Anakinra in the Management of Immune-Related Adverse Effects (irAEs)

A guide for members on the prescribing and monitoring of Subcutaneous anakinra when used in the management of irAEs because of treatment immune-checkpoint inhibitors.

It should be noted that this use may be off-label use; relevant governance processes within each organisation should be followed to ensure the risks associated with this are mitigated

British Oncology Pharmacy Association in Collaboration with The Immuno-Oncology Clinical Network

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Contents

1. Introduction

- Anakinra neutralises the biologic activity of interleukin-1α & interleukin-1β by competitively inhibiting their binding to interleukin-1 type I receptor. Interleukin-1 play a pivotal pro-inflammatory cytokine mediating many cellular responses

- ASCO guidance[2] on the management of irAE highlights anakinra potential use in haematologic toxicity. Other indications may include: severe or refractory arthritis; chronic inflammatory demyelinating polyradiculonevritis (CIDP); psoriasis-like reactions/psoriasis exacerbation; severe and/or anti-TNFα refractory colitis; myasthenia gravis; encephalitis; aseptic meningitis; myocarditis; pneumonitis[3]. It can also be used for haemophagocytic lymphohistiocytosis (HLH). There is also an emerging role for it in the treatment of immunotherapy induced Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS)as it has the ability to cross the blood-brain barrier.

- In England anakinra's use is supported by a Clinical Commissioning Policy for Haemophagocytic Lymphohistiocytosis (HLH) for adults and children in all ages as a result of any cause.https://gettingitrightfirsttime.co.uk/wp-content/uploads/2025/11/HLH-Guide-final-version-v1.4-November-2025.pdf

- This document is intended to be used as a monograph to provide prescribing and monitoring advice once the decision has been made to initiate anakinra in adult patients. It is not a clinical guideline, but a consensus view of current use of anakinra when used for irAEs. It should be used in conjunction with any local policies/procedures/guidelines and should be approved for use according to the trust clinical governance processes.

2. Prescribing and Monitoring Advice

2.1 Contraindications

- Hypersensitivity to anakinra.
- Hypersensitivity to E. coli–derived proteins.
- Hypersensitivity to any of the excipients.
- Active infection.

2.2 Precautions:

- **Allergic reactions** (anaphylactic reactions, angioedema, urticaria and pruritus);
- Injection site reactions;
- Hepatic events;
- Serious infections;
- Renal impairment;
- Neutropenia;
- Thrombocytopenia;
- Pulmonary events;
- Drug reaction with eosinophilia and systemic symptoms (DRESS);
- Amyloidosis (systemic);
- Vaccinations: Live vaccines should **not** be given concurrently with anakinra.

Commented [AT1]: Should we include this or not? It is important to make people aware f this, but not relevant for the whole of the UK - NHS England only.

Commented [AO2R1]: Definitely think it needs to be in and linked to the GIRFT guidance (worth including the link if possible)

Commented [AO3R1]: https://gettingitrightfirsttime.co.uk/wp-content/uploads/2025/11/HLH-Guide-final-version-v1.4-November-2025.pdf

2.3 Pregnancy advice

- There are limited amount of data from the use of anakinra in pregnant women.
- Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.
- As a precautionary measure, it is preferable to avoid the use of anakinra during pregnancy and in woman of childbearing potential not using contraception.

2.4 Pre-treatment assessment

- Baseline FBC, U+Es, LFTs.
- Baseline temperature, pulse, respiratory rate, oxygen saturations and blood pressure.
- Baseline virology: Hepatitis Core Antibody, Hepatitis C, HIV.
- Baseline screen for latent tuberculosis.
- **Neutrophil counts should be assessed before initiating anakinra treatment and while receiving anakinra, monthly for 3 months, and thereafter quarterly for a period up to 1 year.**

2.5 Pharmaceutical form

Solution for injection in a preservative-free, graduated, pre-filled syringe.

2.6 Dosage

- Dosage, frequency and route of administration may vary depending on indication and patient's condition,
- Although there is no specific dose for immune-related-HLH available in the literature, the NHS commissioning guidance recommends 1-2mg/kg/day in two divided doses up to a max of 8mg/kg/day
- Starting dose is often considered to be 4mg/kg/day in two divided doses and then dose titrated in 2mg/kg/day dosing bands dependant on response.
- Caution if renal function 30-59ml/min
- Consider using every other day if renal function <30ml/min
- Of note the dosing considerations in haemofiltration and haemodialysis are different and specialist pharmacy advice should be sort to ensure appropriate dose calibration.
- Following response to treatment the dose is titrated down by 2mg/kg/day aliquots before going to 1mg/kg in a OD dosing regime.

2.7 Method of administration

Anakinra is licensed to be administered by subcutaneous injection. However, in the treatment of HLH the anakinra is generally initiated intravenously and then converted to S/C as condition stabilises (see section 2.7.2).

- The dosing is the same for both routes.

- In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

2.7.1 Subcutaneous injection

- Anakinra is available as a graduated sterile unpreserved pre-filled syringe. The graduated pre-filled syringe allows for doses between 20 and 100 mg.

- Alternating the injection site to avoid discomfort at the site of injection. Cooling of the injection site, warming the injection liquid to room temperature, use of cold packs (before and after the injection), and use of topical glucocorticoids and antihistamines after the injection can alleviate the signs and symptoms of injection site reactions.

- Do not shake. Allow the pre-filled syringe to reach room temperature before injecting.

- Before administration, visually inspect the solution for particulate matter and discolouration. Only clear, colourless-to-white solutions that may contain some product-related translucent-to-white amorphous particles should be injected.

2.7.2. Intravenous Infusion:

- At the point of a diagnosis HLH is generally administered via the intravenous route, despite this being and **unlicensed route of administration**
- Intravenous is recommended in this setting for several reasons
    - the unpredictability of SC absorption in the unwell patient.
    - the pharmacology is also more predictable via the intravenous route.
    - the dosage of anakinra required at the onset and early management points mean the volume of treatment required for S/C administration is often impractical, especially in light of the additional risks in this patient population.
    - it avoids the need for subcutaneous injection in patients who are either thrombocytopenic or at risk of evolving thrombocytopenia and who have falling fibrinogen levels. Both these factors lead to a significant risk of bleeding so it is considered that intravenous route is preferred in the initial stages of HLH management.
- The dosing strategy is the same as in the S/C setting
- Preparation of IV route:
    - Uncap the required number of pre-filled anakinra syringe(s);
    - Add the appropriate dose to a 50ml syringe, making up the total volume of 50ml with sodium chloride 0.9%;
    - Infuse over 30 minutes via syringe pump.
    - Note: Anakinra should not be administered concomitantly via Y-site or mixed with any other medications due to lack of compatibility information.

2.8 Is there therapeutic Drug Monitoring?

- No therapeutic drug monitoring is required.

2.9 Renal impairment.

- Caution if renal function 30-59ml/min
- Consider using every other day if renal function <30ml/min
- Of note the dosing considerations in haemofiltration and haemodialysis are different and specialist pharmacy advice should be sort to ensure appropriate dose calibration.

2.10 Adverse effects

- The table below outlines the broad range of adverse events that patients can experience with anakinra.
- This is not an exhaustive list. See SmPC for further details.
- Allergic reactions, including anaphylactic reactions and angioedema have been reported uncommonly. The majority of these reactions were maculopapular or urticarial rashes. If a severe allergic reaction occurs, administration of anakinra should be discontinued and appropriate treatment initiated.

System	Adverse Effects
Infections & Infestations	Serious infections
Blood and lymphatic system disorders	Neutropenia Thrombocytopenia
Immune system disorders	Allergic reactions including anaphylactic reactions, angioedema, urticaria and pruritus
Nervous system disorders	Headache
Hepatobiliary disorders	Hepatic enzyme increased Non-infectious hepatitis
General disorders and administration site conditions	Injection site reaction
Skin and subcutaneous tissue disorders	Rash Injection site amyloid deposits
Investigations	Blood cholesterol increased

2.11 Drug Interactions

- The table below lists the most common interactions but is not exhaustive. The SmPC and other drug interactions resources should be further consulted.

Drug	Interaction
Live attenuated virus vaccines	Should **NOT** be given concurrently with anakinra.
Concurrent anakinra & TNF-α antagonist	Higher rate of serious infection & neutropenia
Cytochrome P450 Substrates	Plasma concentrations and effects of drugs that are CYP450 substrates may be altered following the initiation of anakinra.

	This would be clinically relevant for CYP450 substrates with a narrow therapeutic index (e.g. warfarin and phenytoin.

Test	**Interaction**
Serological assays	Anakinra may effect CRP, ESR, serum ferritin, D-dimer

3. Appendix 1 Anakinra Patient Information Leaflet

What is anakinra?

Anakinra is a type of cytokine (an immunosuppressive agent) that is used to treat inflammatory diseases.

Cytokines are proteins made by your body that co-ordinate communication between cells and help control cell activity. When your body produces too much of a cytokine this can result in inflammation, causing the symptoms of the disease. Normally, your body produces a protein that blocks the harmful effects of cytokines. Anakinra blocks the cytokines.

How do I take anakinra?

Anakinra will be administered either injected under your skin (subcutaneous) or via an intravenous infusion (drip) in the hospital.

How long will I need to have anakinra?

This will be determined by what immune related side effect you have and how much the anakinra is helping with this.

Does anakinra have any side-effects?

If any of the following happen, tell your doctor immediately:

- **Serious infections** such as pneumonia (a chest infection) or infections of the skin can occur during anakinra treatment. Symptoms might be persistent high fever, shivers, cough, headache, and redness and tenderness of the skin. Also persistent low-grade fever, weight loss, and persistent cough can be signs of an infection.
- **Serious allergic reactions** are uncommon. However, any of the following symptoms may indicate an allergic reaction to anakinra, so you should seek immediate medical attention. Do not inject more Anakinra.
    - Swelling of the face, tongue or throat
    - Trouble swallowing or breathing
    - Suddenly feeling fast pulse or sweating
    - Itchy skin or rash.
- **Very common side effects** (may affect more than 1 in 10 people):
    - Redness, swelling, bruising or itching at the injection site. These symptoms are generally mild to moderate and are more common at the start of your treatment.
    - Headaches.
- **Common side effects** (may affect up to 1 in 10 people):
    - Neutropenia (low white blood cell count) determined after a blood test. This might increase the risk of you getting an infection. Symptoms of infection might include a fever or a sore throat.
    - Serious infections such as pneumonia (a chest infection) or infections of the skin.
    - Thrombocytopenia (low level of blood platelets.
- **Uncommon side effects** (may affect up to 1 in 100 people):

- Serious allergic reactions including swelling of the face, tongue or throat, trouble swallowing or breathing, suddenly feeling fast pulse or sweating and itchy skin or rash.
- Elevated levels of liver enzymes determined after a blood test.

- **Side effects with frequency not known** (frequency cannot be estimated):
  - Signs of liver disorders such as yellow skin and eyes, nausea, loss of appetite, dark-coloured urine and light-coloured stools.
  - If anakinra is injected repeatedly at the same place, there is a risk of a lump (amyloid deposit) forming under the skin. Rotate the injection site to avoid this.

Can I still be vaccinated?

Live vaccines should not be given concurrently with anakinra.

Is it safe to become pregnant or breast feeding while I am receiving anakinra?

You may have already had these conversations with your oncology team before starting immunotherapy.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Anakinra has not been tested in pregnant women and use is not recommended during pregnancy or in women of childbearing potential not using contraception.

It is not known whether anakinra is excreted in human milk. You must not breast-feed if you use anakinra.

Can I take other medicines whilst I am receiving anakinra?

You should always check with your oncology team or pharmacist if you are started on any new medicines, including anything you may buy over the counter.

Supply of anakinra.

It will be prescribed and administered in the hospital.

Who can I contact for further information?

If you have any queries about your anakinra, the best people to speak to are the oncology team who you are under, the team of specialists who have prescribed the anakinra for you, or an oncology pharmacist.

4. References

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5. Acknowledgements

6. Document control

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