HEMATOLOGY-ONCOLOGY ASSOCIATES OF CNY

DEPARTMENT: Pharmacy	**POLICY DESCRIPTION: CRS Treatment Protocol**
PAGE: 1 of 1	**REPLACES POLICY DATED: n/a**
APPROVED: Nick Bouchard, PharmD	**RETIRED: n/a**
EFFECTIVE DATE: 11/21/23	**REFERENCE NUMBER:**

PURPOSE: Cytokine release syndrome (CRS) including life threatening or fatal reactions can occur in patients receiving bispecific antibodies. All patients receiving bispecifics should be evaluated for signs and symptoms of CRS.

SCOPE: All Clinical Staff

POLICY: CRS assessment and grading scale will be completed prior to initiation of bispecifics.

- If normal baseline CRS assessment, patients and caregivers should be educated on potential manifestations of CRS and monitor or and changes in status from baseline
    - Patients and caregivers will be instructed to take temperature and blood pressure 3 times/day during step up dosing phases and to call with any change in status
    - Staff will follow grading scale and management
- If abnormal baseline CRS assessment, clinical team to review prior to initiating treatment
- See below treatment chart for management of CRS in patients receiving bipecifics

CRS Grade	Supportive Care	Glucocorticoids	Anti-cytokine therapy
Grade 1: Temp ≥ 100.4	Support with antipyretics & encourage hydration • APAP 1000 mg every 8 hours PRN for elevated temperature • Monitor neurologic status • If grade 1, pt will check temp and BP every 2hrs while awake at home, call HOACNY for advisement if BP goes less that 10mm HG below baseline AND <90mm Hg systolic, new orthostatic symptoms, weakness, confusion, dizziness or new hypoxia (<90%)	Dexamethasone 12 mg PO may be given & repeated daily if grade 1 CRS continues • Consider for administration for refractory fever, must be reviewed with clinical team or covering MD prior to administration • Must be seen for clinical evaluation same day or next day	May consider tocilizumab for high risk patients (advanced age, high tumor burden, heart failure, pulmonary disease) or fever persisting > 48hr • Must be evaluated in clinic and reviewed with clinical team or covering MD prior to administration

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Grade 2: Temp ≥ 100.4 plus hypotension not requiring a vasopressor and/or hypoxia requiring low flow nasal cannula	Must be evaluated urgently in clinic or ED • APAP 1000 mg Q8H for elevated temperature • NS 1000 ml over 30-60 minutes (may bolus as needed for BP) • Monitor neurologic status • O2 to maintain O2 Sats	Dexamethasone 12 mg (take at home before coming to clinic or ED) • If hypotension continues despite tociluzumab and fluids then administer 10 mg IV every 12 hours	Administer tociluzumab 8 mg/kg (max 800 mg) • May repeat every 8 hours to a max of 3 doses in 24 hours and 4 doses total if not responsive to IV fluids or increasing supplemental oxygen
Grade 3: Temp ≥ 100.4 plus hypotension requiring one vasopressor and/or requiring high flow nasal cannula	Hospital admission (consider ICU) • Management per grade 2 • Hemodynamic monitoring, IV fluids, O2 support, vasopressor support	Dexamethasone 10 to 20 mg every 6 hours (or equivalent) & continue until event is grade 1 or less. Taper over 3 days once patient is grade 1	• As per grade 2 recommendations
Grade 4: Temp ≥ 100.4 plus hypotension requiring greater than one vasopressor and/or requiring positive pressure (CPAP, BiPAP, intubation, and mechanical ventilation)	Hospital admission (ICU) • Manage per grade 3 • Mechanical ventilation may be required	Dexamethasone 10 to 20 mg every 6 hours (or equivalent) & continue until event is grade 1 or less. Taper over 3 days once patient is grade 1 • Alternatively may administer methylprednisolone 1000 mg IV daily X 3 days	• As per grade 2 recommendations

** Atypical CRS presentations: (ie. Persistent CRS-like symptoms for >1 week despite appropriate supportive measures; febrile illness outside of the normal CRS timeframes, or with accompanying significant organ dysfunction) consider diagnostic work up to rule out alternative diagnosis such as infections or HLH/MAS