APPENDIX D: RECOMMENDED PAIN AND SEDATION MEDICATION

Recommended Pain and Sedation Medication			
Name	**Purpose/Dose**	**Side Effects and Notes**	**Pharmacology**
Ketamine (Ketalar)	**Background pain:** • Use low dose 10–20mg (0.1–0.2mg/kg) OV/IO PRN. • Avoid oversedation **Breakthrough pain** in hemodynamically stable or unstable patient: IV/IO push: dose every 5 minutes until goal achieved or nystagmus occurs or RR < 10/min. • 10–20mg (or 0.1–0.2mg/kg) slow push **IM/IN**: every 15 minutes until goal achieved or nystagmus occurs • 40–60mg (or 0.5–0.75mg/kg) **Sedation**: IM sedation dose: • 250–400mg (or 4–5mg/kg) **IV/IO sedation** loading dose: • 1mg/kg IV push over 60 seconds Then **IV/IO drip** for ongoing sedation (load above dose, then drip): • Nonintubated: 1mg/kg/h • Intubated 1–2mg/kg/h	• Cataleptic-like state (dissociated from the surrounding environment) • Respiratory depression at higher doses (>1mg/kg), especially with fast administration IV/IO • Sialorrhea (hypersalivation) (can be problematic in an austere setting). • Releases endogenous catecholamines (epinephrine, norepinephrine), which maintain (or increase) blood pressure and heart rate. • *Consider adding midazolam to avoid emergence phenomenon (e.g., delusions, agitation, irrational/violent behavior) in adults with higher doses (>0.3mg/kg IV/IO)* • *Consider glycopyrrolate if significant sialorrhea* • *Consider antiemetic (e.g., odansatron) empirically (may vomit when recovering from sedation)* • *To avoid rapid respiratory depression, IV/IO administration should be slow: Push no faster than over 60 seconds* • No additional sedation or analgesic effects with doses >1.5mg/kg—only longer duration of effects. • There are no absolute contraindications for the use of ketamine; ketamine is safe for use in TBI and/or eye injury.	• NMDA antagonist • Time to onset: 30 seconds IV or 1–5 minutes IM • Duration of action: 10–15 minutes IV or 20–30 • minutes IM • S(+) ketamine has four times the affinity of R(−) ketamine for the NMDA receptor (S ketamine is common in non-US pharmacies) • In practice, S(+) ketamine (e.g., Esketamin, Ketanest) is twice as potent; use half the recommended dose in mg as racemic ("regular") ketamine • Mid-range dose (0.3–0.8mg/kg IV/IO) has the highest incidence of emergence reactions and dysphoria. AVOID THIS DOSE WHENEVER POSSIBLE. Treat with midazolam or other benzodiazepine (or rebolus ketamine with sedation dose) • Metabolized in the liver to an active metabolite, norketamine, which has a potency one-third that of ketamine • Renal excretion
Hydromorphone (Dilaudid)*	Breakthrough pain in hemodynamically stable patient: IV/IO/ IN: dose every 5 minutes until goal achieved or RR < 10/min. • Nonintubated: 0.25–2mg • Intubated: 1–4mg IM: not recommended	• Respiratory/cardiac/mental status depression • Nausea/vomiting • Pruritus (itching) • Constipation	• Onset <5 minutes • Duration of action 1–4 hours • Hepatic metabolism • Renal clearance (~10% as unchanged drug) • Caution in hepatic/renal impairment (reduce dose by 25%) • IM dose variable and delayed

Recommended Pain and Sedation Medication			
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Fentanyl* (Actiq)**	**Background pain:**
	Oral: only in NONINTUBATED, awake patients, per TCCC guidelines
	• OTFC 800µg
	  • Place lozenge between the cheek and the gum
	  • Do not chew the lozenge
	Breakthrough pain in hemodynamically stable patient:
	IV/IO/ IN: dose every 5 minutes until goal achieved or RR < 10/min.
	• Nonintubated: 25–50µg
	• Intubated: 50–200µg
	**IV push should be over 30–60 seconds, monitor for difficulty breathing (e.g., rigid chest syndrome)
	IM: not recommended
		• Respiratory/cardiac/mental status depression
		• Nausea/vomiting
		• Pruritus (itching)
		• Constipation
		
		Unique concerns:
		• Chest-wall muscle rigidity with rapid IV infusion (rare)
		• Bradycardia (rare)
		• QT-interval prolongation (rare)
		• Highly lipophilic
			• Rapid IV onset (<2 minutes)
			• Duration of action: 30–60 minutes
			• Hepatic metabolism
			• Renal clearance (~10% as unchanged drug)
			• Caution in hepatic/renal impairment (reduce dose by 25%)

Morphine**	**Breakthrough pain** in hemodynamically stable patient: IV/IO/ IN: dose every 5 minutes until goal achieved or RR < 10/min. • Nonintubated: 2.5–10mg • Intubated: 5–10mg IM: not preferred; can give 5–10mg IM if necessary	• Respiratory/cardiac/mental status depression • Nausea/vomiting • Pruritus (itching) • Constipation • Anticholinergic like effects, particularly urinary retention	• Onset <5 minutes. • Active metabolites. • **Duration of action: 1–4 hours** • 85% renal clearance; 7%–10% bile/stool clearance • Significantly reduced clearance in renal failure • IM dose variable and delayed
Percocet	**Background pain** Contains oxycodone (5mg) AND acetaminophen (325mg) **PO/enteral (may be crushed):** 1–2 tabs every 4–6 hours. • DO NOT exceed 4,000mg total acetaminophen per day.	• Respiratory/cardiac/mental status depression • Nausea/vomiting • Pruritus (itching) • Constipation • Hypersensitivity (rare) • Liver toxicity (acetaminophen) at high doses or if compromised liver function at baseline	• Oxycodone • Hepatic metabolism • Active metabolites • Urinary excretion • **Duration of effect: 4–6 hours** Acetaminophen (see below)
Midazolam (Versed)	**Sedation** (includes anxiety or agitation): **IV/IO**: dose every 5 minutes until goal achieved or RR < 10/min. • Nonintubated: 0.5–2mg • Intubated: 1–4mg **IM**: not recommended	• Respiratory/cardiac/mental status depression • Amnestic • Nausea/vomiting • Hypotension • Constipation • Personnel and equipment needed for standard respiratory resuscitation should be available during midazolam administration.	• Onset: 1–5 minutes • **Duration of effect: 1–4 hours** • Hepatic metabolism (active metabolites) • Renal excretion
Glycopyrrolate (Robinul)	Antisialogogue (i.e., to stop hypersalivation from ketamine) **SC/IM/IV/IO**: • 0.1–0.2mg every 4 hours	• Tachycardia/palpitations • Nausea/vomiting • Flushing • Urinary retention • Not to exceed 4 doses/d	• Anticholinergic • Rapid onset • Duration of effect: 2–6 hours • Renal excretion (85%, 80% unchanged)

Recommended Pain and Sedation Medication			
Name	**Purpose/Dose**	**Side Effects and Notes**	**Pharmacology**
Acetaminophen (Tylenol)	For mild to moderate pain: **IV/PO**: 500–1000mg every 6 hours	• Hypersensitivity (rare) • Increased serum transaminases • Nausea/vomiting (IV) • **Acute liver failure: limit daily dose of acetaminophen and acetaminophen-containing products (e.g., Percocet) to 4,000mg**	• Onset: <1 hour PO, 5–10 minutes IV • Duration of effect: 4–6 hours • Hepatic metabolism • Renal excretion
Odansatron (Zofran)	For nausea and vomiting: • 4mg ODT/IV/IO/IM, every 4–8 hours PRN • Can repeat once at 15 minutes if nausea and vomiting are not improved	• Maximum 8mg in any 8-hour interval • QT-interval prolongation (rare) • Constipation • Dizziness/headache	• Selective serotonin 5-HT3 receptor antagonist • Hepatic metabolism • Excreted in the urine and feces
Flumazenil (Romazicon)	For reversal of benzodiazepine overdose (e.g., midazolam) • 0.2mg IV over 15 seconds	• DO NOT USE IN CHRONIC BENZODIAZEPINE USERS! (May cause seizures) • Use only to reverse benzodiazepines YOU have given the patient.	• Specific benzodiazepine receptor antagonist • **Resedation may occur 20–60 minutes after initial dose, may require redosing** • Hepatic metabolism • Renal excretion
Naloxone (Narcan)	For reversal of opioid overdose • 0.4–2mg IV/IM/SC/IN; repeat every 2–3 minutes PRN; not to exceed 10mg (0.01mg/kg)	• Withdrawal reaction precipitated • Abrupt reversal of opioid depression may result in nausea, vomiting, sweating, tachycardia, increased blood pressure, and tremulousness • **Short duration of action relative to longer-acting opioids (e.g., morphine); may need to redose before opioid effect has worn off**	• Competitive opioid antagonist • Onset: 2 minutes IV; 2–5 minutes IM/SC • **Duration of effect: 30–60 minutes, may require redosing** • Hepatic metabolism • Renal excretion
Diphenhydramine (Benadryl)	For itching or allergic reaction (may also cause drowsiness) • 25–50mg IV/IO/PO every 4–6 hours PRN (maximum: 400mg daily)	• May potentiate the effect of other sedative agents • May reduce seizure threshold • May cause paradoxical CNS stimulation (e.g., agitation or anxiety) and/or psychosis • Mild anticholinergic and may cause dry secretions (dry mouth, constipation, urinary retention), blurred vision, flushing, fever, tachycardia • May reduce nausea	• Histamine receptor (H1) antagonist • Hepatic metabolism • Renal excretion

CNS, central nervous system; IM, intramuscular; IN, intranasal; IO, interosseous; IV, intravenous; NMDA, N-methyl-d-aspartate; ODT, oral disintegrating tablet; OTFC, oral transmucosal fentanyl citrate; PO, *per os* (by mouth); PRN, as needed; RR, respiratory rate; SC, subcutaneous; TBI, traumatic brain injury; TCCC, Tactical Combat Casualty Care.

***Hydromorphone is selected as the opioid medication of choice in the PFC setting for the following reasons:**

1. Long acting
2. Lower likelihood of accumulating in the setting of organ dysfunction (particularly renal injury/insufficiency) and, therefore, less likely to cause respiratory depression or hypotension
3. Smaller doses produce greater effect; thus, less medication needs to be carried for longer duration of treatment
4. Less histamine activation, less pruritus, better tolerated

****Morphine**

1. Long acting
2. Can give IM if necessary, but not preferred
3. More side-effects compared with hydromorphone (e.g., higher rate of respiratory depression, hypotension, and pruritus)

*****Fentanyl**

1. Short acting
2. Faster onset
3. Greatest risk of respiratory depression; highly recommend monitoring SpO2 (oxygen saturation)
4. Be prepared to support breathing if necessary
5. Reserved for severe pain or procedures