

Anakinra in the Treatment of Secondary Haemophagocytic Lymphohistiocytosis (sHLH)

UCLH Guideline

Trust Wide

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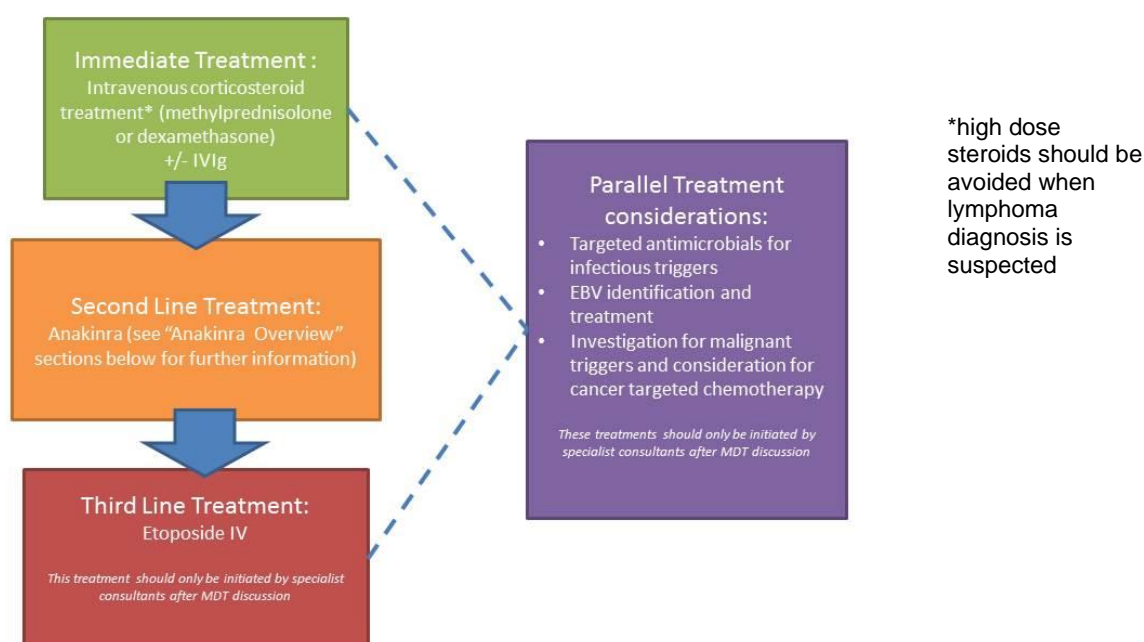
When suspecting Secondary Haemophagocytic Lymphohistiocytosis (sHLH)

When suspecting a diagnosis of sHLH please:

- Contact on-call rheumatologist, haematologist or infectious diseases team through switch board

Contact the HLH MDT via email: jessica.manson@nhs.net for non-urgent advice, and in order to alert the team of a new patient.

sHLH Treatment Overview:



Adapted from Carter et al. (2018)⁽¹⁾

Initiation of Anakinra Treatment

If steroid treatment is inappropriate or has led to an inadequate response, then anakinra may be commenced.

Anakinra can only be continued for 5 working days (Monday to Friday) before submission to the High Cost Drugs (HCD) panel for approval for continuation beyond this. The HCD panel will require differential diagnosis; dose, stopping criteria and estimation as to how long anakinra treatment will be required (see Appendix B). Anakinra may be continued until HCD panel response.

This should allow sufficient time for relevant diagnostic imaging/biopsies – it is important to try to avoid steroid treatment when lymphoma is suspected until all appropriate tissue has been sampled.

Anakinra Overview:

Anakinra blocks the biologic activity of IL-1 alpha and beta by competitively inhibiting IL-1 binding to the interleukin-1 type I receptor (IL-1RI), which is expressed in a wide variety of tissues and organs. IL-1 production is induced in response to inflammatory stimuli and mediates various physiological responses including inflammatory and immunological responses⁽²⁾.

Note: anakinra therapy for sHLH is an off-label use of the drug for all routes

Dose: 100mg daily (increased according to response).

- **Max 600mg* in 24hours administered in 1-2 divided doses, or by continuous infusion**
- **Dosed to the nearest 50mg**

**some patients may require dose adjustment up to 8mg/kg/day maximum*

Anakinra should be used with caution in patients with moderate renal impairment (CrCl 30-59ml/min). In severe renal impairment (CrCl <30ml/min) consider administration every other day⁽²⁾.

Route of administration:

1. Subcutaneous injection:

Anakinra is given subcutaneously unless contraindicated/unsuitable (e.g. platelets <20x10⁹/L)

- Anakinra pre-filled syringes are sterile unpreserved solutions and for single use only.
- Do not shake. Allow the pre-filled syringe to reach room temperature before injecting.
- Before administration, visually inspect the solution for particulate matter and discoloration. Only clear, colourless-to-white solutions that may contain some product-related translucent-to-white amorphous particles should be injected. The presence of these particles does not affect the quality of the product⁽¹⁾.

To be administered subcutaneously to⁽²⁾:

- the abdomen (except for the area around the navel)
- the top of the thighs
- the upper outer areas of the buttocks; and
- the outer area of the upper arms

2. Intravenous bolus of anakinra⁽³⁻⁵⁾

Intravenous bolus administration is reserved for patients for whom subcutaneous injections of anakinra is unsuitable (e.g. platelets <20x10⁹/L). Recommended dose remains as above.

- Use prefilled syringe to administer anakinra as a slow IV bolus (over 1-3minutes) followed by NaCl 0.9% flush

Or

- Use prefilled syringe to add anakinra dose to 50ml NaCl 0.9% before infusing intravenously, over 30 minutes.

Note: Anakinra should not be administered concomitantly via Y-site or mixed with any other medications due to lack of compatibility information.

3. Continuous intravenous infusion^(3,6)

Intravenous infusion administration is reserved for patients who are critically unwell or unresponsive to preferred anakinra routes

- Inject 100mg-200mg by slow IV bolus over 1-3minutes (as a loading dose) followed by a continuous IV infusion set at 2ml/hour. Max 400mg per day (*excluding* loading dose)**.
- Infusion must be changed every 6hours due to limited stability data

- **Change to subcutaneous administration as soon clinically appropriate**
- Continuous IV infusion method of administration:
 - Use a syringe pump to administer
 - Change every 6 hours (or sooner if the infusion has finished before 6hours)
- Set the infusion rate to

Drug	Concentration	Diluent	Rate of Infusion	Dose (see notes below)
Anakinra	100mg in 12ml total volume	Sodium chloride 0.9%	2ml / hour	400mg/day SYRINGE MUST BE CHANGED EVERY 6 HOURS

- Note: Anakinra should not be administered concomitantly via Y-site or mixed with any other medications due to lack of compatibility information.

***some patients may require dose adjustment up to 8mg/kg/day maximum*

Anakinra Treatment Duration:

Dependant on trigger for sHLH

Rheumatological Trigger:

e.g. Adult Onset Stills Disease (AOSD), systemic juvenile arthritis/ macrophage activation syndrome (MAS), systemic lupus erythematosus

- Dependant on response, to be continued (often long-term) and review in line with NHS England Commissioning Policy ⁽⁷⁾
- Weaned under HLH specialist consultant
- For Adult Onset Stills Disease ensure Blueteq form is completed and date of anakinra initiation is added.
- If trigger is SLE, consider rituximab/cyclophosphamide; may need to overlap with treatment of sHLH

Haematological/Malignant Trigger:

e.g. Lymphoma (T- Cell, NK-cell or B-cell), non-specified haematologic neoplasms, leukaemia

- Wean anakinra once chemotherapy regime established and patient stabilised.

Viral Trigger:

e.g. EBV, CMV, Adenovirus

- Continue anakinra until confirmation of viral infection obtained via PCR.
- Start treatment as appropriate to treat this viral driver of sHLH. Aim to wean anakinra as response to treatment progresses.

Iatrogenic Trigger:

Some medications are thought to be linked to HLH induction⁽⁸⁾

If a trigger for HLH is not found, patient should be maintained on lowest possible dose of anakinra and further investigations performed. Consider weaning steroids before weaning anakinra to look for lymphoma. Chase genetic results and bone marrow cytogenetics.

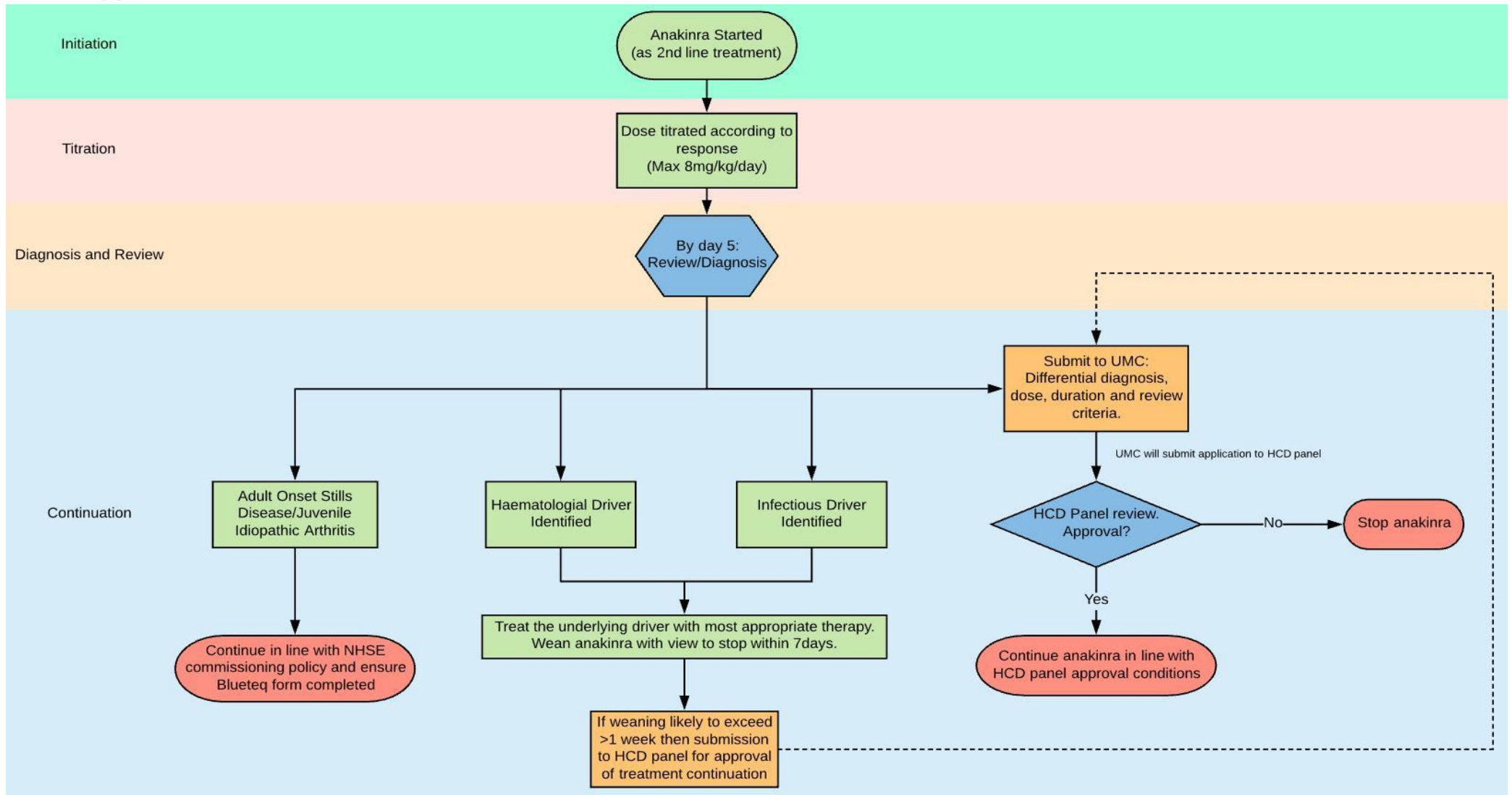
This may require HCD panel application for continuation of treatment (Appendix B)

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Appendix A: Anakinra Treatment/Review Timeline



Appendix B: High Cost Drugs Panel – Anakinra Continuation Form

Anakinra Continuation Form:

Anakinra can be used for up to 5 days empirically, after which continuation form will need to be submitted for High Cost Drugs (HCD) Panel approval. Please complete form below.

Patient Initials: _____ Patient MRN: _____
 Location/Ward: _____ Speciality: _____

Anakinra Details

Date started: _____ Route: _____ Dose/Frequency: _____

Suspected driver for sHLH: _____

Brief background/Rationale for treatment: _____

Tests Completed:	Date:

Further Tests pending:	Booked (yes/no):

Number of days needed for extension: _____ days

Form Completed by: _____ Contact Number/Bleep: _____
 Consultant: _____ Specialty: _____

Please complete the above form and send to uclh.umc@nhs.net for HCD Panel review.
Anakinra treatment may continue whilst awaiting response regarding HCD Panel decision.