Worcestershire NHS
Acute Hospitals NHS Trust

INTERIM GUIDELINE FOR USE OF IL-6 INHIBITORS (TOCILIZUMAB OR SARILUMAB) IN THE MANAGEMENT OF SEVERE COVID-19 INFECTION

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

Overview

This document forms part of the Worcestershire Acute Hospitals NHS Trust (WAHT) Antimicrobial Prescribing Guidelines, published on MicroGuide. It covers the use of Interleukin-6 (IL-6) inhibitors in the management of COVID-19.

This guideline is for use by the following staff groups:

This guideline is intended for use by all clinical staff who prescribe, administer or monitor treatment for patients requiring intensive care for the management of COVID-19.

Lead Clinician(s)	Dr Nicholas Cowley, Consultant Critical Care
Approved by Silver Command on:	
Approved by Medicines Safety Committee on:	Add date
This guideline should not be used after end of:	31/01/2022

Key amendments to this guideline

Date	Amendment	Approved by:
11/01/2021	Guidance published	Silver Command
20/01/2021	Monitoring section expanded, SOP for prescribing, clinically checking and issuing IL-6 inhibitors for COVID-19 added; updated Blueteq Form	

INTERIM GUIDELINE FOR USE OF IL-6 INHIBITORS (TOCILIZUMAB OR SARILUMAB) IN THE MANAGEMENT OF SEVERE COVID-19 INFECTION

Guideline Details

Inclusion criteria

The following patients should be considered for therapy with either tocilizumab or sarilumab if they fulfil all of the following criteria:

- COVID-19 infection is confirmed by microbiological testing or where a multidisciplinary team has a high level of confidence that the clinical and radiological features suggest that COVID-19 is the most likely diagnosis.
- Is not eligible, refused participation in or a decision is taken to not recruit into a clinical trial with immunomodulation arm including an IL-6 inhibitor.
- Admitted to intensive care or a repurposed area designed to offer enhanced organ support, without palliative intent.
- Initiated on respiratory support (non-invasive ventilation/CPAP, high flow nasal oxygen, invasive mechanical ventilation) or cardiovascular support with vasopressors/inotropic drugs.
- Treatment initiation must be prescribed within 24 hours of respiratory or cardiovascular support.

Exclusion criteria

- Known hypersensitivity to tocilizumab or sarilumab
- Co-existing infection that might be worsened by tocilizumab or sarilumab
- More than 24 hours has elapsed since ICU/High Care admission or more than 24 hours after starting respiratory support (whichever is the greater)
- A baseline alanine aminotransferase (ALT) or aspartate aminotransferase (AST) more than 5 times the upper limit of normal (caution is recommended if hepatic enzymes are more than 1.5 times the upper limit of normal)
- A baseline platelet count of less than 50 x 10^9/L
- A baseline absolute neutrophil count of less than 2 x 10^9/L
- A pre-existing condition or treatment resulting in ongoing immunosuppression

Referral

Authorisation for prescription must be from a consultant respiratory physician, intensive care physician, or microbiologist.

Blueteq authorisation must completed (see attached). This may be done retrospectively but ideally within 24 hours.

Monitoring

Please ensure the following are checked prior to tocilizumab initiation:

- Hepatitis B diagnostic serology – do not wait for the result before giving IL-6 inhibitor.
- Consider sending samples for Quantiferon TB (IGRA) test if the patient is thought to be at risk of latent TB.

Standard frequency monitoring of renal and hepatic function and FBC for critical care patients.

IL-6 inhibitors suppress CRP production irrespective of the clinical status of the patient and surveillance for secondary infections is recommended. Consider using procalcitonin levels for patients treated with IL-6 inhibitors.

Gastrointestinal perforation has been reported in patients receiving sarilumab or tocilizumab. Consider CT abdomen and pelvis in deteriorating patients where no other cause has been found.

Report any suspected adverse reactions. This should be arranged through the ward pharmacist or Medicines Information (ext. 45776 or wah-tr.druginfo@nhs.net).

Treatment

Choice will depend on stock availability – please check prior to prescribing

Tocilizumab 8 mg/kg (actual body weight – see table below) (to max. 800 mg) as an intravenous infusion, repeated after 12 to 24 hours at consultant clinician discretion if there is no clinical improvement. The second dose should not be prescribed before clinical review of the patient response.

Tocilizumab should be diluted in a 100 mL bag of 0.9% sodium chloride, after removing an equivalent volume of saline (total volume 100mL) and given over 1 hour.

Weight	<41kg	≥41 and ≤45kg	≥46 and ≤55kg	≥56 and ≤65kg	≥66 and ≤80kg	≥81 and ≤90kg	≥91kg
Dose	8mg/kg (nearest 20mg)	360mg	400mg	480mg	600mg	680mg	800mg

Record the name and the batch number of the administered product on the patient dug chart.

OR

Sarilumab 400 mg in 100 ml sodium chloride 0.9% as intravenous infusion over 1 hour as single dose.

Please select drug link to view preparation and administration guide.

Record the name and the batch number of the administered product on the patient dug chart.

Co-administration of corticosteroids

Administration of dexamethasone is recommended in severe or critical COVID-19.

Co-administration of remdesivir

There is no interaction of either tocilizumab or sarilumab with remdesivir expected. Follow local protocol for the use of Remdesivir for the management of COVID-19.

Reference:

1. Department of Health & Social Care, National Health Service. COVID-19 Therapeutic Alert - Interleukin-6 inhibitors (tocilizumab or sarilumab) for patients admitted to ICU with COVID-19 pneumonia (adults). Published 8th January 2021.
2. Department of Health & Social Care, National Health Service. Interim Position Statement: Interleukin-6 inhibitors (tocilizumab or sarilumab) for patients admitted to ICU with COVID-19 pneumonia (adults). Published 8th January 2021.
3. The REMAP-CAP Investigators. Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19 – Preliminary report. Published 7th January 2021. doi: https://doi.org/10.1101/2021.01.07.21249390
4. Roche Products Limited. RoActemra 20mg/ml Concentrate for Solution for Infusion – Summary of Product Characteristics. Last updated 02nd September 2020.

SOP for prescribing, clinically checking and issuing IL-6 inhibitors for COVID-19

To ensure prompt access to treatment, tocilizumab will be held as stock in ICU and repurposed ICU areas.

1. Consultant respiratory physician, intensive care physician, or microbiologist makes the decision to prescribe IL-6 inhibitor in line with Interim Guideline for Use of IL-6 inhibitors (Tocilizumab or Sarilumab) in the management of severe COVID-19 infection

2. Consultant respiratory physician or intensive care physician completes Tocilizumab Blueteq Form and files this in the patient record paper or completes on-line at https://www.blueteq-secure.co.uk/Trust/Default.aspx
3. Consultant respiratory physician or intensive care physician prescribes treatment on patient drug chart.
4. Nurse uses ward stock and completes stock accountability log for each patient.
5. Nurse prepares dose prescribed following guidance on Medusa for Tocilizumab. For Sarilumab administration guidance, follow drug link.
6. Nurse documents brand name and batch number of preparation administered on patient drug chart.
7. Ward pharmacist checks stock accountability log daily Mon - Fri (accountability period) and reconciles this against patient records (prescription chart and notes/Blueteq online portal for completion of Blueteq form). If prescribing is identified outside Interim Guideline for Use of IL-6 inhibitors (Tocilizumab or Sarilumab) in the management of severe COVID-19 infection, ward pharmacist informs lead pharmacist for Critical Care or his deputy.
8. Ward pharmacists checks tocilizumab prescription and checks/ completes on-line Blueteq registration for patient, where necessary. Ward pharmacists completes requisition form for each patient detailing patient name, NHS number, drug, dose and number and strength of vials used and sends requisitions form to pharmacy. Alternatively, phone dispensary for completion of verbal order or send copy of accountability log to dispensary, clearly marking for which patients supply is to be replaced.
9. Dispensary staff issues tocilizumab/sarilumab for each patient on EMIS as per requisition form.
10. Dispensary staff sends stock replacement equivalent to the stock issued on the requisition form unlabelled as ward stock to relevant ICU ward area.
11. Nursing staff/ pharmacy ATO stores stock on ward fridge and completes accountability log with number of vials received into ward stock.

Tocilizumab Blueteq Form

Standard Operating Procedure	Worcestershire NHS Acute Hospitals NHS Trust

TOCCV1_ver3.0 Interim Position Statement: Tocilizumab for patients admitted to ICU with COVID-19 pneumonia (adults)			
Patient NHS No:		**Trust:**	WORCESTERSHIRE ACUTE HOSPITALS NHS TRUST
Patient Hospital No:		**GP Practice Code:**	
Patient's Initials and DoB:		**GP Postcode:**	
Consultant Name:		**Other Contact Details:**	
Consultant Notification Email Address:			@NHS.net account ONLY
Treatment Start Date:			

Please indicate whether patient meets the following criteria:	**Please tick (All required)**
1. I confirm that the patient is an adult with SARS-CoV-2 infection* * In the absence of a confirmed virological diagnosis, tocilizumab should only be used when a multidisciplinary team have a high level of confidence that the clinical and radiological features suggest that COVID-19 is the most likely diagnosis.	☐ **Yes** ☐ **No**
2. I confirm intravenous tocilizumab has been prescribed as the patient is an adult who has been admitted to ICU with severe pneumonia requiring respiratory support**, such as high-flow nasal oxygen, CPAP or non-invasive ventilation, or invasive mechanical ventilation and **all** of the following apply: • No more than 24 hours has elapsed since ICU admission or more than 24 hours after starting respiratory support (whichever is the later) • The patient will receive tocilizumab according to the Interim Position Statement: IL-6 inhibitors (tocilizumab or sarilumab) for patients admitted to ICU with COVID-19 pneumonia (adults)*** and does not meet any of the exclusion criteria • The patient will receive a maximum number of two doses ** Or admitted to ICU with organ failure requiring support as infusion of vasopressor or inotropes or both. ICU includes areas within the hospital repurposed to deliver one or more of the organ failure supports required to meet eligibility criteria. *** As part of the interim position statement hospitals are strongly encouraged to submit data through the ISARIC 4C Clinical Characterisation Protocol (CCP) case report forms (CRFs), as coordinated by the COVID-19 Clinical Information Network (CO-CIN) **NB: For adult patients with SARS-CoV-2 infection who have not been admitted to ICU, sites should consider randomisation to the immunomodulator arm in the RECOVERY trial if this is available**	☐ **Yes** ☐ **No**

Consultant signature:			
GMC number:		**Date:**	

Adapted from Blueteq HICost/PriorApproval/IFR Database, National Trust Edition TOCCV_ver3.0

Version	3	Date	13/01/2021
Written by	Astrid Gerrard	Approved by	

Monitoring Tool

This should include realistic goals, timeframes and measurable outcomes.

How will monitoring be carried out?

Who will monitor compliance with the guideline?

Page/ Section of Key Document	Key control:	Checks to be carried out to confirm compliance with the policy:	How often the check will be carried out:	Responsible for carrying out the check:	Results of check reported to: *(Responsible for also ensuring actions are developed to address any areas of non-compliance)*	Frequency of reporting:
	WHAT?	**HOW?**	**WHEN?**	**WHO?**	**WHERE?**	**WHEN?**
all	Compliance with protocol	Check of compliance of prescription with guidance including dose, frequency, route, eligibility criteria and completion of Blueteq form	Within 72 hours of each prescriptions	Clinical ward pharmacists for critical care areas	Critical Care Governance meeting	

Contribution List

This key document has been circulated to the following individuals for consultation:

Designation
Antimicrobial Stewardship Pharmacist
Keith Hinton, Lead Pharmacist Surgery and Critical Care
Critical Care consultants
ID consultants
Microbiology consultants
Respiratory consultants

This key document has been circulated to the chair(s) of the following committee's / groups for comments;

Committee
Medicines Safety Committee

Supporting Document 1 - Equality Impact Assessment Tool

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

		Yes/No	Comments
	Does the policy/guidance affect one group less or more favourably than another on the basis of:		
	• Race	No	
	• Ethnic origins (including gypsies and travellers)	No	
	• Nationality	No	
	• Gender	No	
	• Culture	No	
	• Religion or belief	No	
	• Sexual orientation including lesbian, gay and bisexual people	No	
	• Age	No	
2.	**Is there any evidence that some groups are affected differently?**	No	
3.	**If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?**	No	
4.	**Is the impact of the policy/guidance likely to be negative?**	No	
5.	**If so can the impact be avoided?**	n/a	
6.	**What alternatives are there to achieving the policy/guidance without the impact?**	n/a	
7.	**Can we reduce the impact by taking different action?**	n/a	

If you have identified a potential discriminatory impact of this key document, please refer it to Human Resources, together with any suggestions as to the action required to avoid/reduce this impact.

For advice in respect of answering the above questions, please contact Human Resources.

Supporting Document 2 – Financial Impact Assessment

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

	Title of document:	Yes/No
1.	Does the implementation of this document require any additional Capital resources	No
2.	Does the implementation of this document require additional revenue	No
3.	Does the implementation of this document require additional manpower	No
4.	Does the implementation of this document release any manpower costs through a change in practice	No
5.	Are there additional staff training costs associated with implementing this document which cannot be delivered through current training programmes or allocated training times for staff	No
	Other comments:	n/a

If the response to any of the above is yes, please complete a business case and which is signed by your Finance Manager and Directorate Manager for consideration by the Accountable Director before progressing to the relevant committee for approval