COVID19 Tocilizumab Treatment Protocol

Interim RECOVERY trial data on 11th February 2021 showed that Tocilizumab improves survival of patients with COVID-19 by up to a third. The incremental effect is independent of the survival benefits with Dexamethasone for the condition. NHS England has expressed support for commissioning the use of tocilizumab for patients with COVID-19.

Tocilizumab is an Interleukin-6 (IL-6) inhibitor licenced for treatment of rheumatoid arthritis, giant cell arteritis, and chimeric antigen receptor T cell-induced severe or life-threatening cytokine release syndrome in adults. Please visit [here](#) for the spc of the medication.

Use of Tocilizumab for patients with COVID-19 is outside its licenced indications. For this reason, a clear documentation of the justification of its use in patients would be advisable.

Criteria for use of Tocilizumab in patients with CPVID-19

We recommend that the use of Tocilizumab should be considered after the consultant’s ward round when patient’s eligibility for the treatment and the potential risks of use of the medication are considered.

Patients must meet all the following criteria and none of the exclusion criteria in order to be receive tocilizumab:

Eligibility criteria (all must be met):
- Being an in-patient
- Age older than 18
- Tested positive for SARS-CoV-2 infection
- Already on Dexamathasone for COVID-19
- Oxygen saturation of less than 92% on room air or requiring oxygen supplementation
- CRP of equal to or greater than 75 mg/L

Exclusion criteria (none must be present):
- Having received an IL-6 inhibitor in the 48 hours of commencement of oxygen supplementation
- Known hypersensitivity to Tocilizumab or Sarilumab
- Serum ALT or AST greater than five times of the upper limit of normal (ALT: greater than 270 U/L, AST: greater than 170 U/L)
- Active Tuberculosis, fungal infection or sepsis
- Neutrophil count less than $2 \times 10^9$/L
- Platelet count less than $50 \times 10^9$/L

Discuss with Respiratory, or ID consultants when required.

Pregnancy and breast feeding:
Data on the use of Tocilizumab during pregnancy is scant. The potential risk to human foetus is unknown. The use of Tocilizumab in pregnancy is not recommended unless clearly necessary. In those cases, clear documentation of a discussion on the risks to the foetus with the patient and their partner is advised.

There are currently no data on the risk to infants through breast milk. Breast feeding women requiring Tocilizumab must be advised to formula feed their babies for seven weeks after the dose of tocilizumab.

**Dose of Tocilizumab for COVID-19 patients:**

The recommended dose is 8 mg/kg administered intravenously with 0.9% sodium chloride over one hour and as a single dose.

The total dose of Tocilizumab must not exceed 800 mg.

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;41kg</td>
<td>8mg/kg, rounded to 20mg</td>
</tr>
<tr>
<td>≥ 41kg and ≤ 45kg</td>
<td>360mg</td>
</tr>
<tr>
<td>≥ 46kg and ≤ 55kg</td>
<td>400mg</td>
</tr>
<tr>
<td>≥ 56kg and ≤ 65kg</td>
<td>480mg</td>
</tr>
<tr>
<td>≥ 66kg and ≤ 80kg</td>
<td>600mg</td>
</tr>
<tr>
<td>≥ 81kg and ≤ 90kg</td>
<td>680mg</td>
</tr>
<tr>
<td>≥91kg</td>
<td>800mg</td>
</tr>
</tbody>
</table>

**Administration of Tociluzumab for COVID-19 patients:**

Tocilizumab must be diluted in a 100 mL bag of 0.9% sodium chloride after removing equivalent volume of saline for a total volume of 100 mL and given over one hour. Tocilizumab must not be infused concomitantly in the same iv line with other medications.

See [appendix 1](#) for how to initiate Tocilizumab

See [appendix 2](#) for how to prepare Tocilizumab for administration

**Co-administration:**

There is no significant interaction between dexamethasone or hydrocortisone and tocilizumab. Please use the University of Liverpool COVID-19 Drug Interactions Website for more information: [https://www.covid19-druginteractions.org/checker](https://www.covid19-druginteractions.org/checker)

**Side effects and events:**

Tocilizumab is not licenced for use in patients with COVID-19. Please ensure that adverse reactions are reported via the dedicated yellow card reporting site: [https://coronavirus-yellowcard.mhra.gov.uk/](https://coronavirus-yellowcard.mhra.gov.uk/).

**Safety considerations:**
Tocilizumab can cause immunosuppression that renders patients at risk of bacterial and fungal infections. Low clinical threshold for identification and management of infection must be used.

**Monitoring:**
Patients must be regularly clinically assessed for bacterial infection. A blood culture must be obtained for all patients with fever and where treatment for bacterial infection is commenced. Discuss with ID and microbiology consultants when required.

All patients receiving Tocilizumab must be tested for HIV, Hepatitis B, and Hepatitis C infections. Please request HIV antibody, hepatitis B surface antigen, hepatitis B core antibody and Hepatitis C antibody tests. Please discuss the results with microbiology or ID physicians if unsure on how to interpret the results.
Appendix 1.

INITIATING TOCILIZUMAB FLOWCHART

DIAGNOSTIC CRITERIA
Patient matches diagnostic criteria for treatment
Patient has not received Tocilizumab as part of a trial or randomised to mAb arm of a covid-19 trial

BLUETEQ FORM
Consultant looking after patient to complete Blueteq form
https://www.bluteq-secure.co.uk/Trust/Default.aspx
Once completed contact pharmacy- unit pharmacist for review. Out of hours- see Pharmacy Supply below

PRESCRIBING
QE site- Prescribe on the Infusion tab on PICS (Reg/Consultant)
HGS- Prescribe via JAC/Paper drug chart
Add Blueteq number onto the prescription as a note
Inform bed space nurse of prescription

PHARMACY SUPPLY
Pharmacy team will confirm the patient meets the diagnostic criteria and that Blueteq approval has been received.
A named patient supply will be made for the dose. Note vial sizes 80mg, 200mg and 400mg are available and require FRIDGE storage. A separate guide is available to support ward preparation (see appendix 2).
Supply should be made promptly within working hours.
The infusion must be prescribed and approved within 24 hours from organ support, an additional 12 hours is acceptable to complete the infusion. If this time window will be breached please contact the on-call pharmacist for out of hours supply.
Appendix 2.

TOCILIZUMAB DRUG PREPARATION AND ADMINISTRATION GUIDANCE

For Critical Care and Respiratory Support unit use only
To be prepared by suitably trained nursing staff

This method uses Tocilizumab vials (RoActemra)

Tocilizumab dose = ..................mg (check it fits the dosebanding table to the right)

Volume of tocilizumab 20mg/mL concentrate required =

Dose of tocilizumab (mg) ÷ 20 (mg/mL) = ..............................mg ÷ 20 (mg/mL) = ......................mL

Number of vials required =_____ x 200mg vial(s) and/or _____ x 80mg vial(s) and/or _____ x 400mg vial(s)

Calculation completed by and date
Calculation checked by and date

Materials Required

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Storage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tocilizumab 80mg in 4mL vial (RoActemra)</td>
<td>Fridge</td>
</tr>
<tr>
<td>Tocilizumab 200mg in 10mL vial (RoActemra)</td>
<td>Fridge</td>
</tr>
<tr>
<td>Tocilizumab 400mg in 20mL vial (RoActemra)</td>
<td>Fridge</td>
</tr>
<tr>
<td>Sodium Chloride 0.9% 100mL Infusion Bag</td>
<td>Fluid</td>
</tr>
</tbody>
</table>

Record batch details in PICS/on JAC/on Paper Chart

1. Preparation, administration and disposal of intravenous tocilizumab infusion

In addition to the information provided in the table below, please follow the general principles of preparing injectable medicines in a clinical area.

1. Ensure the preparation area is clean and clear. Collect the appropriate number of tocilizumab vials from the fridge and a 100mL IV infusion of sodium chloride 0.9%.

2. Ensure the appropriate personal protective equipment (PPE) is worn as per Critical Care guidance. However, this must include gloves, an apron, an FFP3 face mask and goggles (or a visor).

3. Tocilizumab solutions should be clear to opalescent, colourless to pale yellow and free of visible particles, in order to be deemed suitable for administration.

4. Using an appropriate volume IV syringe, withdraw XmL of sodium chloride 0.9% from the 100mL sodium chloride 0.9% IV infusion. (XmL is the volume of tocilizumab calculated as required for the patient’s dose. E.g. if a dose of 800mg (40mL) of tocilizumab 20mg/ml solution is prescribed, then remove 60mL of sodium chloride 0.9% from the 100mL infusion).

5. Discard the withdrawn sodium chloride 0.9% inside the syringe and needle into a yellow sharps bin.

6. Using an appropriate volume IV syringe, draw up XmL of tocilizumab 20mg/mL solution required for the prescribed dose from the vial(s), as calculated above. (XmL is the volume of tocilizumab 20mg/ml required, as calculated for the patient’s dose. E.g. if 800mg Tocilizumab is prescribed, 40mL of tocilizumab 20mg/ml is needed).

7. SLOWLY add the tocilizumab solution to the sodium chloride 0.9% IV infusion to make a final
8. Dispose of the tocilizumab needle and syringe in a sharps bin.

9. Mix the tocilizumab solution by gently inverting several times to avoid foaming. **DO NOT SHAKE THE SOLUTION - THIS WILL CAUSE THE SOLUTION TO FOAM AND YOU WILL NOT BE ABLE TO USE IT.**

10. Complete and apply an IV infusion label to the tocilizumab IV infusion.

11. Obtain a second check for the IV tocilizumab infusion from a colleague and sign for preparation and administration on PICS.

12. Record baseline observations for the patient before starting the infusion – heart rate, BP, temperature, respiratory rate.

13. Connect the tocilizumab IV infusion to the patient IV line and administer over 1 hour via a volumetric infusion pump. Do not infuse any other medicines via the same IV line whilst the tocilizumab is being administered.

14. Complete patient observations and monitor the patient for signs of hypersensitivity to tocilizumab as follows: 15 minutes after starting the infusion, then every 30 minutes during the infusion and for 1 hour after the end of infusion. Monitoring time points after starting the infusion: 15mins, 45mins, 1hour 15mins, 1 hour 45mins.

15. Acute infusion reactions can occur during the administration of tocilizumab or within 24 hours of infusion. For mild reactions such as flushing and chills, the infusion rate can be slowed down and the patient continually monitored. Notify the doctors of the patient reaction. For severe reactions such as hives, difficulty breathing, chest pain, high or low blood pressure, swelling of face and hands, fever, chills or anaphylaxis or when mild reactions persist despite slowing the infusion, **stop the infusion and inform the doctors immediately for additional treatment.**

16. Once the tocilizumab infusion is complete, take down the infusion and flush the giving set with 20mL of sodium chloride 0.9% over 15 minutes to ensure all the tocilizumab has been given.

17. Dispose of the infusion and giving set in a sharps bin.