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SPECIAL ARTICLE

# Care process for severe epileptic seizures in the Community of Madrid: The Seizures Code

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**KEYWORDS**
Urgent epileptic seizures;
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**Abstract**
*Introduction:* The Urgent Epileptic Seizures Care Process (UESP), also known as the Seizure Code, is a care process implemented in the Community of Madrid with the objective of standardizing and optimizing the urgent management of epileptic seizures (ESs) in pediatric and adult patients.
*Material and methods:* The aim of this care process, which is based on the recommendations of the national consensus guideline in Spain and international guidelines, is to standardize the diagnosis, treatment, and follow-up of severe ESs across all levels of care. It was developed through a multidisciplinary collaborative effort involving professionals in emergency medicine, intensive care, neurophysiology, pediatric neurology, and primary care, and was structured into twelve sub-processes reviewed and endorsed by Spanish scientific societies.
*Results:* The Seizures Code establishes operational criteria for activation and defines specific algorithms for management in different clinical settings. It includes intervention times, therapeutic sequences with early and systematic use of benzodiazepines and early combination

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therapy with antiseizure medications, as well as strategies for coordination between care levels. It also promotes early use of electroencephalography (EEG), ongoing training for health care professionals and families, and a standardized registry of care activity.
*Conclusions:* The Seizure Code is the first comprehensive model for urgent management of severe ESs implemented in a Spanish autonomous community. Its design promotes an early, homogeneous, and evidence-based response, with particular impact on the pediatric population. It enhances interhospital coordination and therapeutic adherence and is a dynamic tool that supports continuous evaluation and improvement of care quality in pediatric neurology.
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**PALABRAS CLAVE**
Crisis epiléptica urgente;
Estatus epiléptico;
Tratamiento precoz;
Código Crisis;
Epilepsia pediátrica

**Proceso asistencial «Crisis epilépticas graves en la Comunidad de Madrid: Código Crisis»**

**Resumen**
*Introducción:* El Proceso Asistencial ''Crisis Epilépticas Graves: Código Crisis'' es una iniciativa implementada en la Comunidad de Madrid con el objetivo de estandarizar y optimizar el tratamiento urgente de las crisis epilépticas (CE) en pacientes pediátricos y adultos.
*Material y métodos:* Basado en las recomendaciones del consenso nacional y en guías internacionales, este proceso busca homogeneizar el diagnóstico, tratamiento y seguimiento de las CE graves en todos los niveles asistenciales. Se desarrolló mediante un trabajo colaborativo multidisciplinar que incluyó profesionales de urgencias, cuidados intensivos, neurofisiología, neuropediatría y atención primaria, estructurado en doce subprocesos asistenciales revisados y avalados por sociedades científicas nacionales.
*Resultados:* El Código Crisis establece criterios operativos para la activación del proceso y define algoritmos específicos para el manejo en los distintos escenarios asistenciales. Incluye tiempos de actuación, secuencias terapéuticas con uso precoz y sistematizado de benzodiacepinas y biterapia con fármacos anticrisis, así como estrategias de coordinación entre niveles asistenciales. Asimismo, promueve el empleo temprano del electroencefalograma (EEG), la formación continuada de profesionales y familiares, y el registro sistemático de la actividad asistencial.
*Conclusiones:* El Código Crisis representa el primer modelo integral de atención urgente a las CE graves implantado en una comunidad autónoma española. Su diseño favorece una actuación precoz, homogénea y basada en la evidencia, con especial impacto en la población pediátrica. Mejora la coordinación intercentros, la adherencia terapéutica y constituye una herramienta dinámica orientada a la evaluación continua y a la mejora de la calidad asistencial en neuropediatría.
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## Introduction and rationale for a pediatric Seizure Code

Epilepsy is the most common chronic neurologic disorder in childhood, with a prevalence of 0.5%–1%.[1,2] Epileptic seizures are a common reason for emergency department visits, accounting for up to 1% of all visits and between 20% and 40% of cases classified in the highest-priority triage categories.[3,4]

Convulsive status epilepticus (SE) is one of the most clinically significant pediatric neurologic emergencies, with an annual incidence of 17–23 cases per 100,000 children, and occurring in 10%–20% of patients with epilepsy.[5] It is defined as a tonic, clonic, or tonic-clonic seizure, or two or more such seizures between which consciousness was not regained, lasting for at least 30 min, and it is a condition associated with a high morbidity and mortality that therefore requires immediate intervention.

The recent evidence underscores the need to optimize the response to epileptic seizures, in and out of hospital, to prevent its progression to SE. In children without a prior history of epilepsy, seizures may be a warning sign of severe diseases requiring early diagnosis and treatment. In those with a known history of epilepsy, urgent intervention is indicated if there are changes in the characteristics, duration or frequency of seizures, adverse events of medication, or poorly controlled seizures.[6]

The ''time is brain'' principle is particularly critical in the pediatric population, Prolonged duration of seizures is associated to an increased risk of brain damage, develop-

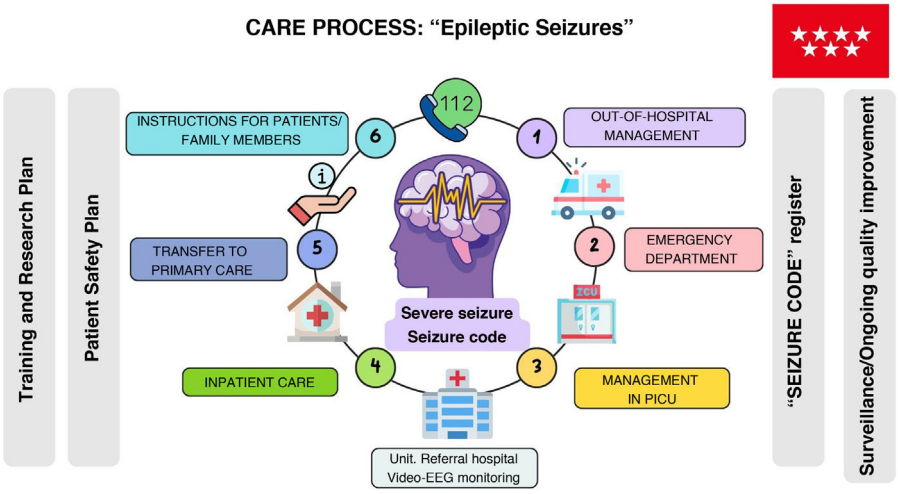


**Figure 1** Urgent Epileptic Seizure care process.

mental disorders and death.[7–9] In adults, delayed treatment increases the risk of secondary epileptogenesis, as well as health care costs[10,11]; in children, the available evidence, although more limited, shows poorer outcomes and more frequent recurrence in association with delayed treatment.[12,13]

Despite this, there is still considerable variation among centers in terms of treatment protocols, the time to administration of rescue medication, and the criteria for referral to specialists. Less than 30% of children with SE receive benzodiazepines (BZD) at the appropriate time and dosage.[13] A study conducted in Norway found a mean delay of 13 min to the administration of the first rescue drug (BZD) and a mean delay of 83 min to administration of second-line treatment in patients with refractory SE,[12] in excess to the intervals recommended by international guidelines.

Current guidelines advocate for stepwise treatment algorithms with well-defined schedules to facilitate standardization, reduce errors, and improve coordination across levels of care.[14–17]

The project presented in this article was developed in the framework of the development of the Severe Epileptic Seizures: Seizure Code care process, an initiative of the Community of Madrid that seeks to standardize the management of severe seizures in children and adults to guarantee an early, coordinated and evidence-based response.[18]

## Development and validation of the care process

The lack of solid evidence and the need to standardize guidelines for the emergency treatment of status epilepticus motivated the Sociedad Española de Epilepsia (SEEP, Spanish Epilepsy Society) to undertake a three-year collaborative project that culminated in 2020 with a consensus document on the management of adult and pediatric SE in the emergency department.[19] In parallel, the World Health Organization published the Global Intersectoral Action Plan on Epilepsy and Other Neurological Disorders in 2022, which outlines strategic objectives and recommendations for early diagnosis, effective treatment, and comprehensive care (https://www.who.int/publications/i/item/9789240076624).

In this context, the Community of Madrid developed the ''Severe Epileptic Seizures: Seizure Code'' care process to establish a protocol for the comprehensive care of patients with severe seizures from initial management out of hospital to post-discharge follow-up. Its main objectives are to structure emergency care, reduce delays in treatment, standardize protocols across levels of care, optimize resources, and prevent progression to SE.

The document was developed with participation of 94 professionals from the medical emergency system of the Community of Madrid and the City of Madrid (SUMMA-112/SAMUR), emergency departments, pediatric intensive care units, pediatric neurology and primary care. The final document was structured into 12 subprocesses, including the following (Fig. 1):

- Operational definitions and clinical criteria;
- Sequential management algorithms;
- Specific protocols for each stage of care (prehospital, emergency department, intensive care, inpatient care, and follow-up);
- High-risk points for patient safety and monitoring;
- Care transition strategies to ensure continuity of care.

The text was reviewed and endorsed by the SEEP, the Epilepsy Group of the SEN, the Neuro-Stroke Group of the Sociedad Española de Urgencias y Emergencias (Spanish Society of Urgent and Emergency Medicine), and the Sociedad Española de Neuropediatría (Spanish Society of Pediatric Neurology), with additional feedback from the Federación Española de Epilepsia (Spanish Epilepsy Federation), which represented the perspective of patients.

Its implementation began in November 2023 after all the teams involved in the code had completed training. The ''Severe Epileptic Seizures: Seizure Code'' care process is the first international comprehensive model for the management of severe epileptic seizures, covering everything from pre-hospital care to monitoring and post-discharge follow-up.

**Table 1** Characteristics of a referral hospital for the management of severe epileptic seizures.

| |
|---|
| *Health care resources* |
| Pediatric neurology unit |
| Pediatric intensive care unit |
| Intermediate care unit |
| Availability of urgent CT scans |
| On-call neurosurgeon |
| Capability to deliver all available treatment options: |
| 1 Antiseizure medications |
| 2 Immunomodulators |
| [3]Dietary therapy |
| Capability to perform and interpret video-EEG within the first 24 h |
| *Material resources* |
| Video-EEG |
| CT and CT angiography |
| Brain MRI |
| Performance of specific tests |
| Emergency laboratory services |

Abbreviations: CT, computed tomography; EEG, electroencephalogram; MRI, magnetic resonance imaging.

## Implementation of the care process: specific actions

To achieve the objectives set for the Seizure Code care pathway, a series of key actions were defined that form the backbone of the care model and enable a consistent, coordinated response based on the best available evidence:

## Operational definition and risk stratification of epileptic Seizures: identification of patients with severe epileptic Seizures and activation of the Seizure Code (SC)

The care process is called ''Urgent Epileptic Seizures Code'' rather than ''Status Epilepticus Code'' to emphasize its preventive intent: its main objective is the early identification and treatment of seizures before they progress to SE.

One of the key elements in the development of the SC was the redefinition of urgent epileptic seizures and their stratification into three risk levels to allow adaptation of the medical emergency response to the severity of the seizures and guide clinical decision-making:

1 *Urgent seizures:* requiring immediate evaluation by emergency medical services, but not transport to a hospital.
2 *Potentially severe seizures:* requiring urgent transport to a referral hospital due to the risk of complications or progression to SE (Table 1).
3 *Severe seizures:* SE or epileptic seizures with a high risk of progression to SE, requiring immediate activation of the SC.

Early detection of severe seizures makes it possible to activate a care pathway that prioritizes patients for treatment in specialized units and prevents progression to refractory forms or those with a poorer prognosis.

## Activation of the Seizure Code and coordination of care

Early intervention in the prehospital phase by both caregivers and emergency services is one of the innovative aspects of this care process. The prehospital care subprocess involves activating the SC in various scenarios, integrating primary care, prehospital emergency care services, and regional and referral hospitals.

Activation is based on defined clinical criteria, and care coordination starts by alerting the physician in charge of the SC (neurologist or pediatric intensivist). Care delivery is prioritized in proportion to the risk to avoid both unnecessary medicalization and delays in severe cases.

## Criteria for activating the Seizure Code

- Generalized or focal SE, with or without altered level of consciousness, excluding typical febrile seizures controlled with a single dose of BZD.
- Suspected nonconvulsive status epilepticus: decreased level of consciousness, confusion with no identifiable cause, or postictal state with altered level of consciousness lasting longer than 1 h.
- New-onset postictal focal deficit, after ruling out a vascular cause. If suspected, the STROKE Code should be activated rather than the SC.
- Seizure cluster: two or more focal or generalized tonic-clonic seizures with altered level of consciousness in less than 12 h or an at least threefold increase in seizure frequency, not meeting the criteria for SE.
- First epileptic seizure in an infant aged less than 1 month.

Patients managed by a level 3 palliative care unit are excluded.

The code prioritizes transport of the patient in an advanced life support ambulance to the assigned referral hospital.

Early standardized treatment of severe epileptic seizures

The care process includes standardized treatment protocols for both out-of-hospital (Figs. 2 and 3) and hospital (Figs. 4 and 5) settings with the aim of ensuring rapid, consistent, and evidence-based care.

## First-line treatment: benzodiazepines

Benzodiazepines are the first-line treatment for SE due to their activity as GABA-A receptor modulators (level A evidence). In the hospital setting, intravenous administration is recommended, preferably of midazolam or diazepam.[20–23]

When intravenous delivery is not feasible, the most accessible route is used: oral or intramuscular midazolam, or rectal diazepam—which have been found to be as effective as intravenous administration.[24–28]

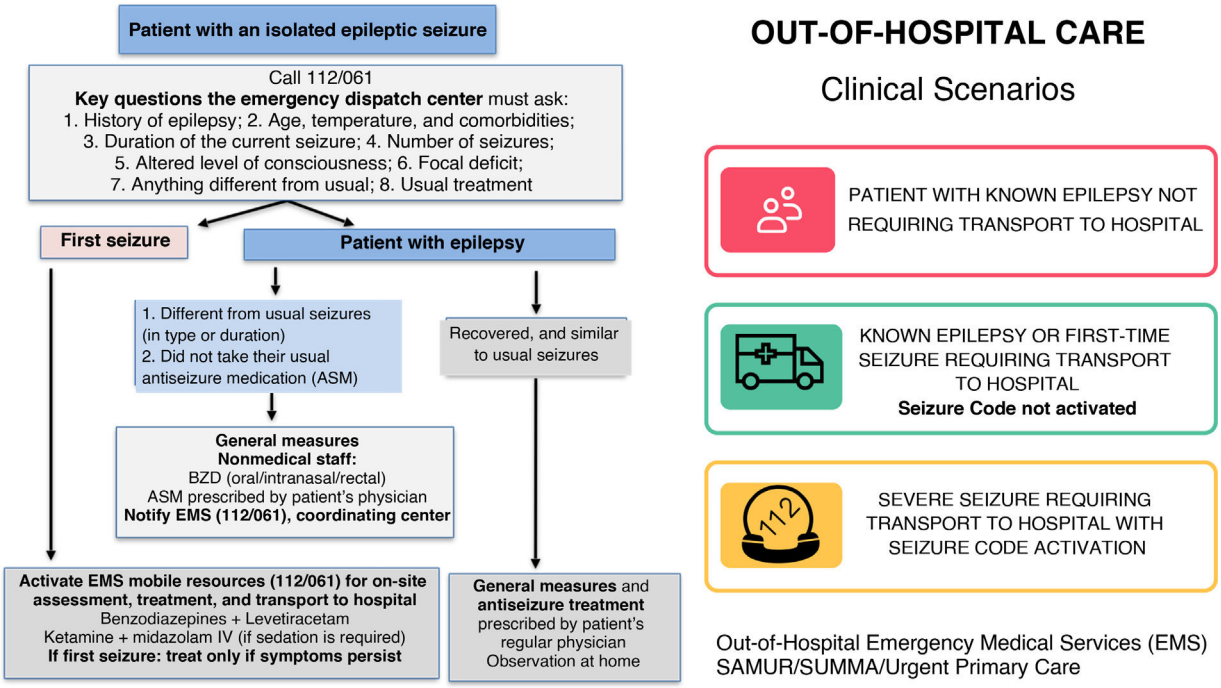


**Figure 2** Clinical scenarios in the out-of-hospital setting.

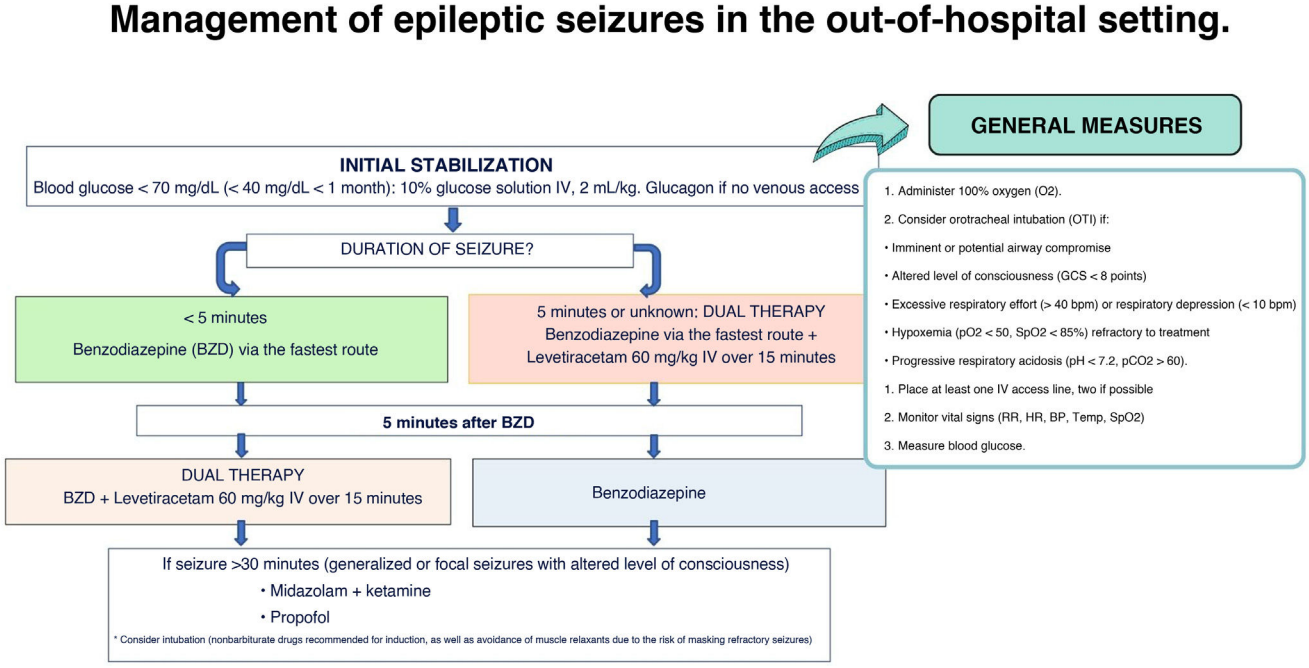


**Figure 3** Management of epileptic seizures in the out-of-hospital setting.

## Early dual therapy: rationale and implementation

The loss of efficacy of benzodiazepines (BZDs) in advanced stages of epilepsy is associated with GABA-A receptor internalization, which justifies the early initiation of dual therapy combining a BZD with a non-BZD antiseizure medication (ASM).[20,29–31]

Contrary to other protocols that reserve addition of a second ASM for later stages, the SC pioneers early rational polytherapy through the combined administration of an ASM with the second dose of BZD in the hospital setting.

In the out-of-hospital setting, where stringent timing proves challenging the concurrent administration of a non-BZD ASM is allowed from the outset or if the seizures last longer than 5 min.

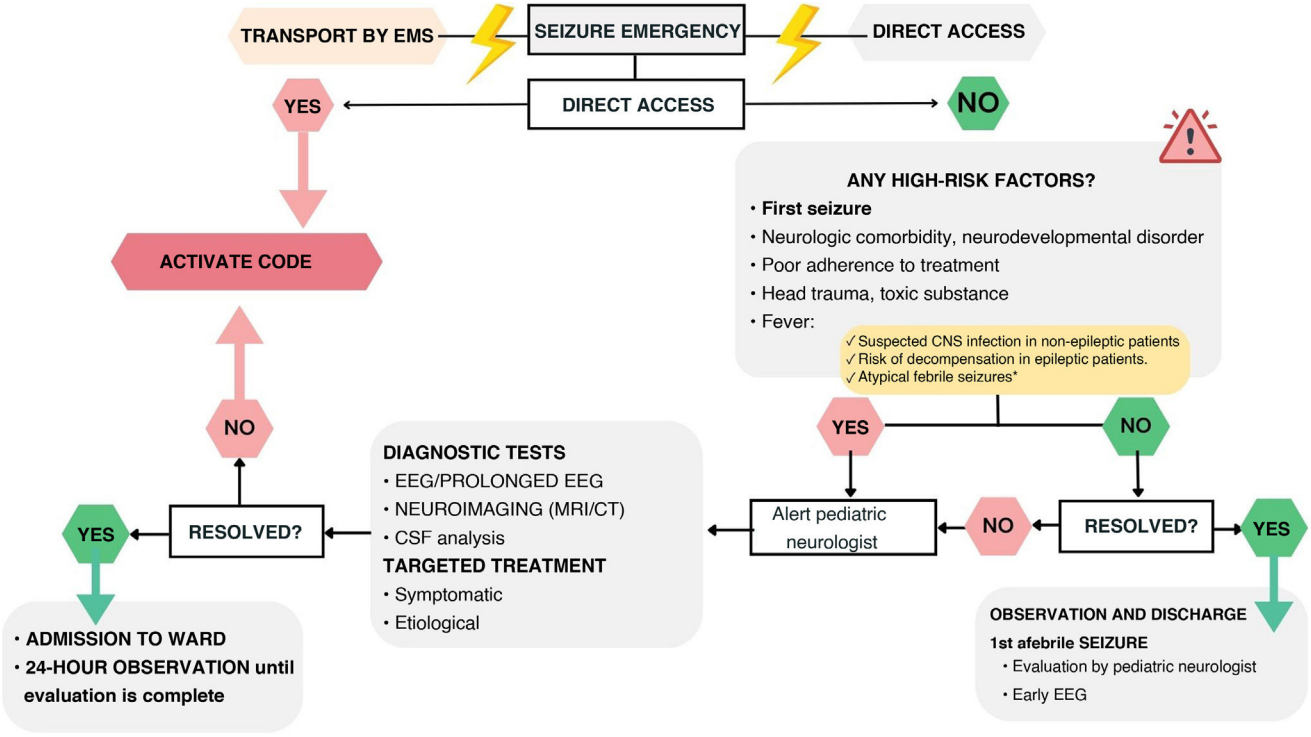


**Figure 4** Management of epileptic seizures in the hospital setting.

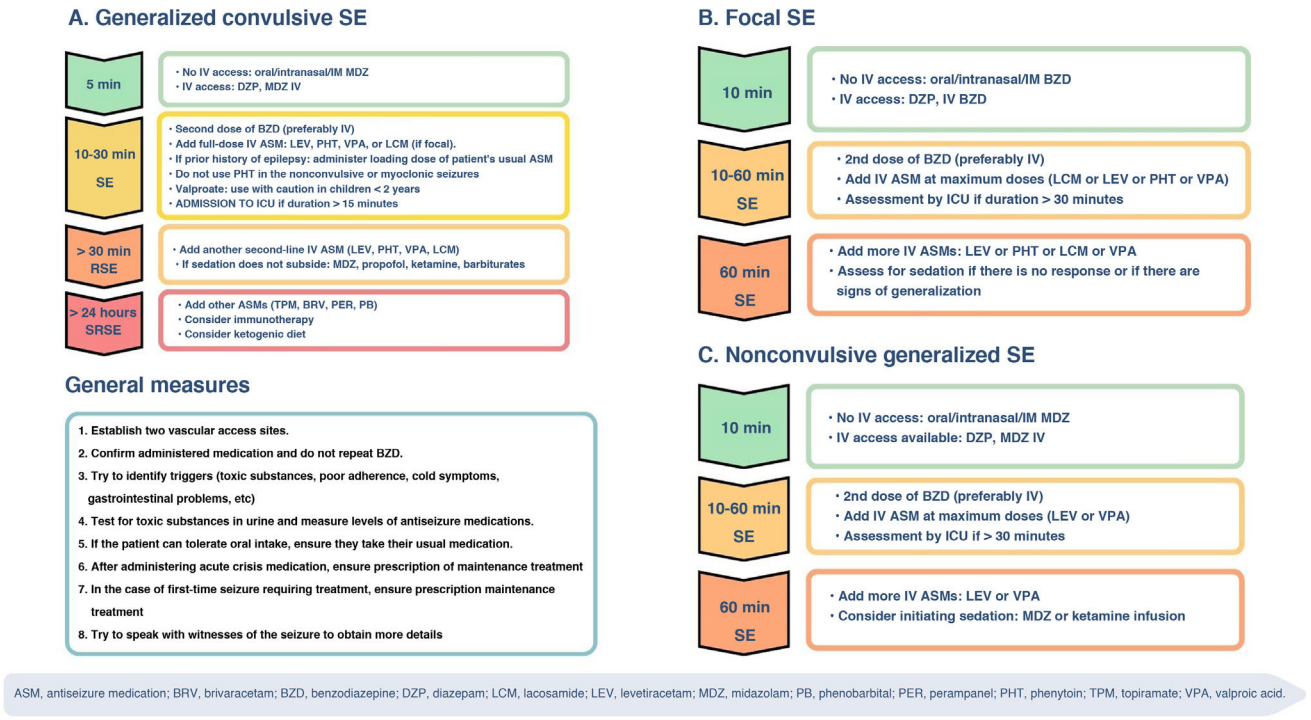


**Figure 5** Algorithms for the hospital-based treatment of status epilepticus (SE).

## Second- and third-line treatment

If the patient does not respond to BZDs, administration of a second-line ASM is recommended, with selecting the drug according to the type of seizure and the profile of the patient. The options most supported by the evidence are: levetiracetam (40–60 mg/kg); valproic acid (40 mg/kg) and/or phenytoin (20 mg/kg) and lacosamide (5 mg/kg) for

**Table 2** Dosage of antiseizure medications used in patients with acute epileptic seizures.

| | Route | Dose | Complications |
|---|---|---|---|
| *First-line* | | | |
| Diazepam (DZP) | IV<br>IM<br>Rectal | 0.3 mg/kg; max 5 mg (<50 kg), 10 mg (>50 kg)<br><15 kg: 5 mg; >15 kg: 10 mg | Respiratory depression |
| Midazolam (MDZ) | IM<br><br>IM, IV | 0.3 mg/kg<br>0.2 mg/kg<br>Max 10 mg | Respiratory depression |
| MDZ oral solution | PO | 0.5 mg/kg (max 10 mg)<br>3 months–1 year: 2.5 mg<br>1–5 years: 5 mg<br>5–10 years: 7.5 mg<br>10–18 years: 10 mg | Respiratory depression |
| *Second-line* | Most commonly used antiseizure medications | | |
| Phenytoin (PHT) | IV | 18–20 mg/kg, max 1 g/20 min | Extreme bradycardia<br>Hypotension<br>Arterial ischemia due to extravasation |
| Phenobarbital (PB) | IV | 15–20 mg/kg/20 min | Excessive sedation<br>Respiratory depression |
| Valproate (VPA) | IV | 20–40 mg/kg<br>Max 1500 mg<br>Infusion 1–3 mg/kg/h | Hyperammonemic encephalopathy: avoid in children younger than 2 years of age and those with mitochondrial disease |
| Levetiracetam (LEV) | IV<br>PO | 40–60 mg/kg (max 4500 mg/kg) | |
| Lacosamide (LCM) | IV<br>PO | 5–10 mg/kg<br>Max 200–400 mg | ECG monitoring (bradycardia, second- and third-degree heart block) |
| Brivaracetam (BRV) | IV<br>PO | 3–5 mg/kg<br>Max 100–200 mg | Excessive somnolence |
| Perampanel (PER) | Oral/NG-tube | 20 kg: 2–4 mg (max 6 mg)<br>20–30 kg: 4–6 (max 8 mg)<br>>30 kg: 4–8 (max 12 mg) | |
| Topiramate (TPM) | PO | 5 mg/kg: 200 mg | |
| *Third-line* | Minimum doses of anesthetics for treating SE | | |
| Midazolam | IV | 0.03–0.3 mg/kg at 4 mg/min | 0.05–0.2 mg/kg/h<br>Max: 1.3–3 mg/kg/h |
| Ketamine | IV | 0.5–3 g/kg | 0.05–0.2 mg/kg/h.<br>Max: 1.3–3 mg/kg/h |
| Propofol | IV | 2–2.5 mg/kg | 0.3–4 mg/kg/h |

Abbreviations: ECG, electrocardiogram; IV, intravenous; NG, nasogastric; PO, oral; SE, status epilepticus.

focal seizures. Studies to date have not found any of them to be significantly superior to the others.[13,32–35]

In the case of refractory SE, treatment should be delivered in pediatric intensive care units (PICUs), using combinations of anesthetics (midazolam, propofol, barbiturates), ketamine, or immunomodulatory therapies, as well as dietary measures, such as the ketogenic diet.[29–35]

Table 2 details the dosages of the different ASMs.

## Tailoring treatment to the type of seizure

Different management algorithms are defined according to the type of seizures (generalized tonic-clonic, focal, or nonconvulsive). In convulsive SE, addition of a third-line drug is recommended from minute 30, while in focal or nonconvulsive SE, this threshold is delayed to up to 60 minutes[31] (Fig. 5).

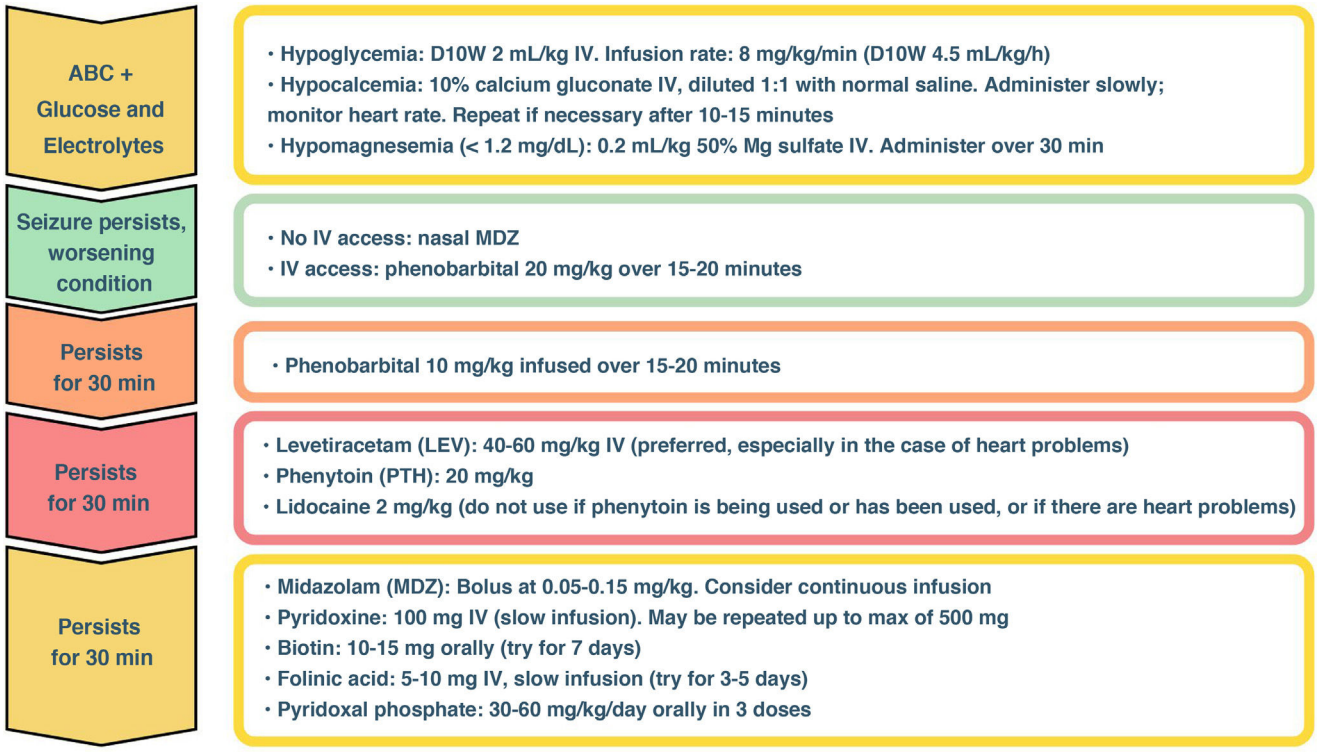


**Figure 6** Management of neonatal seizures.

## Specific protocol for neonatal seizures

A specific protocol is implemented for term newborns (up to 28 days of age) and preterm infants (up to 44 weeks of corrected age), which includes urgent referral and specialized neonatal transport to any of the four referral hospitals with Level IIIb-c neonatal intensive care units (NICUs) (Fig. 6). Given that neonatal seizures are predominantly secondary, the algorithm prioritizes the identification of inborn errors of metabolism and other potential underlying conditions.[36]

## Optimization and standardization of the emergency management of severe epileptic seizures

Various strategies have been implemented in the care process to optimize and standardize emergency care for children with seizures, ensuring a structured and early response based on the best available evidence. Among the key developments is the design of a specific algorithm for emergency departments (Fig. 4), which outlines the initial management and the indications for diagnostic tests, regardless of the type of seizure.

This algorithm includes a standardized history-taking and physical examination to facilitate rapid identification of risk factors for SE, relevant medical history, and key clinical features, thereby reducing variability in care delivery and guiding the prioritization of diagnostic and therapeutic resources.

## Early electroencephalography: diagnosis and therapeutic drug monitoring

The electroencephalogram (EEG), and video-EEG in particular, is the most valuable technique for diagnosis of seizures, including cases presenting as medical emergencies. It is particularly useful for identifying nonconvulsive status epilepticus (NCSE), a condition that can develop in up to one-third of pediatric patients following an episode of convulsive SE.[37]

In this context, early video-EEG is considered a priority diagnostic modality, and, if possible, should be performed in the 24 h following a seizure. In cases in which NCSE is strongly suspected or in the presence of recurrent seizures with subtle manifestations, the test should be performed within 30 min of admission to the hospital.

In PICUs, continuous EEG monitoring allows therapeutic monitoring of patients in a medically induced coma and guides the adjustment of sedation in super-refractory SE, with the goal of achieving a burst-suppression pattern.

The main advantages of early EEG include:

- Rapid differential diagnosis between epileptic seizures and other non-epileptic clinical conditions (such as status dystonicus or paroxysmal sympathetic hyperactivity), which are particularly common in children with developmental and epileptic encephalopathies.[30]
- Continuous monitoring of epileptiform activity, useful in patients under neuromuscular blockade or deep sedation.
- Guiding the adjustment of ASMs and anesthetic agents in cases of refractory and super-refractory SE.

In the neonatal setting, amplitude-integrated EEG or continuous brain-function monitoring is recommended, ideally to be initiated within 2 h of arrival in infants admitted to the NICU (Fig. 6).

## Transfer of care and family empowerment

Care does not end with hospital discharge: a seamless transition to primary care must be ensured, and families must be trained on the initial management of additional seizures. A key innovation in the care process is the home use of rescue BZDs, to be administered by family members, a measure that reduces the risk of progression to SE and the need for emergency care.[14,38] For the Community of Madrid, the BZDs recommended for home use are oral midazolam and rectal diazepam.

The evidence supports training family members and school staff in the early identification of seizures and the correct administration of rescue medication,[30] a priority recommendation in the SC.[4,39]

To facilitate the transition, the discharge summary must include:

- A personalized report detailing the type of seizures and the treatment;
- Warning signs indicating the need for urgent referral or activation of the SC;
- Home or school seizure action plan including indications for the use of BZDs;
- Contact information for the epilepsy unit, ensuring two-way communication with primary care.
- Comprehensive care for epileptic seizures: safety, training, surveillance, and research

Although multiple protocols on the management of SE and seizures have been published in the international literature,[29,35] the heterogeneity of the samples and methodological differences impede the extrapolation of results and the formulation of robust recommendations based on high-quality evidence.

In this context, the ''Severe epileptic seizures: Seizure Code'' care process has been designed as a comprehensive model that incorporates the following among its core elements:

- A systematic patient registry for cases of severe seizures, enabling standardized collection of data on clinical and therapeutic variables throughout the entire care process. This registry will enable the performance of observational studies, both prospective and retrospective, and facilitate the identification of clinical patterns and the evaluation of the effectiveness of the ASMs used for treatment.
- A specialized research committee to generate scientific evidence on the urgent management of epileptic seizures, with the ultimate goal of promoting continuous improvement in clinical practice based on real-world data.
- A comprehensive patient safety plan focused on preventing adverse events associated with the use of ASMs and on the early detection of complications of prolonged seizures.
- A structured training program aimed both at health care professionals and at family members and caregivers, covering aspects ranging from the identification of high-risk seizures to the safe and effective administration of rescue benzodiazepines, as well as understanding how the SC works.

Thus, the care process serves as a robust clinical tool, grounded in coordination across care levels, early diagnosis supported by EEG, early therapeutic intervention, and the empowerment of the family as key elements in the management of seizure emergencies.

## Limitations, conclusions, and future directions

The concept of seizure emergency is a novel contribution compared to the traditional approach, which focuses solely on SE, by including other high-risk situations such as repetitive or cluster seizures. The novel operational definition enabled the development of a networked care model integrating out-of-hospital emergency services, hospitals, primary care, and specialized units, promoting a consistent response and the application of consensus-based protocols, including the ASM sequence and early EEG performance.

Among the limitations, we ought to highlight that certain criteria—such as classifying the occurrence of two or more febrile seizures within 24 h as a seizure emergency—may not be appropriate for specific situations, such as atypical febrile seizures, and make it difficult to compare results with studies that use more restrictive criteria. This variability underscores the dynamic nature of the SC, which is subject to ongoing review by a multidisciplinary committee tasked with proposing modifications based on emerging evidence.

Another challenge is the consistent implementation of the SC in a region with more than 6.8 million inhabitants and over 30 hospitals, where variations in resources, internal organization, and staff training can affect adherence to the protocol and the effectiveness of the intervention.

- Looking ahead, the care process brings up several priority areas for evaluation and research:
  - Early dual therapy: evaluate the efficacy of early addition of a non-benzodiazepine antiepileptic drug in terms of seizure control and prevention of refractory SE.
  - Treatment according to seizure type: analyze differential outcomes in generalized, focal, and nonconvulsive epileptic seizures to define specific strategies.
  - Out-of-hospital use of benzodiazepines: conduct prospective studies to assess the impact of early home treatment administered by family members.
  - Unified patient registry: implementation of a systematic database to monitor clinical, therapeutic, and outcome-related variables.
  - Implementation evaluation: assess adherence, response times, and coordination across care levels, as well as their impact on clinical and organizational outcomes.

## Declaration of competing interest

The authors have no conflicts of interest to declare.

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