

E. Dose adjustments for blinatumomab

Toxicity	Grade	Advise
Cytokine release syndrome(CRS), tumor lysis syndrome (for grading CRS see other table below)	Grade 3	Stop blinatumomab until resolved and restart with 9 µg/day. After 7 days increase dose to 28 µg/day (if toxicity recurs, stop treatment). Also tocilizumab 8 mg/kg over 1h is an option and can be repeated every 4-6h if needed and responsive.
	Grade 4	Permanently stop blinatumomab Also tocilizumab 8 mg/kg over 1h should be started and can be repeated every 4-6h if needed and responsive.
Neurological	Convulsions	Permanently stop blinatumomab
	Grade 3	Stop blinatumomab until resolved till grade 1, then restart with 9 µg/day. After 7 days increase dose to 28 µg/day (if toxicity recurs, stop treatment). Always repeat dexamethasone 20 mg before restart. Also tocilizumab 8 mg/kg over 1h is an option and can be repeated every 4-6h if needed and responsive. Permanently stop blinatumomab when toxicity occurs at 9 µg/day or when toxicity lasts longer than 7 days.
	Grade 4	Permanently stop blinatumomab Also tocilizumab 8 mg/kg over 1h should be started, and can be repeated every 4-6h if needed and responsive.
Liver enzymes	Grade 3	If clinically relevant, stop until grade 1, then restart with 9 µg/day. After 7 days increase dose to 28 µg/day (if toxicity recurs, stop treatment). Also tocilizumab 8 mg/kg over 1h is an option and can be repeated every 4-6h if needed and responsive.
	Grade 4	Permanently stop blinatumomab Also tocilizumab 8 mg/kg over 1h should be started, and can be repeated every 4-6h if needed and responsive.
Other clinically relevant side effects	Grade 3	If clinically relevant, stop until grade 1, then restart with 9 µg/day. After 7 days increase dose to 28 µg/day (if toxicity remits, stop treatment). Also tocilizumab 8 mg/kg over 1h is an option and can be repeated every 4-6h if needed and responsive.
	Grade 4	Permanently stop blinatumomab Also tocilizumab 8 mg/kg over 1h should be started, and can be repeated every 4-6h if needed and responsive.