Treatment Guideline

Gloucestershire Hospitals
NHS Foundation Trust

Tocilizumab: Prescribing and Administering in Adults

1. Background

- Tocilizumab is a humanized monoclonal antibody that binds to soluble and membrane-bound interleukin-6 (IL-6) receptors. It is from a group of drugs called cytokine inhibitors. Cytokines are small protein molecules, which occur in the body and are involved in inflammatory conditions. By inhibiting the release of IL-6, physiological processes which increase inflammation can be modulated, including T-cell activation and immunoglobulin secretion.

- Tocilizumab is currently used at GHNHSFT within the NICE Technology Appraisal process to treat severe rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA) after the failure of other disease modifying anti-rheumatic drugs (DMARDs). **This guidance is not applicable to patients being treated with tocilizumab for Covid-19 or to paediatric patients where separate guidance is available**

- For full guidance the NICE Technology Appraisals can be found at: www.nice.org.uk

- Tocilizumab is available as an intravenous infusion and as a subcutaneous injection designed for the patient to self-administer at home, this will usually be supplied via Homecare. The decision as to which formulation the patient will receive will be decided by the rheumatology team on the basis of clinical need and suitability for each patient

2. Prescribing

Contraindications

- Hypersensitivity to the active substance or any excipients
- Severe or uncontrolled infections such as sepsis and opportunistic infections
- Use in combination with TNF inhibitor medicines
- Live vaccines must not be given concurrently

3. Prescribing Tocilizumab Infusions for Day Case Patients

- Tocilizumab must be prescribed on the “Gloucestershire Hospitals Tocilizumab Day Case Prescription Chart”

- All details on the chart must be completed. This includes patients’ name, DOB, address and hospital number. An addressograph is sufficient

- The allergy section of the chart must be completed and patients’ weight must be documented on the chart

- **Declaration**
  All tocilizumab prescription charts must have the declaration for treatment completed by the prescriber. He/She must indicate if treatment is in line with the appropriate NICE Technology Appraisal by adding the technology appraisal reference number and countersigning. If treatment is outside the NICE criteria but has been agreed by a commissioner, the Individual Funding Request box must be ticked and the chart countersigned

Dosing of Intravenous Infusion in RA:

- Dose of tocilizumab infusion is 8mg/kg given four weekly

- For individuals whose body weight is more than 100kg, doses exceeding 800mg are not recommended.

- Doses may be reduced to 4mg/kg monthly if ALT/AST are raised or haematological parameters are abnormal, as per the manufacturer's SPC

Dosing of Intravenous Infusion in JIA:

- The dosing in patients above 2 years of age is 8mg/kg every two weeks in patients weighing 30kg or over, or 12mg/kg in patients weighing less than 30kg.

Frequency of dosing:

- No loading dose is required

- Actual dose for administration is checked by nursing staff upon patient admission based on current weight using the Tocilizumab dose banding table (See Appendix Two)

- The Day Case Prescription charts are valid for 6 months only

- Pharmacy will be unable to dispense tocilizumab for charts which are out of date, incorrectly completed or where the declaration is incomplete.

4. Dose Calculation (For Day Case Patients attending for Infusions)

- Dose calculation is carried out on admission by nursing staff on the Medical Day Unit, CGH using a dose-banding table for patients 40kg and over (see Appendix Two)

- Patient must be weighed upon admission. Weight must be documented on the chart for each admission.

- For patients >40kg, using the Tocilizumab dose banding table for rheumatology patients only, find the appropriate patient weight band for the relevant dose in mg/kg to locate the dose banded dose. For example, for a 73kg patient receiving 8mg/kg, the dose would be 600mg.

- Dose must be documented on the prescription chart and a second calculation check must be carried out by another staff nurse or healthcare professional.

5. Prescribing Tocilizumab for Subcutaneous (SC) Injection via Homecare (only for Rheumatoid Arthritis)

- The subcutaneous product is administered weekly at a dose of 162mg into the abdomen, thigh or upper arm

- Patients switching from tocilizumab intravenous therapy to subcutaneous administration should administer the first subcutaneous dose instead of the next scheduled intravenous dose

- The Pharmacy Homecare Office will provide the relevant Homecare registration and prescription forms for completion which should be returned to them for processing.

6. Patient Preparation and Pre-Treatment Investigations

- Prior to administration of the first dose, the following investigations must be performed:
  →Medical History, chest X ray and T spot test to exclude tuberculosis (as per local policy)
  →Hepatitis B and C serology, HIV if appropriate
  →History to confirm previous exposure to Varicella Zoster or serology test
  →Baseline lipid profile
  →Baseline U and E, LFTs to include AST, ESR, PV and FBC

- The patient will be fully counselled on the risks and benefits of treatment by the rheumatology specialist nurses

- For subsequent infusions bloods must be taken (for FBC, U&E's, LFT's and CRP) 2 weeks prior to date of infusion and will be checked by the infusion unit staff prior to the day of the infusion

- Lipid profile is required after the second infusion only

- On admission complete the patient care plan "Patients receiving tocilizumab infusions" – Y0970

- Carry out baseline observations to include Blood Pressure (BP), Pulse (P), Temperature, Urine Dip and patient weight

- Check blood results – (refer to blood monitoring guidance below)

- Ensure no evidence of sepsis or clinically manifested infection.

- Check medication history to ensure no drug contraindications or changes to medication which the rheumatology team are unaware of

- Ensure no previous reactions, if this is the case, patient may require pre-treatment with paracetamol and/or antihistamine, contact rheumatology for advice. **Severe reactions are a contraindication to further treatment.**

- Cannulate patient.

- For patients receiving subcutaneous injections, bloods should be monitored at intervals of monthly unless stated otherwise and will be monitored by the rheumatology specialist nurses.

7. Preparation of Infusion

<u>Reconstitution for patients with RA and JIA weighing 30kg or more</u>

- Withdraw a volume of sterile, non-pyrogenic sodium chloride 0.9% solution for injection from a **100 ml** infusion bag, equal to the volume of tocilizumab concentrate required for the patients dose, under aseptic conditions

- The required amount of tocilizumab concentrate should be withdrawn from the vial and placed in the 100 ml infusion bag. This should be a final volume of 100 ml.

- To mix the solution, gently invert the infusion bag to avoid foaming. Do not shake.

- Check the infusion with another trained member of staff and label the bag using a white sticker.

8. Administration of Infusion

- Administer the tocilizumab infusion intravenously over a period of 1 hour.
- It is recommended that the administration of the solution for infusion is started as soon as possible and within 24 hours of preparation if stored refrigerated at 2°C to 8°C
- Do not infuse tocilizumab in the same intravenous line as any other agents

9. Monitoring of Infusion

- Serious hypersensitivity reactions have been reported as associated with infusions of tocilizumab
- Acute infusion reactions including anaphylactic reactions may develop within seconds or within a few hours following infusion
- As this is rare, pre-treatment to prevent an infusion reaction is not required
- Check observations every 15 minutes (infusions 1-5) and every 30 minutes for subsequent infusions
- If acute reactions occur, the infusion must be stopped immediately.
- Check observations again before patient leaves the unit to go home

10. Treatment of Infusion Reaction

- An infusion reaction is any reaction occurring during or within 1-2 hours of an infusion. This can be classified into mild, moderate and severe.

- ***Mild*** reactions include: Mild fever, chills, nausea, headache, pruritis, dizziness and cough
- ***Moderate*** reactions include: Chest pain, shortness of breath, hypo/hypertension, palpitations, urticarial, elevated temperature
- ***Severe*** reaction include significant hypo/hypertension, stridor, chest discomfort or shortness of breath, bronchospasm, angiooedema of upper airway, elevated temperature

If a patient has a ***mild*** or ***moderate*** reaction:
→ STOP infusion immediately
→ Give PO paracetamol 1g and/or IV chlorpheniramine 10mg if appropriate
→ Monitor vital signs every 10 minutes
→ Wait 20 minutes
→ Restart infusion at half the original rate
→ Refer for medical assistance

If a patient has a severe reaction or anaphylaxis is suspected:
→ STOP infusion immediately
→ Treat as per anaphylaxis protocol

If a patient has any reaction:
→Contact the consultant rheumatologist responsible for the patient's care

- The decision to retreat a patient with tocilizumab who has had a reaction to it will be made by the consultant rheumatologist responsible for that patient's care. **A severe or anaphylactic reaction is a contraindication to on-going treatment**

References:

Summary of Product Characteristics for *RoActemra 20mg/ml Concentrate for Solution for Infusion* ®
Last updated on the Electronic Medicines Compendium 22/11/2022. Accessed via the Electronic Medicines Compendium http://emc.medicines.org.uk on *16/3/2023*

Summary of Product Characteristics for *RoActemra 162mg solution for injection in pre-filled syringe*®
Last updated on the Electronic Medicines Compendium 03/08/2023. Accessed via the Electronic Medicines Compendium http://emc.medicines.org.uk on *16/03/2023*

National Institute for Health and Clinical Excellence (NICE)
www.nice.org
NICE TA373 – Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs only have failed

NICE TA373 – Abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis

Appendix One

TOCILIZUMAB BLOOD MONITORING GUIDANCE

Dose adjustments due to laboratory abnormalities (see section 4.4).

• Liver enzyme abnormalities

Laboratory Value	Action
> 1 to 3 x Upper Limit of Normal (ULN)	Modify the dose of the concomitant MTX if appropriate For persistent increases in this range, reduce RoActemra dose to 4 mg/kg or interrupt RoActemra until alanine aminotransferase (ALT) or aspartate aminotransferase (AST) have normalised Restart with 4 mg/kg or 8 mg/kg, as clinically appropriate
> 3 to 5 x ULN (confirmed by repeat testing, see section 4.4).	Interrupt RoActemra dosing until < 3 x ULN and follow recommendations above for > 1 to 3 x ULN For persistent increases > 3 x ULN, discontinue RoActemra
> 5 x ULN	Discontinue RoActemra

• Low absolute neutrophil count (ANC)

In patients not previously treated with RoActemra, initiation is not recommended in patients with an absolute neutrophil count (ANC) below **1.8**

Laboratory Value (cells x 10^9/ l)	Action
ANC > 1	Maintain dose
ANC 0.5 to 1	Interrupt RoActemra dosing When ANC increases > 1 x 10^9/ l resume RoActemra at 4 mg/kg and increase to 8 mg/kg as clinically appropriate
ANC < 0.5	Discontinue RoActemra

• Low platelet count

Laboratory Value (cells x 10^3/ µL)	Action
50 to 100	Interrupt RoActemra dosing When platelet count > 100 x 10^3/ µ resume RoActemra at 4 mg/kg and increase to 8 mg/kg as clinically appropriate
< 50	Discontinue RoActemra

NORMAL BLOOD RANGES

Liver function tests:

ALT (alanine aminotransferase) and AST
Men: ALT < 50
Women: ALT < 35

Alkaline phosphatase (alk phos)
Men and women (30-130) Seek advice if alkaline phosphatase >160

Appendix Two

Tocilizumab dose banding for rheumatology patients only

While we have availability of all vial combinations rheumatology patients should receive dosing as per the relevant dose banding tables below. The standard dose is 8mg/kg, capped to a maximum dose of 800mg, but patients may receive dose reductions to 6mg/kg or 4mg/kg if they develop blood dyscrasias or abnormalities of liver function.

8mg/kg dose		6mg/kg dose		4mg/kg dose	
Patient weight	**Dose**	**Patient weight**	**Dose**	**Patient weight**	**Dose**
40-42kg	320mg	**40-43kg**	240mg	**40-43kg**	160mg
43-47kg	360mg	**44-50kg**	280mg	**44-46kg**	180mg
48-52kg	400mg	**51-56kg**	320mg	**47-55kg**	200mg
53-57kg	440mg	**57-63kg**	360mg	**56-65kg**	240mg
58-62kg	480mg	**64-70kg**	400mg	**66-75kg**	280mg
63-67kg	520mg	**71-76kg**	440mg	**76-85kg**	320mg
68-72kg	560mg	**77-83kg**	480mg	**86-95kg**	360mg
73-77kg	600mg	**84-90kg**	520mg	**96-105kg**	400mg
78-82kg	640mg	**91-96kg**	560mg	**106-115kg**	440mg
83-87kg	680mg	**97-103kg**	600mg	**116-125kg**	480mg
88-92kg	720mg	**104-110kg**	640mg	**126-135kg**	520mg
93-97kg	760mg	**111-116kg**	680mg		
98->100kg	800mg	**117-123kg**	720mg		
		124-130kg	760mg		
		131->134kg	800mg		

Pharmacy dispensing guide

Dose	Vials to dispense
160mg	2 x 80mg
180mg	1 x 200mg
200mg	1 x 200mg
240mg	3 x 80mg
280mg	1 x 200mg and 1 x 80mg
320mg	4 x 80mg
360mg	1 x 200mg and 2 x 80mg
400mg	1 x 400mg
440mg	1 x 200mg and 3 x 80mg
480mg	1 x 400mg and 1 x 80mg
520mg	1 x 200mg and 4 x 80mg
560mg	1 x 400mg and 2 x 80mg
600mg	1 x 400mg and 1 x 200mg
640mg	1 x 400mg and 3 x 80mg
680mg	1 x 400mg, 1 x 200mg and 1 x 80mg
720mg	1 x 400mg and 4 x 80mg
760mg	1 x400mg, 1 x 200mg and 2 x 80mg
800mg	2 x 400mg