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Which terms should be used to describe medications used in the treatment of seizure disorders? An ILAE position paper

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Abstract

A variety of terms, such as “antiepileptic,” “anticonvulsant,” and “antiseizure” have been historically applied to medications for the treatment of seizure disorders. Terminology is important because using terms that do not accurately reflect the action of specific treatments may result in a misunderstanding of their effects and inappropriate use. The present International League Against Epilepsy (ILAE) position paper used a Delphi approach to develop recommendations on English-language terminology applicable to pharmacological agents currently approved for treating seizure disorders. There was consensus that these medications should be collectively named “antiseizure medications”. This term accurately reflects their primarily symptomatic effect against seizures and reduces the possibility of health care practitioners, patients, or caregivers having undue expectations or an incorrect understanding of the real action of these medications. The term “antiseizure” to describe these agents does not exclude the possibility of beneficial effects on the course of the disease and comorbidities that result from the downstream effects of seizures, whenever these beneficial effects can be explained solely by the suppression of seizure activity. It is acknowledged

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that other treatments, mostly under development, can exert *direct* favorable actions on the underlying disease or its progression, by having “antiepileptogenic” or “disease-modifying” effects. A more-refined terminology to describe precisely these actions needs to be developed.

KEYWORDS

antiepileptic drugs, antiseizure medications, recommendations, terminology

1 | INTRODUCTION

Since the original description by Sir Charles Lockock in 1857 of the clinical effectiveness of potassium bromide in controlling seizures in women with epilepsy, over 40 medications have been introduced for the treatment of seizure disorders.^{1,2} Historically these medications have been referred to in the medical literature by a variety of terms, such as “antiepileptic,” “anticonvulsant,” or “antiseizure.” Names matter, and some of those terms have increasingly come under criticism. For example, using the term “anticonvulsant” to collectively denote these medications is less than appropriate, because not all seizure types are convulsive.³ Likewise, the term “antiepileptic drug” (AED), although still widely used, has been considered inaccurate³⁻⁵ because currently used medications are symptomatic therapies, that is, they suppress the symptoms (seizures) but have no demonstrated direct activity on the underlying disease (epilepsy).^{6,7} It has also been argued that in some settings the term “antiepileptic” has stigmatizing undertones, as it could be perceived as hostile to an “epileptic,” that is, a person with epilepsy.⁴ Other arguments have been raised against use of the term “drugs,” which in the English medical literature can be used interchangeably with “medicines” or “medications” but in community settings (and in its literal translation into other languages) can be extended to denote compounds associated with non-therapeutic, illegal recreational abuse and dependence.⁴ The importance of avoiding the label “antiepileptic” was highlighted more than a decade ago by the Report “*Epilepsies Across the Spectrum*” published by the influential U.S. Institute of Medicine, which used consistently the term “seizure medications.”⁸ In recent years, the terms “antiseizure medicines” and “antiseizure medications” (ASMs) have been used increasingly in the medical literature.^{3,5} The use of etymologically correct terminology becomes particularly important in the current era, when efforts are ongoing to identify and develop novel treatments that do not have a purely symptomatic effect against seizures, but may actually treat the underlying pathophysiology leading to

Key points

- The terminology used to describe treatments should reflect accurately the nature of their primary action.
- Because medications currently used in the treatment of seizure disorders exert a symptomatic effect against seizures, they should be referred to as “antiseizure medications”.
- The term “antiseizure” does not exclude the possibility of suppression of seizure activity having a favorable influence on the course of the disease and on comorbidities that result from the downstream effects of seizures.
- A more-refined terminology needs to be developed to describe treatments, mostly under investigation, which has direct (seizure-unrelated) actions on the underlying disease process leading to seizures or disease progression.

epilepsy, prevent the occurrence of epilepsy, or modify its course.⁹⁻¹¹

Based on the preceding background, the International League Against Epilepsy (ILAE) considered it necessary to provide guidance on use of appropriate terminology to describe treatments that are currently available or may become available in the future. The present position paper from the ILAE Nomenclature Task Force provides recommendations on English-language terminology to be applied to pharmacological treatments that exert a symptomatic effect against seizures.

2 | METHODS

Consensus on the recommended terminology was achieved using a modified Delphi process.¹² The Delphi panel, which included all 16 members of the Nomenclature Task Force, was appointed by the ILAE

Executive Committee in consultation with the Task Force co-chairs (E.P. and J.F.). Membership included representation from every ILAE region, from the International Bureau for Epilepsy (IBE), and from clinical as well as basic science expertise.

To finalize the key statements of the consensus paper, an iterative approach was used. First, a set of 16 statements drafted by the Nomenclature Task Force co-chairs and worded to ensure relevance to the goal was submitted via electronic survey to the panel members, who were given an opportunity to propose additional statements. Two additional statements were proposed at this stage, bringing the total to 18. A link to each statement was then sent electronically to each panelist, whose responses were anonymous. Panelists rated each statement on a 9-point Likert scale from 1 (“strongly disagree”) to 9 (“strongly agree”), with a no judgment option to reflect “no opinion.” Panelists were given the opportunity for comments, particularly if they did not agree with the concept expressed by the statements or their wording. According to a predefined procedure, statements that received median ratings of 3 or less without discordance (defined as >25% of panelists rating the statement 7 or higher) were to be discarded. Statements with median ratings of 7 or higher without discordance (defined as >25% of panelists rating the item as 3 or lower) were accepted. Statements with median ratings of 4–7, or those showing discordance, were reviewed by the co-chairs, reworded based on the feedback received by panelists and resubmitted for a second round of ratings. Items that did not achieve consensus following the second round could be resolved by the co-chairs following consideration of any further comments received, but no adjudication was needed because consensus on each of the 18 items was achieved at the end of the second round. The finalized statements and associated ratings for level of agreement (Table 1), provided the basis for production of the initial version of the consensus document, which was submitted to the ILAE Executive Committee for overall approval of concept and content.

After review by the Executive Committee, the document was submitted to the journal for peer review and simultaneously placed on the ILAE website for a period of 2 months for public consultation. Comments from the epilepsy community worldwide were solicited repeatedly during this period. A total of 191 comments were received. All comments were reviewed and incorporated as appropriate into the manuscript by a separate ad hoc Task Force. The revised article was then submitted to the Executive Committee for final approval prior to resubmission to the journal. All authors accepted the final version. More details of the procedure for the publication of position papers are available on the ILAE website (<https://www.ilae.org/files/dmfile/publication-procedures-for-ilae-reports-14-july-2022.pdf>).

3 | RECOMMENDATIONS

3.1 | “Antiseizure” as preferred term for medications having a symptomatic effect

There was consensus within the Task Force that most medications currently used to treat epilepsy exert their effects by suppressing symptoms (seizures). In fact, these medications have been approved by regulatory authorities based solely on the evidence of a symptomatic effect on seizure activity. Therefore, the term “antiseizure” is the most appropriate term to describe these medications. The Task Force considered that the term “antiseizure” is sufficiently explanatory in the English language, and that including the term “epileptic” when describing the effect of these medications is redundant in this language.

3.2 | “Seizure” versus “epileptic seizure”

Although the term “seizure” in the English language is used predominantly in the context of epileptic seizures, the same term has been applied also to indicate psychogenic non-epileptic seizures (PNES), currently renamed functional/dissociative seizures (FDS). PNES/FDS are paroxysmal events that might be mistaken for epileptic seizures. However, their underlying neurobiology differs from that of epileptic seizures and is likely to reflect a complex episodic brain network dysfunction not involving epileptic activity.¹³ Although initially, the Nomenclature Task Force proposed that the term “seizure” should be reserved preferably to indicate epileptic seizures, feedback from public comments showed that no consensus could be reached on this proposition. Consequently, following further consultation within the ILAE membership, including the ILAE Task Force on FDS, it was agreed that the term “seizure” can also be applied to non-epileptic events. When the term “seizure” describes PNES/FDS, the context must clearly distinguish these events from epileptic seizures to reduce the risk of confusion.

ASMs act to suppress epileptic seizures by modulating neuronal excitability through their actions on receptors, ion channels, and other molecules. These actions link them to the neurobiology of epileptic seizures as manifestations of abnormal excessive or synchronous neuronal activity in the brain.¹⁴ When applied to these medications, “antiseizure” refers to epileptic seizures. Because of their

TABLE 1 List of statements in their final (approved) wording.

Statement #	Statement (Percent of Agreement)
1	Terms used to describe classes of therapeutic agents should convey at best the nature of their primary therapeutic action (100%)
2	Terms used to describe classes of therapeutic agents have implications, including potential association with stigma on how their use is perceived by health professionals, patients, and the lay public at large. Therefore, the views of different stakeholders should be considered when making recommendations about applicable terminology (100%)
3	Most of the medications currently used to treat epilepsy exert their effect by suppressing the symptoms of epilepsy (seizures) and are approved based on evidence of a symptomatic effect on seizure activity, and therefore the term “antiseizure” is the most appropriate term to describe medications that alter or suppress the symptom of seizure, either in persons with epilepsy, or in persons with symptomatic seizures (87%)
4	In the same way as it is correct to use the term “antiseizure medications (ASMs)” to describe drugs that act primarily by suppressing seizures, it is appropriate to say that such medications have antiseizure actions, or antiseizure effects (87%)
5	The term “antiepileptic medication” is not recommended for a medication that suppresses the symptom of seizure and only indirectly (through seizure suppression) may affect the underlying disease (epilepsy) or comorbidities (94%)
6	The term “antiepileptic medication” should be reserved for drugs that have been demonstrated to have a direct effect on the course of epilepsy, the likelihood of developing epilepsy, or the likelihood of developing more severe epilepsy (94%) ^a
7	The terms “antiseizure medication” and “antiepileptic medication” are not mutually exclusive (80%) ^a
8	It is understood that a medication that alters the symptom of seizure by providing seizure control (including suppression of epileptic EEG discharges) can impact positively on other measures such as cognitive development and, possibly, susceptibility to further seizures (93%)
9	Use of the term “antiepileptic” when referring to these drugs may mislead people with epilepsy, their caregivers, the lay public, and some health care professionals into believing that these drugs treat the disease, and that disappearance of the symptoms could necessarily signal disappearance of the underlying disease (88%)
10	Applying the term “antiseizure” to treatments that have symptomatic effects does not exclude that the same treatments may have additional actions on the underlying epilepsy, epileptogenic processes, or co-morbidities. For example, a medication could have antiseizure effects and have an independent effect on epileptogenesis (80%)
11	When referring to treatments used in the management of epileptic seizures, the term “antiseizure” may be sufficiently explanatory in the English language, and including the term “epileptic” when describing the effect of medications adds unnecessary redundancy. In other languages, the term “epileptic” may need to be retained, which may justify recommending the wording “anti-(epileptic, optional) seizure” (94%)
12	To minimize potential misunderstanding in the English language, the term “seizure” should preferably be reserved to indicate “epileptic seizures.” ^b In other languages, the term “epileptic seizures” can be used as necessary (94%)
13	The acronym for “antiseizure drugs” is ASDs, which is a widely used acronym to indicate autism spectrum disorder. Therefore, “antiseizure medicines (ASMs)” or “antiseizure medications (ASMs)” is the preferred choice (93%)
14	“Medication” refers more specifically to therapeutic products, whereas “medicine” is used to indicate both the science of treating diseases as well as the products used to treat disease (93%)
15	Although the remit of the Task Force is to make recommendations about English-language terms, the Task Force realizes that the issue has high relevance in all languages (100%)
16	Regional and national stakeholders within the International League Against Epilepsy (ILAE) organization should be encouraged to take appropriate action to address the issue and make recommendations about adequate terminology to be applied in their local language(s), taking into consideration the specific social and cultural context and the need for broad stakeholders’ involvement (93%)
17	Among drugs with antiseizure effect, grouping and naming according to their major mechanism of action would be a further step of potential clinical benefit (e.g., helping the clinician to design a rational polytherapy), while taking into account their frequent clinical use in other, unrelated conditions (80%)
18	Although exceeding the scope of this Task Force, and in order to help lay people understand treatment algorithms in epilepsy, similar considerations may apply to treatment modalities other than drugs (e.g., surgery, stimulation, diet); once defined by their mechanism of action and/or impact, they should be included in the corresponding “antiseizure”, “antiepileptic” ^a , or other category of treatment (93%)

Note: Percentage agreement (percentage of ratings in the 7–10 range) achieved during the Delphi process for each statement is shown in parentheses.

^aBased on feedback from public consultation, this recommendation was subsequently revised to indicate that the use of the term “antiepileptic” is undesirable (see text).

^bBased on feedback from public consultation, this recommendation was subsequently revised to indicate that the term “seizure” may also be applied to non-epileptic events.

complex pharmacology, some ASMs can also be effective in other indications, such as neuropathic pain, psychiatric disorders, and migraine.

A diagnosis of PNES/FDS does not warrant the use of ASMs unless epileptic seizures co-exist. Well-established treatments for PNES/FDS consist of a well-structured explanation of the diagnosis, psychoeducation, psychological therapies, and, sometimes, antidepressants or other psychoactive drugs (including certain ASMs) that target mood or anxiety disorders.^{15,16}

3.3 | “Medication” versus “medicine” or “drug”

The Task Force also discussed alternatives to the term “medication.” “Medication” in the English language refers only to therapeutic products, whereas “medicine” is used to indicate both the science of treating symptoms/diseases as well as the products used to treat these conditions. This may justify a preference for the term “antiseizure medication” (ASM), although both “medication” and “medicine” can be used interchangeably in this context. On the other hand, the term “antiseizure drug” (ASD) is not recommended because the acronym “ASD” is widely established to indicate autism spectrum disorder and is also used in cardiology as acronym for atrial septal defect.

3.4 | When should the term “antiepileptic” be used?

Use of the term “antiepileptic” is not recommended when describing medications that have a purely symptomatic effect. The Task Force acknowledged that a medication that alters the symptom of seizure, by providing seizure control (including suppression of epileptic electroencephalography [EEG] discharges), can have an *indirect* favorable impact on other outcomes such as cognitive development and, possibly, susceptibility to further seizures. Any such favorable effect on the underlying disease, however, could be solely a consequence of symptom suppression. In fact, using the term “antiepileptic” in this setting may mislead people with epilepsy, their caregivers, the lay public, and health care professionals into believing that these medications treat more than just the symptoms of the disease and that the disappearance of the symptoms could necessarily signal disappearance of the underlying disease.

The Task Force initially suggested that the term “antiepileptic” be reserved for medications that have been demonstrated to directly affect the course of epilepsy, the likelihood of developing epilepsy, or the likelihood of developing more severe epilepsy. However, based on

feedback from the public consultation, the Task Force agreed that using the label “antiepileptic” is undesirable because of stigma-related implications and the possibility that it could be misinterpreted as meaning “against a person with epilepsy.” This term could also create confusion with earlier literature where the term “antiepileptic” was applied to medications having a symptomatic effect on seizures.

Applying the term “antiseizure” to treatments that have symptomatic effects does not exclude that the same treatments may have, in addition, *direct* actions on the underlying epilepsy, epileptogenic processes, or co-morbidities. For example, a medication could have antiseizure effects and have an independent effect on epileptogenesis. Therefore, “antiseizure” and “antiepileptic” (or whatever term is chosen to indicate treatments with direct effects on the course of the disease) should not be regarded as being mutually exclusive. The provision of recommendations on the terminology to be used for treatments that are not purely symptomatic is beyond the purpose of the present paper.

3.5 | Application to non-pharmacological treatments

In addition, appropriate terminology should be used to describe not only pharmacological treatments (medications), but also the actions of other therapeutic modalities such as surgery, neurostimulation, and dietary treatments. However, providing specific recommendations on this topic is beyond the purpose of this article.

3.6 | Language-specific issues

Although the remit of our Task Force was to develop recommendations for English-language terminology, we acknowledge that there is a need for a similar effort to be applied to the development of correct terminology in all other languages. Accordingly, the ILAE encourages the development at the regional and national level of corresponding terminology in languages other than English, considering the specific social and cultural context and the need for broad stakeholders’ involvement.

4 | DISCUSSION AND CONCLUSIONS

The terms used to describe diseases and their treatment carry important medical and social implications. This is particularly true when dealing with diseases such as

epilepsy that are commonly associated with misperception, prejudice, and stigma, all of which could be affected by how specific terms are interpreted by health care professionals, patients, and the public at large.¹⁷ Accordingly, recommendations concerning specific terminology should be undertaken in consultation with all stakeholders involved. The present position paper was developed through involvement of health care professionals with disparate expertise and geographical location, as well as representation from the IBE, the leading lay organization representing people with epilepsy. This paper also incorporates feedback obtained by public consultation with members of the ILAE and IBE communities.

Ideally, the terminology used to describe therapeutic agents should reflect accurately the nature of their primary action. Based on this principle, the medications currently used in the treatment of epilepsy should be collectively described by the term “antiseizure medications” or “anti-seizure medications” (or ASMs), which may be used interchangeably, although the term without a hyphen may be preferred for simplicity. This term, which has been used increasingly in recent years,⁵ reflects accurately the primarily symptomatic effect of these medications against seizures, and reduces the possibility of health care practitioners, patients, or caregivers having undue expectations, or an incorrect understanding of the real action of these medications. These medications may be further categorized by classifying them according to their molecular mechanism(s) of action, which could be relevant for their rational clinical use.^{18,19} Of note, the term “antiseizure” to describe these agents does not exclude the possibility of a favorable influence on the course of the disease and associated comorbidities, as long as these beneficial effects can be explained solely by suppression of seizure activity. For example, rapid achievement of seizure control in children with epileptic encephalopathies often impacts favorably on cognitive outcome. This effect can be ascribed to the cessation of epileptic discharges and their consequent damaging effect on the developing brain.²⁰ The possibility that some treatments do or will exert direct favorable effects on the underlying disease, or its progression is acknowledged. One example of treatments that target the underlying pathophysiology are the immune therapies used to treat autoimmune-associated seizure disorders, which often respond poorly to conventional ASMs.²¹

The focus of the present position statement is to provide recommendations on the terminology to be applied to treatments having a symptomatic effect against seizures. Extensive preclinical and clinical research is ongoing with the aim to develop innovative treatments that target the underlying disease. These treatments could succeed in achieving effects that are often described with terms

such as “antiepileptogenic,” “disease-modifying,” or other. Recommendations on which labels should be used to describe these actions, and how related terminology should be defined, will be provided by the ILAE in due course.

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CONFLICT OF INTEREST STATEMENT

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ETHICS STATEMENT


We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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