Table S1. Red flags and escalation criteria for peripartum care in Wolfram syndrome type 1 (WS1).

Domain	Red flags (examples)	Immediate actions (per local pathway)	Escalation / who to involve	Key refs
Pregestational diabetes mellitus	• Recurrent hypoglycemia (<70 mg/dL; <3.9 mmol/L) or any severe episode requiring assistance • Persistent hyperglycemia (>180 mg/dL; >10 mmol/L for >2 h) • Positive ketones, vomiting, abdominal pain, Kussmaul breathing, or clinical concern for DKA	• Confirm CGM with capillary/venous glucose as per protocol • Treat hypoglycemia promptly (oral/IV glucose) and reassess every 15 min until resolved • Review insulin/dextrose regimen; consider ketone testing and acid–base evaluation if indicated • Avoid prolonged fasting; ensure postpartum dose reassessment early	Endocrinology + Anesthesiology/Obstetrics; consider ICU/Medicine if DKA suspected or unstable	(20,22,23)
CDI / fluids & electrolytes	• Rapidly rising or falling Na; Na >145 mmol/L or symptomatic hypernatremia • Na <130 mmol/L or symptomatic hyponatremia • Sustained polyuria (e.g., >300 mL/h or >2 mL/kg/h) with thirst, hypotension, tachycardia, or signs of hypovolemia • New confusion, seizures, or severe headache	• Strict intake/output; hourly urine output in acute phase • Check serum Na/osmolality urgently and repeat per protocol • Review desmopressin timing/dose and fluid strategy; avoid inappropriate free-water administration • Correct dysnatremia according to endocrine/obstetric pathways	Endocrinology + Anesthesiology; ICU if seizures, severe symptoms, or unstable Na	(13)
Hemodynamic instability (labor/neuraxial)	• Post-neuraxial hypotension (SBP <90 mmHg or >20% fall from baseline) especially with symptoms or fetal concerns • Refractory hypotension despite initial measures • Syncope/near-	• Left uterine displacement; optimize positioning • Fluid co-load and vasopressor treatment per protocol • Evaluate for alternative causes (bleeding, high spinal block, sepsis) • Continuous fetal	Anesthesiology + Obstetrics; ICU if shock or refractory instability	(16,24)

	syncope or suspected autonomic instability	monitoring when applicable		
Respiratory compromise / aspiration risk	• SpO_2 <94% despite supplemental oxygen • Abnormal capnography or rising CO_2 when monitored • Inability to clear secretions, repeated choking/aspiration signs • Reduced consciousness after sedatives/analgesics	• Escalate oxygen delivery and airway support as needed; consider noninvasive support per pathway • Minimize additional sedatives; suction/positioning • If general anesthesia is required, use aspiration precautions and awake extubation when safe	Anesthesiology; ICU/Respiratory support team if persistent compromise	(24)
Airway (if GA required)	• Difficult mask ventilation or failed intubation • Cannot intubate/cannot oxygenate scenario	• Activate institutional difficult-airway algorithm early • Use video laryngoscopy/supraglottic devices; call for help • Prepare front-of-neck access per institutional pathway	Senior anesthesiologist + ICU; ENT if required	(24)
Urology / UTI / sepsis	• Fever ≥38 °C or systemic symptoms • Flank pain, rigors, or suspected pyelonephritis • Obstructed catheter/no urine output; worsening dysuria/urinary symptoms	• Check catheter patency; ensure aseptic technique • Urinalysis/culture if symptomatic; start antibiotics per obstetric/UTI pathway • Maintain strict urine output monitoring	Obstetrics + Urology as needed; Infectious Diseases/ICU if sepsis suspected	(7,8)
Bleeding / anemia	• Postpartum hemorrhage per obstetric criteria • Ongoing bleeding with tachycardia/hypotension • Symptomatic anemia or clinically significant Hb drop per local thresholds	• Activate PPH protocol; uterotonics and surgical hemostasis as indicated • Type and screen/crossmatch; transfuse per institutional thresholds • IV iron therapy when appropriate	Obstetrics + Anesthesiology; blood bank; ICU if massive transfusion	(24)
VTE / thromboembolism	• Unilateral leg swelling/pain; sudden dyspnea; chest pain; hemoptysis • Persistent unexplained	• Urgent assessment and diagnostic imaging per pregnancy pathway • Ensure mechanical prophylaxis; initiate anticoagulation if	Obstetrics + Medicine/Hematology; ICU if suspected PE with instability	(18,21)

	tachycardia or hypoxemia • High-risk features (reduced mobility, prior VTE) with new symptoms	clinically indicated per protocol		
Cochlear implant / electrosurgery	• Need for extensive monopolar electrosurgery • Suspected device malfunction or unexpected loss of function • Communication barrier impacting immediate safety	• Prefer bipolar electrosurgery when feasible • If monopolar electrosurgery is required, follow manufacturer and institutional precautions (grounding pad away from implant; minimize current path near **the head and neck**) • Document device status; ensure communication support	Operating room team + Anesthesiology; ENT if malfunction suspected	(17)
Communication and anxiety (deafblindness)	• Escalating anxiety/panic interfering with cooperation • Inability to confirm understanding in urgent decisions	• Use pre-agreed communication method; involve partner/interpreter • Provide anticipatory guidance and reassurance • Consider low-dose anxiolysis with continuous respiratory monitoring when appropriate	Anesthesiology + Obstetrics; mental health support if needed	(9,10,12)

Note: Thresholds are intended to support situational awareness and escalation; clinical decisions should follow institutional obstetric/endocrine/anesthesia pathways and be individualized to maternal–fetal status.
Abbreviations: CDI, central diabetes insipidus; CGM, continuous glucose monitoring; CO_2, carbon dioxide; DKA, diabetic ketoacidosis; ENT, ear, nose, and throat; Hb, hemoglobin; ICU, intensive care unit; IV, intravenous; Na, serum sodium; PE, pulmonary embolism; PPH, postpartum hemorrhage; SBP, systolic blood pressure; SpO_2, peripheral oxygen saturation; UTI, urinary tract infection; VTE, venous thromboembolism.