Management of Bispecific Antibody Treatment-related Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS)

All reactions grade 1 or above should be discussed with a Consultant Haematologist. For patients requiring ITU input: Registrar Bleep #702 Outreach Nurses Bleep #421/422 Neurology Team bleep		
Presenting Symptoms	**Initial management**	**Ongoing management**
Grade 1 and Grade 2 ICANS- Inform ICU and Consider Transfer		
Grade 1: ICE score 7–9 Awakens Spontaneously **Grade 2:** ICE score 3–6 Awakens to voice	• Interrupt bispecific infusion (if running) • Vigilant supportive care; aspiration precautions; IV hydration • Withhold oral intake of food, medicines and fluids and assess swallowing. Liaise with pharmacist for medicines that need converting from oral preparations. • Avoid sedating medications • Initiate regular neurological observations every 4 hourly • ICE score TDS- QDS • Initiate consultation with a neurologist • Consider non-sedating, anti-seizure medicinal products **(Levetiracetam IV 500mg BD, or up to 2000 mg BD)** • Consider **Dexamethasone IV 10 mg every 6 hours** until symptom resolution, then taper. • Consider **Tocilizumab**, if neurotoxicity is associated with CRS. • If ICANS persistent (>48 hours), consider **Anakinra**	• Early EEG ideally within 24 hours, repeated if condition deteriorates • Fundoscopic exam to assess for papilloedema • Consider MRI brain and CT brain; diagnostic LP including opening pressure; MRI spine if focal neurological deficits; CT brain can be performed if MRI brain not feasible • Consider **antifungal prophylaxis** in patients receiving steroids
Grade 3 ICANS (Medical Emergency) – Transfer to ICU		
ICE score 0–2 Awakens only to tactile stimulus Clinical seizures that resolve rapidly or non-convulsive seizures on EEG that resolve with intervention Focal cerebral oedema on imaging	• Supportive care, treatment and neurological work-up as indicated for Grade 1 and Grade 2 ICANS • For steroid treatment, consider **methylprednisolone 1mg/kg IV every 12 hours**. Taper when symptoms improve.	• Repeat MRI brain for refractory or worsening ICANS • For first occurrence of Grade 3 ICANS, bispecific may be re-introduced once symptoms have resolved according to protocol **(Discuss with Consultant Haematologist)** • For recurrent Grade 3 ICANS, discontinue bispecific therapy permanently

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Grade 4 ICANS (Medical Emergency) – Transfer to ICU		
ICE score 0 Un-rousable Prolonged (>5 minutes) or frequent seizures Motor weakness Diffuse cerebral oedema on imaging or symptoms of oedema	• Supportive care, treatment and neurological work-up as indicated for Grade 1 and Grade 2 ICANS • For steroid treatment, consider **methylprednisolone 1000 mg IV OD for 3 days.** Taper when symptoms improve. • May consider Intrathecal steroids or lymphodepleting drugs such as cyclophosphamide or other drugs if unresponsive to standard immunosuppressive therapies such as Anakinra • Consider hyperosmolar therapy with mannitol	• Consider repeat neuroimaging every 2-3 days for persistent ICANS • Permanently discontinue bispecific therapy

ICE Assessment Tool	
Question	**Points**
What year is it?	1
Which month is it?	1
Which city/town are we in?	1
Which hospital are we in?	1
Follow an instruction e.g. touch your nose	1
Name 3 objects (point to three different objects)	3
Write a sentence	1
Count backwards from 100 in 10's	1