Tocilizumab Dosing for the Treatment of COVID-19

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This document was developed by Ontario Health's Infectious Diseases Advisory Committee based on best available evidence and expert consensus. There are limitations to the evidence that is currently available. **Prescribers should conduct a comprehensive risk-benefit analysis when applying the recommendations to inform individualized treatment decisions.**

Purpose

The objective of this document is to provide clinicians with recommendations for intravenous (IV) tocilizumab dosing for adults age 18 years and above.

Tocilizumab (Actemra) is indicated for hospitalized patients with COVID-19 who are on recommended doses of dexamethasone therapy (or a dose-equivalent corticosteroid) and are within 14 days of hospital admission (or within 14 days of a new COVID-19 diagnosis if the infection was hospital acquired) **AND**:

1. Require new respiratory support (e.g., high-flow oxygen, non-invasive ventilation, mechanical ventilation) and/or vasopressor/inotropic support **OR**
2. Have evidence of systemic inflammation, defined as a serum C-reactive protein of 75 mg/L or higher AND have evidence of disease progression (i.e., increasing oxygen or ventilatory requirements to maintain a resting oxygen saturation of 92%) despite 24-48 hours of recommended doses of dexamethasone therapy (or a dose-equivalent corticosteroid)[1]

Background

The recommended dosing strategy for tocilizumab can vary between different health authorities and references. The Ontario COVID-19 Science Advisory Table's guidance document from Mar 1, 2021 recommended using either a weight-based dosing strategy (8 mg/kg, maximum dose 800 mg) or a weight-based dose banding strategy (800 mg if weight greater than 90 kg; 600 mg if weight greater than 65 and equal or less than 90 kg; 400 mg if weight greater than 40 and equal or less than 65 kg; and 8 mg/kg if weight equal or less than 40 kg).[2] In drug shortage situations, a fixed dose of tocilizumab 400 mg was recommended.[3]

Assessment

The efficacy and safety of tocilizumab dosing using a weight-based dosing strategy or a weight-based dose banding strategy are supported by clinical evidence from the REMAP-CAP and RECOVERY trials.[4,5] The two dosing strategies have not been directly compared in a clinical trial. A pharmacokinetic simulation study predicted comparable tocilizumab exposures for weight-based dosing and weight-based dose banding.[6] Observational studies that have compared weight-based dosing and fixed-dosed strategies (e.g., 400 mg or 600 mg for all patients irrespective of weight) did not find any significant difference for mortality and hospital length of stay when a fixed dose of 400 mg was compared with weight-based dosing.[7–10]

Neither the RECOVERY nor the REMAP-CAP trials provided sufficient information to understand the role of a second dose in patients who did not respond to a first dose.[3] Observational studies reported similar benefits between a single tocilizumab dose compared to multiple doses.[11–13] Treatment with multiple doses of tocilizumab was associated with higher odds of pneumonia compared to a single dose, that may be related to tocilizumab-induced immunosuppression.[11]

Tocilizumab is supplied in 80 mg, 200 mg and 400 mg single-use vials. Single-use vials do not contain preservatives and must immediately be discarded after use to prevent microbial contamination of the IV solution if not compounded under sterile preparation according to National Association of Pharmacy Regulatory Authorities standards.[3]

It is currently unclear whether there are any advantages for weight-based dosing compared to weight-based dose banding or a fixed-dosing strategy for mortality and other clinical outcomes. Weight-based dose banding and fixed-dose strategies have practical and safety advantages such as reducing dosing errors and avoiding unnecessary drug waste.

Recommendations

The Committee recommends the tocilizumab dosing strategy outlined in Table 1 based on the best available evidence, safety and logistical considerations.

Table 1. Tocilizumab Dosing

Patient Weight	Tocilizumab Dosing in Non-drug Shortage Situations (Single Dose IV)	Tocilizumab Dosing in Drug Shortage Situations (Single Dose IV)
Less than or equal to 40 kg	8 mg/kg	8 mg/kg
Greater than 40 kg to less than or equal to 65 kg	400 mg	400 mg
Greater than 65 kg to less than or equal to 90 kg	600 mg	400 mg
Greater than 90 kg	800 mg	400 mg

Questions

For any questions on the contents of this document, please contact the Provincial Drug Reimbursement Programs (PDRP) at OH-CCO_InfoPDRP@ontariohealth.ca.

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