Guidelines for Management of Intravenous Chemotherapy-related Allergic Reactions, including Anaphylaxis, in Adults

These guidelines refer only to the management of intravenous **chemotherapy-related** reactions

(for management of acute reactions to blood / blood product transfusions, and general anaphylaxis not related to intravenous chemotherapy, refer to the relevant Trust guidelines)

Signs and symptoms of an acute allergic reaction

An allergic or hypersensitivity reaction can include some or all of the following signs and symptoms:

- skin reactions, such as urticaria (hives), local flare, facial flushing or angioedema (subcutaneous swelling)
- rhinitis (runny nose)
- pyrexia, rigors, tachycardia
- GI symptoms, such as nausea, cramps or diarrhoea

In most cases, prompt and appropriate action in response to initial hypersensitivity symptoms, as specified in these guidelines, will prevent an allergic reaction to an infusion developing into a full-blown anaphylactic reaction.

Anaphylaxis

Anaphylaxis is a severe, life threatening generalized or systemic hypersensitivity reaction. It is characterised by rapidly developing life-threatening airway and/or breathing and/or circulation problems, usually associated with skin and mucosal changes (flushing, urticarial, angioedema).

Airway problems:	throat and tongue swelling, stridor, hoarse voice
Breathing problems:	wheeze, increased respiratory rate, fatigue, confusion caused by hypoxia, cyanosis (SpO_2 < 92%)
Circulation problems:	hypotension, tachycardia, dizziness, pale, clammy, loss of consciousness, cardiac arrest

Anaphylaxis is associated with sudden onset and rapid progression of symptoms (the patient will look and feel unwell, will become anxious and may experience a "sense of impending doom")

Chemotherapy causes of allergic reactions, including anaphylaxis

- In haematology and oncology, medications containing 'foreign' protein which are likely to cause such reactions include: asparaginase; monoclonal antibodies e.g. rituximab, cetuximab
- Chemotherapy drugs with a > 25% risk of immediate hypersensitivity reactions include docetaxel and paclitaxel
- Chemotherapy drugs with a metallic base - e.g. cisplatin, carboplatin, oxaliplatin - may be more likely to cause a reaction with successive treatments (rather than the first treatment), due to drug sensitisation
- Chemotherapy drugs with a lower risk of immediate hypersensitivity reaction include amsacrine, anthracyclines, bleomycin, etoposide, liposomal doxorubicin, melphalan, methotrexate, mitomycin C

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Treatment Pathway

First sign of a reaction during IV administration of chemotherapy

Stop IV administration
(maintain IV access)

Anaphylactic Reaction?

Yes

Symptoms and signs
Sudden onset and rapid progression of symptoms
Life-threatening problems:
Airway: throat and tongue swelling (laryngeal oedema), stridor, hoarseness
Breathing: wheeze (bronchospasm), increased respiratory rate, confusion, cyanosis, hypoxia (O_2 sats < 92%)
Circulation: hypotension, tachycardic, pale, clammy, dizziness, loss of consciousness

The patient will become anxious and may experience a sense of impending doom

Call for help (crash team)
Lay patient flat, with or without elevating the patient's legs (if the patient has breathing problems, they may prefer to sit rather than lie down)

O_2 at high flow rate (10 – 15L/min)

Initiate cardiac monitoring

ADRENALINE[1] IM 0.5ml of 1:1000 solution
If no improvement after 5 minutes, give a repeat dose[2]
(several doses may be needed at about 5 minute intervals, especially if improvement is transient or the patient deteriorates)

No

Symptoms and signs
Urticaria (hives)
Pruritis (local and generalised)
Flushing / redness (especially face and neck)
Maculopapular rash (trunk, arms, legs, face)
Angioedema (subcutaneous swelling)
Rhinitis (runny nose)
Pyrexia
Rigors
Tachycardia
GI symptoms, such as nausea, cramps or diarrhoea
BUT
No evidence of life-threatening airways, breathing or circulatory symptoms

Lay patient flat, with or without elevating the patient's legs

Consider need for O_2 at high flow rate (10 – 15L/min)

Take observations at least every 15 minutes:
Blood pressure, pulse, respiratory rate, O_2 saturation, temperature

If patient deteriorates and develops symptoms of anaphylaxis, **call for help (crash team)** and follow anaphylaxis pathway

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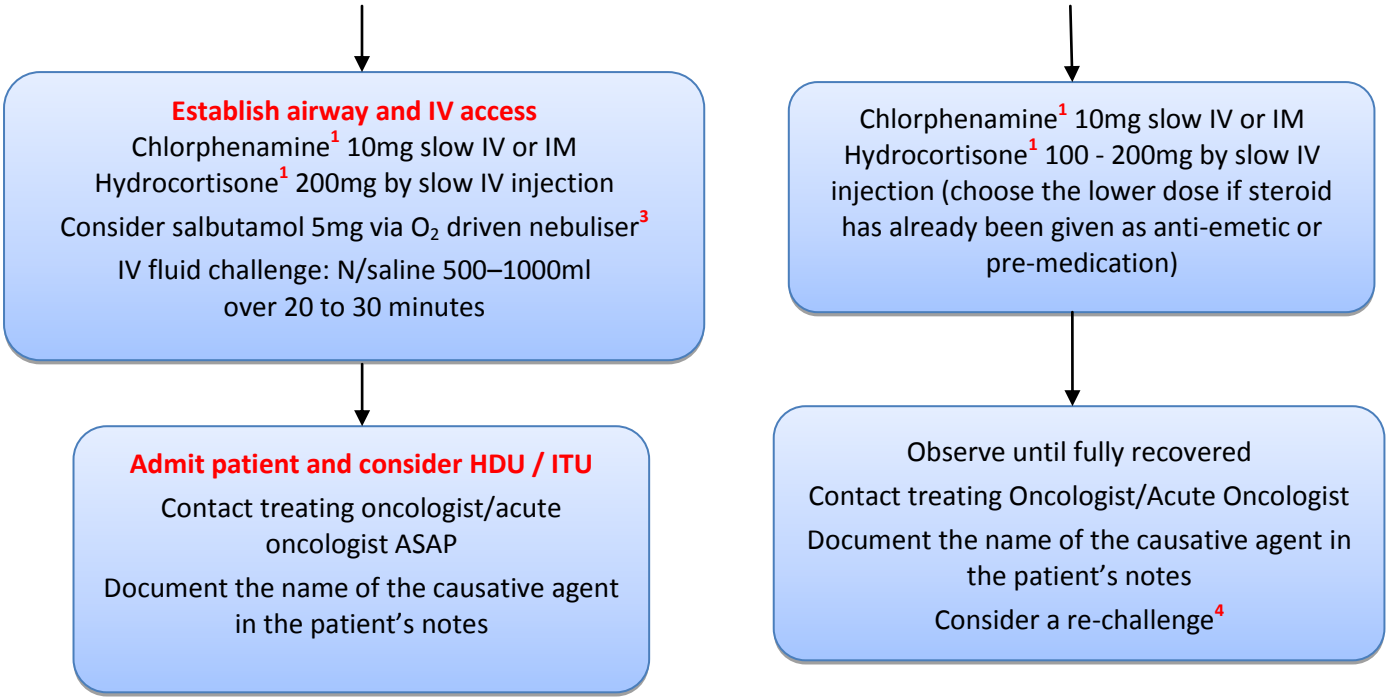

[1] A prescription is not required before administration of chlorphenamine or hydrocortisone or intramuscular adrenaline 1 in 1000, as they are being used to save life in an emergency. However, ensure that the drug(s) and dose(s) administered are documented in retrospect in the patient's healthcare record.

[2] If there is doubt as to adequacy of the circulation and absorption from the IM site, or if platelets low, **IV adrenaline** can be used (0.5ml of 1:10,000 solution by slow IV). **This is hazardous and recommended only for an experienced practitioner (anaesthetist, ITU doctor).** Patients must be monitored with continuous ECG, pulse oximetry and frequent BP measurements as a minimum.

[3] For persistent bronchospasm, use 5mg salbutamol in 500ml sodium chloride 0.9% and start at 5 microgram (0.5ml) per minute by intravenous infusion (dose range 3–20 micrograms (0.3 – 2ml) per minute).

[4] *Re-challenge*

Re-challenge of the offending drug on the same day may be considered if the following criteria are met:

- if the initial reaction was mild.
- if the patient has fully recovered and is haemodynamically stable
- if the infusion is re-started slowly, with a gradual increase in infusion rate only if tolerated.
- if the decision to re-challenge is made by an experienced doctor in agreement with nursing staff

Re-challenge of the offending drug on a later date may be considered if the following criteria are met:

- if antihistamine and steroid cover is prescribed to be administered 30 – 60 minutes before the re-challenge
- if the infusion is started slowly, with a gradual increase in infusion rate only if tolerated.
- if the decision to re-challenge is made by an experienced doctor in agreement with nursing staff

If the patient does not tolerate the re-challenge, no further attempt should be made to continue treatment using this drug, and alternative treatment options need to be considered.

Special Circumstances

- If the patient is experiencing rigors due to rituximab infusion, a further dose of paracetamol may be indicated.
- Laryngopharyngeal spasm due to oxaliplatin must not be confused with an allergic reaction, and it will not respond to anti-allergy treatments.

References: UK Resuscitation Council (2008, annotated with links to NICE guidance 2012), *Emergency Treatment of Anaphylactic Reactions, Guidelines for healthcare providers.*