			
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15/03/2009	V0.2 Draft	Words 'chemotherapy, cytotoxic and monoclonal' replaced by 'systemic anti-cancer therapy' to reflect NCEPOD report	Bryony Neame
2011-09	V2 Published	Document reviewed and updated.	Network Chemotherapy Nursing Group
2017	V3	Change in the management of anaphylaxis	Ruth O'Brien
2019	V3	Document reviewed: no change required.	Ruth O'Brien
July 2019	V4 Published		Approved virtually by Chemotherapy group
April 2022	V4.1 Draft		Ruth O'Brien and Nicola Sell
April 2022	V4.2 Draft	Reformatted by R.Patel	
June 2022	V4.3-V4.4	Updated terminology throughout document: "mild and severe anaphylaxis" changed to "hypersensitivity and anaphylaxis" as advised by EKHUFT resus team	Circulated for virtual approval
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