National Institute for Health and Care Excellence

Final

Epilepsies in children, young people and adults

Methods for changes to valproate and topiramate recommendations after revised MHRA safety advice

NICE guideline NG217

Methods

January 2025

Final

Evidence reviews were developed by NICE

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Introduction

In December 2023 the MHRA announced changes to the regulatory status of valproate. NICE convened a streamlined working group to review the evidence about the effectiveness of valproate and agree if any changes needed to be made to recommendations in NG217, to take into account with the new regulatory position. There were some delays to the final safety information being published by MHRA (the safety alert was published at the end of January 2024 with the safety update on potential fertility risks and risks to children for men being published in September 2024).

The following MHRA guidance was considered:

- MHRA guidance on the use of valproate,
- valproate use in people younger than 55 years,
- valproate use in women and girls, and
- valproate use in men.

Additionally, this update considered the impact of the MHRA drug safety update concerning the use of topiramate.

Methods

The January 2025 update was based on MHRA drug safety updates and did not follow the processes described in the Guidelines Manual. Details of the methods used are provided below.

Forming a working group

The focus of the work was to update the recommendations in response to recent MHRA safety alerts rather than review new evidence, therefore open recruitment and the use of a full committee to update recommendations was not considered to be the most effective approach. Instead, a streamlined working group was convened consisting of an independent chair, 2 paediatric neurologists, 3 adult neurologists, 1 clinical nurse specialist, 1 learning disabilities psychiatrist, 1 pharmacist and 1 lay member. Members of the working group were sought from committee members who had developed NG217. All working group members (for details of group membership see the working group membership list) were asked to declare interests and the Declaration of Interests policy was applied (declared interests and associated actions are listed in the DOI register). An MHRA expert on valproate also attended working group meetings to advise on the evidence on valproate safety and the regulatory position.

Updating the recommendations

Two working group meetings were held during which the effectiveness evidence included in NG217 (2022) for the different seizure types was presented and the original rationales from NG217 were taken into account. The working group agreed changes to recommendations about the use of valproate that were needed in light of the new regulatory position but would also align as much as possible with the effectiveness evidence included in NG217. The rationale and impact text of the guideline and the discussion sections of the evidence reviews were updated accordingly. A decision support tool was developed using data from the existing evidence reviews.

A third working group meeting was planned but given the supportive feedback from the peer review (see below) it was decided that the working group would have sign-off via email.

Consultation

The recommendations were amended to take into account updated MHRA regulations on the use of sodium valproate and topiramate. As such, these changes did not meet the threshold for a full formal stakeholder consultation. Therefore, an external peer review was conducted.

External peer review

Input from independent external peer reviewers was sought during development. The following people provided comments on the amended recommendations and NICE decision support tool:

Dr Suresh Pujar, Chair, British Paediatric Epilepsy Group

Dr Ailsa McLellan, President, BPNA

Professor Tony Marson, Secretary General, European Academy of Neurology, SANAD-II lead

Professor Sofia Eriksson, Consultant neurologist and honorary associate Professor at The National Hospital for Neurology and Neurosurgery at Queen Square and UCL Hospitals NHS Foundation Trust

Dr Lucy Kinton Consultant neurologist and honorary secretary of the Association of British Neurologists

Sarah Morgan, Expert Scientific Assessor Safety and Surveillance, MHRA

Themes and actions

Comments related to generalised tonic-clonic seizures

- All peer reviewers supported the change from recommending sodium valproate as the first-line monotherapy to offering a choice among lamotrigine, levetiracetam, and sodium valproate.
- Some peer reviewers disagreed with removing sodium valproate from the combined list of first-line add-on options and creating a separate recommendation for it. They preferred a combined list that includes sodium valproate.

Decision: Based on this feedback, sodium valproate was retained in the combined list of first-line add-on options, with appropriate caveats and safety warnings.

Comments related to focal seizures

- Peer reviewers supported the removal of sodium valproate from the list of first-line add-on options.
- They agreed it should be included as a second-line add-on option but raised concerns about the order of options presented.

Decision: The order of options was identified as potentially confusing, as sodium valproate was listed last to allow for safety warnings beneath it. To enhance clarity, sodium valproate was repositioned alphabetically within the list, while the safety warnings remain directly underneath, clearly associated with sodium valproate in this recommendation.

Comments related to absence seizures, myoclonic seizures, tonic or atonic seizures, and idiopathic generalised epilepsies

- For these seizure types, reviewers agreed that when sodium valproate is recommended as a first-line or second-line monotherapy (or add-on therapy), other choices (typically lamotrigine, levetiracetam, and sodium valproate) should also be available.
- One reviewer questioned why levetiracetam was not included as a first-line option for tonic or atonic seizures.

Decision: As levetiracetam was not included in the 2022 guideline for tonic or atonic seizures, adding it was outside the scope of this update, which is limited to MHRA regulatory changes related to sodium valproate.

Comments related to treatment of childhood-onset epilepsies

- No comments were made regarding changes in the treatment of childhood-onset epilepsies.

Comments related to the NICE decision support tool

- None of the peer reviewers found the decision support tool helpful, citing concerns that:
    - The data presented were too broad for individual seizure phenotypes,
    - There was insufficient information specific to paediatric populations,
    - Additional statistical checks might be needed and
    - The tool did not adequately support the nuances of individualised decision-making.

Decision: Given the limited data available to address these concerns, the decision support tool will not be further developed or published.

Other comments

- General comments were made regarding the MHRA drug safety updates for topiramate, which have since been addressed with added safety warnings.
- Some reviewers raised other points unrelated to the MHRA drug safety update, which were deemed outside the scope of this update.
- Comments were also made regarding the wording of safety information or advice, but no changes were made to ensure consistency with MHRA safety wording.

Changes to valproate recommendations after revised MHRA safety advice

Based on the discussions with the working group the table below shows the changes that were made with reasons for the change provided in the final column.

In the guideline there will be one box preceding all relevant sections with links to the associated general safety information:

> For more information on treatment in women and girls, see the section on antiseizure medications for women and girls.
>
> Follow the Medicines and Healthcare products Regulatory Agency (MHRA) safety advice on the use of valproate, valproate use by women and girls, valproate use by men, the use of topiramate and antiepileptic drugs in pregnancy.

To avoid repetition specifically related to sodium valproate safety measures and precautionary advice, safety information has been moved into one box so that it can be cross-referred in the related recommendations:

Box 2 Sodium valproate safety measures and precautionary advice

> **Safety measures for under 55s**
>
> Do not start sodium valproate for the first time in people (male or female) younger than 55 years, unless 2 specialists independently agree and document that there is no other effective and tolerated treatment, or there are compelling reasons that the reproductive risks do not apply.
>
> **Safety measures in women and girls able to have children**

Only use sodium valproate in women and girls able to have children (including young girls who are likely to need treatment when they are old enough to have children), if:

other treatment options are unsuccessful

the risks and benefits have been fully discussed, including the risks to an unborn child

the likelihood of pregnancy has been taken into account and the Pregnancy Prevention Programme put in place, if appropriate.

Precautionary advice for boys and men

Advise boys and men that effective contraception (condoms, plus contraception used by a female sexual partner) is recommended throughout the valproate treatment period and for 3 months after stopping valproate. Advise men taking valproate who are planning a family within the next year of the potential fertility risks and treatment options.

Recommendation table – original and amended recommendations and rationale

Previous recommendation in NG217	Revised recommendation(s)	Rationale
5 Treating epileptic seizures in children, young people and adults		
5.1 Generalised tonic-clonic seizures		
5.1.1 Offer sodium valproate as first-line monotherapy for generalised tonic-clonic seizures in: • boys and men	5.1.1 Offer a choice of lamotrigine, levetiracetam or sodium valproate as first-line monotherapy for generalised tonic-clonic seizures. Follow the sodium valproate safety measures and	The recommendations were amended to align with updated MHRA regulations on the use of sodium valproate. Sodium valproate,

Previous recommendation in NG217	Revised recommendation(s)	Rationale
• girls aged under 10 years and who are unlikely to need treatment when they are old enough to have children • women who are unable to have children.	precautionary advice in box 2. If the first choice of treatment is unsuccessful, try another one of these options. If that is also unsuccessful, try the third option. In January 2025, these were off-label uses of lamotrigine in children under 13 years and levetiracetam in adults and children. See NICE's information on prescribing medicines.	levetiracetam and lamotrigine are now all options for first-line treatment of generalised tonic-clonic seizures in boys and men, young girls who are unlikely to need treatment when they are old enough to have children, and women who are unable to have children.
5.1.3 If first-line monotherapy with sodium valproate is unsuccessful for generalised tonic-clonic seizures, offer lamotrigine or levetiracetam as second-line monotherapy treatment. If the first choice is unsuccessful, try the other of these options.	Deleted	Lamotrigine and levetiracetam are now options for first-line treatment
5.1.5 If monotherapy is unsuccessful in people with generalised tonic-clonic seizures, consider 1 of the following first-line add-on treatment options: • clobazam • lamotrigine • levetiracetam	5.1.2 If monotherapy is unsuccessful in people with generalised tonic-clonic seizures, consider 1 of the following first-line add-on treatment options: • clobazam • lamotrigine • levetiracetam • perampanel	Valproate: The recommendations were amended to align with updated MHRA regulations on the use of sodium valproate. Sodium valproate is now only an option for first-line add-on therapy after discussion of the risks and benefits in boys and men, young girls who are unlikely to need treatment when they are old

Previous recommendation in NG217	Revised recommendation(s)	Rationale
• perampanel • sodium valproate, except in women and girls able to have children • topiramate. If the first choice is unsuccessful, consider the other first-line add-on options.	• sodium valproate (follow the sodium valproate safety measures and precautionary advice in box 2) • topiramate (do not use topiramate in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled). In January 2025, these were off-label uses of clobazam as add-on therapy in children under 6 months, lamotrigine in children under 2 years, levetiracetam in children under 12 years, perampanel in children under 7 years, and topiramate in children under 2 years. See NICE's information on prescribing medicines.	enough to have children, and women who are unable to have children. Whilst the balance of benefits and risks of topiramate has changed, this is already at a stage where several options have not been successful. It was considered to be important to keep this as an option so that treatments can be individualised.
5.2 Focal seizures with or without evolution to bilateral tonic-clonic seizures		
5.2.4 If monotherapy is unsuccessful in people with focal seizures, consider 1 of the following first-line add-on treatment options: • carbamazepine • lacosamide • lamotrigine	5.2.4 If monotherapy is unsuccessful in people with focal seizures, consider 1 of the following first-line add-on treatment options: • carbamazepine • lacosamide • lamotrigine	Whilst the balance of benefits and risks of topiramate has changed, this is already at a stage where several options have not been successful. It was considered to be important to keep this as an option so that treatments can be individualised. Safety advice was added.

Previous recommendation in NG217	Revised recommendation(s)	Rationale
• levetiracetam • oxcarbazepine • topiramate • zonisamide. If the first choice is unsuccessful, consider the other first-line add-on options. In April 2022, these were off-label uses of lacosamide in children under 4 years, lamotrigine in children under 2 years, levetiracetam in children under 4 years, oxcarbazepine in children under 6 years, topiramate in children under 2 years, and zonisamide in children under 6 years. See NICE's information on prescribing medicines.	• levetiracetam • oxcarbazepine • topiramate (do not use topiramate in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled) • zonisamide. If the first choice is unsuccessful, consider the other first-line add-on options. In January 2025, these were off-label uses of lacosamide in children under 4 years, lamotrigine in children under 2 years, levetiracetam in children under 4 years, oxcarbazepine in children under 6 years, topiramate in children under 2 years, and zonisamide in children under 6 years. See NICE's information on prescribing medicines.	
5.2.5 If first-line add-on treatments tried are unsuccessful in people with focal seizures, consider 1 of the following second-line add-on treatment options: • brivaracetam	5.2.5 If first-line add-on treatments tried are unsuccessful in people with focal seizures, consider 1 of the following second-line add-on treatment options: • brivaracetam	The recommendations were amended to align with updated MHRA regulations on the use of sodium valproate. Sodium valproate

Previous recommendation in NG217	Revised recommendation(s)	Rationale
• cenobamate (in line with NICE's technology appraisal guidance on cenobamate for treating focal onset seizures in epilepsy) • eslicarbazepine acetate • perampanel • pregabalin • sodium valproate, except in women and girls able to have children. If the first choice is unsuccessful, consider the other second-line add-on options.	• cenobamate (in line with NICE's technology appraisal guidance on cenobamate for treating focal onset seizures in epilepsy) • eslicarbazepine acetate • perampanel • pregabalin. If the first choice is unsuccessful, consider the other second-line add-on options. In January 2025, these were off-label uses of brivaracetam in children under 4 years, eslicarbazepine acetate in children under 6 years, perampanel in children under 4 years, and pregabalin in children. See NICE's information on prescribing medicines.	was moved to a third-line add-on treatment option for focal seizures.
5.2.6 If second-line add-on treatments tried are unsuccessful in people with focal seizures, consider 1 of the following third-line add-on treatment options: • phenobarbital • phenytoin • tiagabine • vigabatrin.	5.2.6 If second-line add-on treatments tried are unsuccessful in people with focal seizures, consider 1 of the following third-line add-on treatment options: • phenobarbital • phenytoin • tiagabine	

Previous recommendation in NG217	Revised recommendation(s)	Rationale
If the first choice is unsuccessful, consider the other third-line add-on options.	• sodium valproate (follow the sodium valproate safety measures and precautionary advice in box 2) • vigabatrin. If the first choice is unsuccessful, consider the other third-line add-on options. In January 2025, this was an off-label use of tiagabine in children under 12 years. See NICE's information on prescribing medicines.	
5.3 Absence seizures		
Absence seizures (including childhood absence epilepsy)		
5.3.2 If first-line treatment is unsuccessful, offer sodium valproate as second-line monotherapy or add-on treatment for absence seizures in: • boys of all ages • girls aged under 10 years and who are unlikely to need treatment when they are old enough to have children • women who are unable to have children.	5.3.2 If first-line treatment is unsuccessful, offer a choice of lamotrigine, levetiracetam or sodium valproate as second-line monotherapy or add-on treatment for absence seizures in. Follow the sodium valproate safety measures and precautionary advice in box 2. If the first choice of treatment is unsuccessful, try another one of these options as monotherapy or add-on treatment. If that is also unsuccessful, try the third option as monotherapy or add-on treatment.	The recommendations were amended to align with updated MHRA regulations on the use of sodium valproate. Sodium valproate, levetiracetam and lamotrigine are now all options for second-line monotherapy or add-on treatment for absence seizures in boys and men, young girls who are unlikely to need treatment when they are old enough

Previous recommendation in NG217	Revised recommendation(s)	Rationale
	In January 2025, these were off-label uses of lamotrigine in children under 2 years and levetiracetam in adults and children. See NICE's information on prescribing medicines.	to have children, and women who are unable to have children.
5.3.3 If second-line treatment is unsuccessful for absence seizures, consider lamotrigine or levetiracetam as a third-line monotherapy or add-on treatment options. If the first choice is unsuccessful, consider the other of these options.	Deleted.	Lamotrigine and levetiracetam are now options for second-line monotherapy or add-on treatment.
Absence seizures with other seizure types		
5.3.5 Consider sodium valproate as first-line treatment for absence seizures with other seizure types (or at risk of these) in: • boys and men • girls aged under 10 years and who are unlikely to need treatment when they are old enough to have children • women who are unable to have children.	5.3.4 Consider a choice of lamotrigine, levetiracetam or sodium valproate as first-line treatment for absence seizures. Follow the sodium valproate safety measures and precautionary advice in box 2). If the first choice of treatment is unsuccessful, try another one of these options as monotherapy or add-on treatment. If that is also unsuccessful, try the third option as monotherapy or add-on treatment. In January 2025, these were off-label uses of lamotrigine as monotherapy and as an add-on therapy for children under 2 years, lamotrigine as	The recommendations were amended to align with updated MHRA regulations on the use of sodium valproate. Sodium valproate, levetiracetam and lamotrigine are now all options for first-line monotherapy or add-on treatment of absence seizures with other seizure types in boys and men, young girls who are unlikely to need treatment when they are old enough to have

Previous recommendation in NG217	Revised recommendation(s)	Rationale
	monotherapy for children under 13 years, levetiracetam as monotherapy for adults and children, and as an add-on therapy for children under 12 years. See NICE's information on prescribing medicines.	children, and women who are unable to have children.
5.3.8 If first-line treatments tried are unsuccessful for absence seizures and other seizure types (or at risk of these), consider: • lamotrigine or levetiracetam as a second-line monotherapy or add-on treatment options or • ethosuximide as a second-line add-on treatment. If the first choice is unsuccessful, consider the other second-line options.	5.3.5 If first-line treatments tried are unsuccessful for absence seizures and other seizure types (or at risk of these), consider ethosuximide as a second-line add-on treatment.	Lamotrigine and levetiracetam are now options for first-line treatment
5.4 Myoclonic seizures		
5.4.2 Offer sodium valproate as first-line treatment for myoclonic seizures in: • boys and men • girls aged under 10 years and who are unlikely to need treatment when they are old enough to have children	5.4.2 Offer a choice of levetiracetam or sodium valproate as first-line treatment for myoclonic seizures. Follow the sodium valproate safety measures and precautionary advice in box 2. If the first choice of treatment is unsuccessful, try the	The recommendations were amended to align with updated MHRA regulations on the use of sodium valproate. Sodium valproate and levetiracetam are now options for first-line monotherapy or add-on treatment of myoclonic seizures in

Previous recommendation in NG217	Revised recommendation(s)	Rationale
• women who are unable to have children.	other one of these options as monotherapy or add-on treatment. In January 2025, this was an off-label use of levetiracetam as monotherapy. See NICE's information on prescribing medicines.	boys and men, young girls who are unlikely to need treatment when they are old enough to have children, and women who are unable to have children.
5.4.4 If sodium valproate is unsuccessful as first-line treatment for myoclonic seizures, offer levetiracetam as a second-line monotherapy or add-on treatment.	Deleted	Levetiracetam is now an option for first line treatment.
5.4.5 If levetiracetam is unsuccessful for myoclonic seizures, consider 1 of the following as monotherapy or add-on treatment options: • brivaracetam • clobazam • clonazepam • lamotrigine • phenobarbital • piracetam • topiramate • zonisamide.	5.4.3 If first-line treatment is unsuccessful for myoclonic seizures, consider 1 of the following as monotherapy or add-on treatment options: • brivaracetam • clobazam • clonazepam • lamotrigine • phenobarbital • piracetam • topiramate (do not use topiramate in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled)	Valproate: Line of treatment amended now that levetiracetam is an option for first-line treatment. Whilst the balance of benefits and risks of topiramate has changed, this is already at a stage where several options have not been successful. It was considered to be important to keep this as an option so that treatments can be individualised. Safety advice was added.

Previous recommendation in NG217	Revised recommendation(s)	Rationale
If the first choice is unsuccessful, consider any other of these options.	• zonisamide. If the first choice is unsuccessful, consider any other of these options. In January 2025, these were off-label uses for brivaracetam in adults and children, clobazam as monotherapy in adults and children, clobazam as add-on therapy in children under 6 months, clonazepam solution in children, lamotrigine as monotherapy for children under 13 years and add-on therapy for children under 2 years, piracetam in children, topiramate in adults and children, and zonisamide in adults and children. See NICE's information on prescribing medicines.	
5.5 Tonic or atonic seizures		
5.5.2 Offer sodium valproate as first-line treatment for tonic or atonic seizures in: • boys and men • girls aged under 10 years and who are unlikely to need treatment when they are old enough to have children • women who are unable to have children.	5.5.2 Offer a choice of lamotrigine or sodium valproate as first-line treatment for tonic or atonic seizures. Follow the sodium valproate safety measures and precautionary advice in box 2. If the first choice of treatment is unsuccessful, try the other one of these options as monotherapy or add-on treatment.	The recommendations were amended to align with updated MHRA regulations on the use of sodium valproate. Sodium valproate and lamotrigine are now options for first-line monotherapy or add-on treatment of tonic or atonic seizures in boys and men, young girls who are unlikely to need treatment when they are old enough to have children,

Previous recommendation in NG217	Revised recommendation(s)	Rationale
	In January 2025, these were off-label uses of lamotrigine as monotherapy for children under 13 years, and as an add-on therapy for children under 2 years. See NICE's information on prescribing medicines.	and women who are unable to have children.
5.5.4 If sodium valproate is unsuccessful as first-line treatment for tonic or atonic seizures, consider lamotrigine as a second-line monotherapy or add-on treatment.	Deleted	Lamotrigine is now an option for first line treatment.
5.5.5 If lamotrigine is unsuccessful for treating tonic or atonic seizures, consider 1 of the following as monotherapy or add-on treatment options: • clobazam • rufinamide • topiramate. If the first choice is unsuccessful, consider any other of these options.	5.5.3 If first-line treatment is unsuccessful for treating tonic or atonic seizures, consider 1 of the following as monotherapy or add-on treatment options: • clobazam • rufinamide • topiramate (do not use topiramate in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled). If the first choice is unsuccessful, consider any other of these options.	Valproate: Line of treatment amended now that lamotrigine is an option for first-line treatment. Whilst the balance of benefits and risks of topiramate has changed, this is already at a stage where several options have not been successful. It was considered to be important to keep this as an option so that treatments can be individualised. Safety advice was added.

Previous recommendation in NG217	Revised recommendation(s)	Rationale
	In January 2025, these were off-label uses for clobazam as monotherapy in adults and children, clobazam as add-on therapy in children under 6 months, rufinamide, and topiramate as monotherapy in children under 6 years, and topiramate as add-on therapy in children under 2 years. See NICE's information on prescribing medicines.	
5.6 Idiopathic generalised epilepsies		
5.6.1 Offer sodium valproate as first-line treatment for idiopathic generalised epilepsies in: • boys and men • girls aged under 10 years and who are unlikely to need treatment when they are old enough to have children • women who are unable to have children.	5.6.1 Offer a choice of lamotrigine, levetiracetam or sodium valproate as first-line treatment for idiopathic generalised epilepsies Follow the sodium valproate safety measures and precautionary advice in box 2. If the first choice of treatment is unsuccessful, try another one of these options as monotherapy or add-on treatment. If that is also unsuccessful, try the third option as monotherapy or add-on treatment. In January 2025, these were off-label uses of lamotrigine as monotherapy for children under 13 years, and as an add-on therapy for children under 2 years, levetiracetam as monotherapy in adults and children. See NICE's information on prescribing medicines.	The recommendations were amended to align with updated MHRA regulations on the use of sodium valproate. Sodium valproate, lamotrigine and levetiracetam are now options for first-line monotherapy or add-on treatment of idiopathic generalised epilepsies in boys and men, young girls who are unlikely to need treatment when they are old enough to have children, and women who are unable to have children.

Previous recommendation in NG217	Revised recommendation(s)	Rationale
5.6.3 If first-line treatments are unsuccessful for idiopathic generalised epilepsies, consider lamotrigine or levetiracetam as a second-line monotherapy or add-on treatment options. If the first choice is unsuccessful, consider the other of these options.	Deleted	Lamotrigine and levetiracetam are now options for first-line treatment
5.6.4 If second-line treatments tried are unsuccessful for idiopathic generalised epilepsies, consider perampanel or topiramate as third-line add-on treatment options. If the first choice is unsuccessful, consider the other of these options.	5.6.2 If first-line treatments are unsuccessful for idiopathic generalised epilepsies, consider perampanel or topiramate as second-line add-on treatment options. If the first choice is unsuccessful, consider the other of these options. Do not use topiramate in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled. In January 2025, this was an off-label use of perampanel for children under years. See NICE's information on prescribing medicines.	Valproate: Line of treatment amended now that lamotrigine and levetiracetam are first-line treatment. Topiramate: keep topiramate in the list but add a safety warning as there is only 1 alternative
6 Treating childhood-onset epilepsies		
6.1 Dravet syndrome		

Previous recommendation in NG217	Revised recommendation(s)	Rationale
6.1.2 Consider sodium valproate as first-line treatment for people with Dravet syndrome. Be aware that sodium valproate should be used with caution in women and girls, but it is recommended as first-line treatment for Dravet syndrome because of the severity of the syndrome and the lack of evidence for other effective first-line treatment options.	6.1.2 Consider sodium valproate as first-line treatment for people with Dravet syndrome. Follow the sodium valproate safety measures and precautionary advice in box 2. Be aware that sodium valproate should be used with caution, but it is recommended as first-line treatment for Dravet syndrome because of the severity of the syndrome and the lack of evidence for other effective first-line treatment options.	Recommendation amended to require use of valproate with caution in all groups (not just women and girls) in line with new MHRA regulations on the use of sodium valproate. 6.1.3 has been deleted because the related safety measures are now covered by the information in the box.
6.1.3 If sodium valproate first-line monotherapy is started or continued for Dravet syndrome in women and girls able to have children (including young girls who are likely to need treatment when they are old enough to have children): • discuss the potential risks and benefits of treatment, including the risks to an unborn child • take into account the likelihood of pregnancy and put in place a pregnancy prevention programme, if appropriate. Follow the MHRA safety advice on valproate use by women and girls.	Deleted	
6.1.6 If triple therapy is unsuccessful for Dravet syndrome in a child aged under 2 years or	6.1.6 If triple therapy is unsuccessful for Dravet syndrome in a child aged under 2 years or	Whilst the benefits and risks of topiramate have changed it was

Previous recommendation in NG217	Revised recommendation(s)	Rationale
second-line treatment is unsuccessful in a child aged over 2 years, consider 1 of the following add-on options under the supervision of a ketogenic diet team or a neurologist with expertise in epilepsy, as appropriate: • ketogenic diet • levetiracetam • topiramate. If the first choice is unsuccessful, consider the other add-on options. In April 2022, these were off-label uses of levetiracetam and topiramate. See NICE's information on prescribing medicines.	second-line treatment is unsuccessful in a child aged over 2 years, consider 1 of the following add-on options under the supervision of a ketogenic diet team or a neurologist with expertise in epilepsy, as appropriate: • ketogenic diet • levetiracetam • topiramate (do not use topiramate in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled). If the first choice is unsuccessful, consider the other add-on options. In January 2025, these were off-label uses of levetiracetam and topiramate. See NICE's information on prescribing medicines.	decided that it should be an option for childhood-onset epilepsies. Safety advice was added.
6.2 Lennox–Gastaut syndrome		
6.2.2 Consider sodium valproate as first-line treatment for people with Lennox–Gastaut syndrome. Be aware that sodium valproate should be used with caution in women and girls,	6.2.2 Consider sodium valproate as first-line treatment for people with Lennox–Gastaut syndrome. Follow the sodium valproate safety measures and precautionary advice in box 2. Be	Recommendation amended to require use of valproate with caution in all groups (not just women and girls) in line with new MHRA

Previous recommendation in NG217	Revised recommendation(s)	Rationale
but it is recommended as first-line treatment for Lennox–Gastaut syndrome because of the severity of the syndrome and the lack of evidence for other effective first-line treatment options.	aware that sodium valproate should be used with caution, but it is recommended as first-line treatment for Lennox–Gastaut syndrome because of the severity of the syndrome and the lack of evidence for other effective first-line treatment options.	regulations on the use of sodium valproate. Safety advice was added. 6.2.5 has been deleted because the safety information is covered in box 2.
6.2.3 If sodium valproate treatment is started or continued for Lennox–Gastaut syndrome in women and girls able to have children (including young girls who are likely to need treatment when they are old enough to have children): • discuss the risks and benefits of treatment, including the risks to an unborn child • take into account the likelihood of pregnancy and put in place a pregnancy prevention programme, if appropriate. Follow the MHRA safety advice on valproate use by women and girls.	Deleted	
6.2.5 If second-line treatment is unsuccessful, consider the following as third-line add-on treatment options for people with Lennox–Gastaut syndrome:	6.2.5 If second-line treatment is unsuccessful, consider the following as third-line add-on treatment options for people with Lennox–Gastaut syndrome:	Whilst the benefits and risks of topiramate have changed it was decided that it should be an option for Lennox-Gestaut syndrome. Safety advice was added.

Previous recommendation in NG217	Revised recommendation(s)	Rationale
• cannabidiol in combination with clobazam if the child is over 2 years, in line with NICE's technology appraisal guidance on cannabidiol with clobazam for treating seizures associated with Lennox–Gastaut syndrome • clobazam • rufinamide • topiramate.	• cannabidiol in combination with clobazam if the child is over 2 years, in line with NICE's technology appraisal guidance on cannabidiol with clobazam for treating seizures associated with Lennox–Gastaut syndrome • clobazam • rufinamide • topiramate (do not use topiramate in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled). In January 2025, these were off-label uses of clobazam as add-on therapy in children under 6 months, rufinamide in children under 1 year, and topiramate in children under 2 years. See NICE's information on prescribing medicines.	
6.3 Infantile spasms		
6.3.11 Consider the following as a second-line monotherapy or add-on treatment options for infantile spasms, guided by a ketogenic diet	6.3.11 Consider the following as a second-line monotherapy or add-on treatment options for infantile spasms, guided by a ketogenic diet team	Sodium valproate and topiramate in the list as this population is unlikely to be of childbearing age. Safety

Previous recommendation in NG217	Revised recommendation(s)	Rationale
team or tertiary paediatric epilepsy specialist, as appropriate: • ketogenic diet • levetiracetam • nitrazepam • sodium valproate • topiramate. If the first choice is unsuccessful, consider the other second-line options. In April 2022, these were off-label uses of levetiracetam, nitrazepam and topiramate. See NICE's information on prescribing medicines.	or tertiary paediatric epilepsy specialist, as appropriate: • ketogenic diet • levetiracetam • nitrazepam • sodium valproate • topiramate. If the first choice is unsuccessful, consider the other second-line options. In January 2025, these were off-label uses of levetiracetam, nitrazepam and topiramate. See NICE's information on prescribing medicines.	information not added or linked to for the same reason.
6.5 Epilepsy with myoclonic-atonic seizures (Doose syndrome)		
6.5.2 Consider levetiracetam or sodium valproate as first-line treatments for epilepsy with myoclonic-atonic seizures. If either levetiracetam or sodium valproate is unsuccessful, try the other of these options. In December 2024, this was an off-label use of	6.5.2 Consider levetiracetam or sodium valproate as first-line treatments for epilepsy with myoclonic-atonic seizures. Follow the sodium valproate safety measures and precautionary advice in box 2. If either levetiracetam or sodium valproate is unsuccessful, try the other of these options.	Recommendation amended to require use of valproate with caution in all groups (not just women and girls) in line with new MHRA regulations on the use of sodium valproate. Safety advice was added. 6.5.3 has been deleted because the

Previous recommendation in NG217	Revised recommendation(s)	Rationale
levetiracetam. See NICE's information on prescribing medicines.	In January 2025, this was an off-label use of levetiracetam. See NICE's information on prescribing medicines.	safety information is covered in box 2.
6.5.3 If sodium valproate is started or continued for epilepsy with myoclonic-atonic seizures in girls or women able to have children (including young girls who are likely to need treatment when they are old enough to have children): • discuss the risks and benefits of treatment, including the risks to an unborn child • take into account the likelihood of pregnancy and put in place a pregnancy prevention programme, if appropriate. Follow the MHRA safety advice on valproate use by women and girls.	Deleted	
6.5.5 If second-line treatment for epilepsy with myoclonic-atonic seizures is unsuccessful, consider the following as third-line monotherapy or add-on treatment options: • clobazam • ethosuximide • topiramate	6.5.5 If second-line treatment for epilepsy with myoclonic-atonic seizures is unsuccessful, consider the following as third-line monotherapy or add-on treatment options: • clobazam • ethosuximide	Whilst the benefits and risks of topiramate have changed it was decided that it should be an option for childhood-onset epilepsies. Safety advice was added.

Previous recommendation in NG217	Revised recommendation(s)	Rationale
• zonisamide. If the first choice is unsuccessful, consider the other third-line options. In April 2022, these were off-label uses of clobazam as monotherapy in adults and children, and add-on therapy in children under 6 months, and topiramate and zonisamide in adults and children. See NICE's information on prescribing medicines.	• topiramate (do not use topiramate in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled) • zonisamide. If the first choice is unsuccessful, consider the other third-line options. In January 2025, these were off-label uses of clobazam as monotherapy in adults and children, and add-on therapy in children under 6 months, and topiramate and zonisamide in adults and children. See NICE's information on prescribing medicines.	

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