

# Grading and Management of CRS

While high-grade CRS is rare, prompt and urgent intervention to prevent progression of CRS is required; however, other causes of systemic inflammatory response should be ruled out, including infection and malignancy progression. Empiric treatment for infection is warranted in the neutropenic patient. Organ toxicities associated with CRS may be graded according to CTCAE v5.0 but they do not influence CRS grading.

Fever is defined as temperature >100.4°F not attributable to any other cause. In patients who have CRS then receive antipyretics or anticytokine therapy such as tocilizumab or steroids, fever is not required to grade subsequent CRS severity. In this case, CRS grading is driven by hypotension or hypoxia.

CRS Grade	Anti-IL-6 Therapy	Steroids	Additional Supportive Care
<b>Grade 1</b> Fever ( $\geq 100.4^\circ\text{F}$ )	For prolonged CRS (>3 days) in patients or those with significant symptoms, comorbidities, and/or are >65 years, consider 1 dose of IV tocilizumab 8 mg/kg over 1 hour (not to exceed 800 mg)	For idecabtagene and lisocabtagene, consider IV dexamethasone 10 mg every 24 hours for early-onset CRS (<72 hours after infusion)	<ul style="list-style-type: none"> <li>Sepsis screen and empiric broad-spectrum antibiotics, consider granulocyte colony-stimulating factor (G-CSF) if neutropenic</li> <li>Maintenance IV fluids for hydration</li> <li>Symptomatic management of organ toxicities</li> </ul>
<b>Grade 2</b> Fever with hypotension not requiring low-flow nasal cannula or blow-by	IV tocilizumab 8 mg/kg over 1 hour (not to exceed 800 mg/dose). Repeat in 8 hours if no improvement; no more than 3 doses in 24 hours with maximum of 4 doses total	For persistent refractory hypotension after 1-2 doses of anti-IL-6 therapy: Consider IV dexamethasone 10 mg every 12-14 hours depending on product.	<ul style="list-style-type: none"> <li>IV fluids as needed</li> <li>For persistent refractory hypotension after two fluid boluses, and anti-IL-6 therapy. Start vasopressors, consider transfer to ICU, consider echocardiogram, and initiate other methods of hemodynamic monitoring. Telemetry, ECG, troponin, and BNP If persistent tachycardia</li> <li>Manage per Grade 3 if no improvement within 24 hours after starting anti-IL-6 therapy</li> <li>Symptomatic management of organ toxicities</li> </ul>
<b>Grade 3</b> Fever with hypotension requiring a vasopressor with or without vasopressin and/or hypoxia requiring high-flow cannula, face mask, nonrebreather mask, or Venturi mask	Anti-IL-6 therapy as per Grade 2 if maximum dose not reached within 24-hour period	IV dexamethasone 10 mg every 6-12 hours depending on the product. If refractory, manage as grade 4	<ul style="list-style-type: none"> <li>Transfer to ICU, obtain echocardiogram, and perform hemodynamic monitoring</li> <li>Supplemental oxygen</li> <li>IV fluid bolus and vasopressors as needed</li> <li>Symptomatic management of organ toxicities</li> </ul>
<b>Grade 4</b> Fever with hypotension requiring multiple vasopressors (excluding vasopressin) and/or hypoxia requiring positive pressure (eg, continuous positive airway pressure [CPAP], bilevel positive airway pressure [BiPAP], intubation, mechanical ventilation)	Anti-IL-6 therapy as per Grade 2 if maximum dose not reached within 24-hour period	IV dexamethasone 10 mg every 6 hours. If refractory, consider 3 doses of IV methylprednisolone 1-2 g/day depending on the product. If refractory, consider dosing every 12 hours. Other lines of therapy may be considered.	<ul style="list-style-type: none"> <li>ICU care and hemodynamic monitoring</li> <li>Mechanical ventilation as needed</li> <li>IV fluid bolus and vasopressors as needed</li> <li>Symptomatic management of organ toxicities</li> </ul>