KCNT1-Related Epilepsy

Treatment Landscape and Clinical Decision Context

Educational Overview for Clinicians

Provided by the KCNT1 Epilepsy Foundation
Educational resource only — not clinical guidelines

Purpose of This Document

This document provides an educational overview of the treatment landscape and clinical decision context for patients with KCNT1-related epilepsy.

KCNT1-related epilepsies are rare, heterogeneous, and frequently drug-resistant. Many clinicians encounter only one or two affected patients in their careers. Families, by contrast, often develop deep longitudinal expertise and play a critical role in care.

This resource is intended to support clinical understanding, anticipate commonly encountered challenges, and facilitate effective clinician–caregiver communication. It does **not** replace clinical judgment or institutional protocols.

KCNT1 in Clinical Context

KCNT1 encodes a sodium-activated potassium channel expressed primarily in the central nervous system. Pathogenic variants, most commonly gain-of-function, are associated with a spectrum of developmental and epileptic encephalopathies (DEE).

Reported phenotypes include:

- epilepsy of infancy with migrating focal seizures (EIMFS) (May begin with infantile spasm syndrome)
- early-onset developmental and epileptic encephalopathies
- autosomal dominant sleep-related hypermotor epilepsy (ADSHE), now referred to as sleep-related hypermotor epilepsy (SHE)

Clinical severity, seizure types, comorbidities, and trajectories vary widely, including among individuals with the same variant.

Core Treatment Realities in KCNT1

Several features consistently shape clinical decision-making:

- **Pharmacoresistance is common.** Durable seizure control with a single medication is uncommon.
- **Polytherapy is typical.** Mixed seizure types often require layered approaches.
- **Seizure patterns may evolve.** Semiology and response may change with development, illness, or puberty.
- **Caregiver-generated data is central.** Longitudinal observation often provides the most actionable context.

Medications Commonly Encountered in KCNT1 Care

Children with KCNT1-related epilepsy are frequently exposed to multiple anti-seizure medications (ASMs) over time. Clinicians often review extensive medication histories with partial or transient benefit.

The medications below reflect **agents commonly reported in published case series, registries, and caregiver reports**. Inclusion does **not** imply recommendation, efficacy, or safety.

Maintenance ASMs (variable response)

Phenobarbital; levetiracetam; valproate; topiramate; zonisamide; clobazam

Clinical context:

- Polytherapy is common
- Sedation, behavioral effects, appetite changes, and fatigue are often dose-limiting
- Medication adjustments occur frequently over time

Seizure-type-specific context

Infantile spasms: vigabatrin; prednisolone or ACTH
Evidence in KCNT1 does not clearly favor one steroid approach; access varies by region.

SHE / ADSHE phenotype: carbamazepine or oxcarbazepine may be encountered
Caution is advised, as seizure aggravation has been reported outside this phenotype.

Rescue and emergency medications

- Diazepam nasal spray
- Midazolam nasal spray
- Diazepam rectal gel

- Lorazepam (IV; sometimes oral inpatient)
- Midazolam (IV)

Caregivers often maintain detailed seizure action plans and differentiate clearly between maintenance and rescue therapies.

Presence on this list reflects reported use, not endorsement.

Adjunctive and Non-Pharmacologic Therapies

Ketogenic or modified Atkins diet, pharmaceutical cannabidiol, and neuromodulation (e.g., VNS) may be encountered, typically layered onto medication regimens with variable benefit.

Gastrointestinal Symptoms and Neurogenic Distress

Many individuals with KCNT1 experience significant GI symptoms and episodes of distress not fully explained by seizures alone. These may include feeding intolerance, reflux, constipation or diarrhea, and episodic abdominal discomfort.

Caregivers frequently describe prolonged crying or apparent pain — sometimes termed *neurogenic crying* or *neurogenic distress*. These terms are descriptive rather than diagnostic.

Proposed mechanisms include altered sensory processing, autonomic dysregulation, central pain pathways, GI–brain interaction, or medication effects. Systematic characterization remains limited.

Clinicians are encouraged to consider non-seizure contributors to distress and reassess symptoms longitudinally, particularly around medication changes or illness.

Autonomic Manifestations, Apnea, and Cyanosis

Autonomic manifestations have been described in KCNT1-associated epilepsies, particularly EIMFS, including apnea and perioral cyanosis.

Caregivers may report breathing pauses, bradycardia alerts, or abrupt color changes. These events may occur during seizures, peri-ictally, or as recurrent episodes where seizures are not always clinically apparent.

Terminology varies, and formal autonomic testing is not routinely reported in the literature for KCNT1. Regardless of labeling, these events can significantly impact safety and emergency presentations.

Systemic-to-Pulmonary Collateral Arteries (SPCAs)

A subset of individuals with KCNT1 have been reported to develop abnormal systemic-to-pulmonary collateral arteries (sometimes termed MAPCAs).

Bleeding is often the first recognized sign and may present as hemoptysis, unexplained anemia, respiratory distress, or acute decompensation.

SPCAs may be missed on routine imaging. **CT angiography** is often the most reliable modality for identification, particularly when prior imaging has focused on cardiac structure rather than collateral vasculature.

Caregiver history and prior records may be critical for recognition.

Longitudinal Care and Caregiver Expertise

Baseline function is dynamic. Caregivers often identify subtle changes before they are captured on EEG or imaging.

Clinicians are encouraged to actively solicit caregiver observations, particularly during acute care, medication changes, or unexplained deterioration.

Trial Readiness and Emerging Therapies

Targeted therapies for KCNT1 are in development, including small-molecule inhibitors and antisense approaches. Trial eligibility often depends on longitudinal documentation, seizure tracking, and baseline clarity — areas where caregiver-maintained data is essential.

Disclaimer