Injuries following in utero exposure to sodium valproate

A guide to ACC cover

July 2020

This document summarises the scientific research on the impact of exposure to valproate in utero and discusses when ACC can cover this as treatment injuries under the Accident Compensation Act 2001.

This document is not a guideline for clinical practice. It aims to improve transparency and consistency of ACC cover decisions. ACC considers each claim on its own merit, taking into account all the circumstances of the case.

Background

In utero exposure to anti-seizure medicines (anticonvulsants) is associated with a broad range of pathologies. When a child has dysmorphic features combined with other malformations, sometimes the term 'Fetal Anticonvulsant Syndrome' (FACS) is used.

FACS is an umbrella term that includes a range of pathologies, including Fetal Valproate Spectrum Disorder (FVSD), which is specifically related to exposure to sodium valproate.

The purpose of this document is to clarify the extent of ACC cover for injuries following in utero exposure to sodium valproate, including cover for mental injuries that arise because of physical injuries.

Cover

The assessment of the affected person to establish cover for personal injury is informed by the criteria for diagnosis established through the specialists' consensus [1]. Deciding ACC cover requires a different approach from establishing a potential or definite diagnosis of FVSD.

A diagnostic assessment by a multidisciplinary team will provide all the relevant information to support the claim lodgement and cover assessment. The multidisciplinary team may include paediatrics, general physicians, neurologists, clinical geneticists, speech-language therapists and other relevant clinical experts. Providing the diagnostic assessment and lodging the claim when indicated by the guidance provided below are likely to reduce delays in ACC decisions on cover and will assist in managing any entitlements for covered injuries. If specific diagnostic testing is needed, the lead clinician should contact ACC on 0800 735 566 extension 45275 to discuss the potential for ACC funding.

Consideration criteria for Fetal Valproate Spectrum Disorder (FVSD)

Note: Physical features of FVSD may become more apparent over time.

Each claim is considered on the individual circumstances and treatment provided.

For ACC to cover the injury, all the **essential criteria** described in Table 1 need to be met.

Table 1: Essential criteria

Essential criteria	Notes
Exposure to valproate during this pregnancy is confirmed	Doses and duration of valproate therapy need to be confirmed.
Alternative congenital causes are ruled out	In some circumstances a chromosomal microarray is not indicated (e.g. isolated spina bifida).
Clinical investigations and molecular genetic analysis, appropriate for the clinical presentation, do not reveal an alternative explanation for the phenotype	Variants of uncertain significance may be uncovered with genetic testing. In these circumstances clinical judgement of likelihoods is needed. Evaluation of parents is not required but may assist clinical management in some circumstances.
No other recognisable diagnosis explains the phenotype	Assessment by a relevant medical professional and/or clinical geneticist identifies physical injuries sufficient to reach a positive diagnosis of FVSD, AND excludes other teratogenic disorders which overlap (such as Fetal Alcohol Syndrome).

Injuries that are likely to be accepted

The following are regarded as physical injuries that can be caused by valproate exposure in utero and are likely to be accepted when the essential criteria are met.

Table 2: Injuries that are likely to be accepted

Physical injury	Comment
Spina bifida	
Metopic suture synostosis	
Facial dysmorphism including mandible or temporomandibular joint abnormalities	Where these are typical for valproate exposure.
Cleft palate	

Injuries that might be accepted

The following might be accepted as physical injuries when the essential criteria are met, and the constellation/extent of physical problems noted in Table 2 is sufficient to make a diagnosis of FVSD. If these abnormalities are noted alone, that is without other physical abnormalities also being present, it is unlikely that ACC would accept the claim.

Table 3: Injuries that might be accepted

Physical injury	Comment
Genitourinary malformations	Including cloacal abnormalities or hypospadias that are typical for valproate exposure.
Talipes requiring surgery, digital or hand abnormalities	Where these are typical for valproate exposure.
Congenital cardiac defect	If other typical physical injuries are also present.
Coloboma	If other typical physical injuries are also present.
Laryngomalacia	If other typical physical injuries are also present to explain this finding.

Claims that are unlikely to be accepted

Other features listed in Table 4 by Clayton-Smith et al (2019) are not physical injuries (e.g. social communication difficulty or cognitive dysfunction). Others may be physical injuries but are not sufficiently specific to be regarded by ACC as a physical injury that is part of FVSD (e.g. a Beighton score of six or more is also common in children or adolescents that do not have FVSD).

The following are *unlikely* to be accepted as physical injuries caused by exposure to valproate.

Table 4: Injuries that are unlikely to be accepted

Pathology	Comments
Stridor	Unless this is a result of laryngomalacia with facial dysmorphism also present.
Joint laxity	A non-specific feature commonly found in the general population.
Strabismus/refractive error	A non-specific feature commonly found in the general population.
Enuresis	A non-specific feature commonly found in the general population. Enuresis persisting after six years of age may require further investigation.
Eustachian tube dysfunction/glue ear/ hearing disorders	A non-specific feature commonly found in the general population.
Misshapen, discoloured or unevenly spaced teeth	A non-specific feature commonly found in the general population.

Mental injury

With regard to mental injuries that follow from the covered physical injuries, Wood et al (2014) reported changes to grey matter thickness in a group of seven-year-old children exposed to valproate compared to controls. This finding has not been replicated since no similar studies have been performed. Consequently, these studies are suggestive but still preliminary. Other human studies in the literature do not separate valproate from other exposures, and thus it is not possible to draw conclusions about the specificity of these findings.

ACC's approach to mental injury based on current medical knowledge and the relevant ACC legislation.

Current research results in relation to persons exposed to valproate in utero provide some support for macroscopic brain changes leading to clinically significant behavioural, cognitive or psychological impacts.

A definition of a mental injury is a *clinically significant behavioural, cognitive or psychological dysfunction*. It cannot be assumed that all the communication, behavioural, cognitive, mood or psychological challenges facing a person with physical characteristics typical for FVSD are in fact the result of a physical injury caused by the exposure.

Until further research is available, ACC uses the following approach to considering whether there is a mental injury because of a physical injury.

If **one** of these is present:

1. Facial dysmorphism characteristic of FVSD
2. Facial dysmorphism consistent with FVSD with either cleft palate OR mandible abnormalities also present
3. Facial dysmorphism consistent with FVSD with either cardiac abnormalities OR genitourinary abnormalities also present
4. Spina bifida
5. Metopic suture synostosis

then the following might be accepted as a result of a predicted brain injury from exposure to valproate:

1. Clinically significant social anxiety and communication difficulties diagnosed by a psychologist or psychiatrist.
2. Clinically significant cognitive deficits characteristic of FVSD when measured and confirmed by a psychologist.

The assessing psychologist/psychiatrist must provide an explanation of the clinical significance of these mental injuries, including the treatments or supports that are likely to be needed.

Entitlements

ACC provides a range of supports for people who have cover accepted for personal injury. In general, the support is for the covered injury.

Guideline development

The recent publication of FVSD diagnostic criteria led ACC to invite experts and consumer representatives to discuss the assessment and extent of injuries caused by exposure to valproate in utero.

The advisory group was provided with relevant scientific articles including the Clayton-Smith paper [1,2]. The group noted that Table 4 of that paper included essential, suggestive and supportive features for the diagnosis of FVSD. None of the suggestive or supportive criteria is specific to FVSD, so these features cannot be assumed to be a personal injury due to exposure to valproate.

The advisory group discussed this and other papers in detail and developed this guidance to assist whānau/family of people potentially affected by valproate exposure in utero, registered health professionals, and ACC staff when assessing requests for treatment injury cover or requests for support from ACC.

Future updates

ACC anticipates current and future research will improve understanding of the impacts of valproate and other anticonvulsants on unborn children. ACC will incorporate insights from future research as new scientific evidence becomes available. This guide will be updated in future years.

References

1. Clayton-Smith J, Bromley R, Dean J, Journel H, Odent S, Wood A, et al. Diagnosis and management of individuals with Fetal Valproate Spectrum Disorder; A consensus statement from the European Reference Network for Congenital Malformations and Intellectual Disability. *Orphanet Journal of Rare Diseases*. 2019;14:180.
2. Wood A, Chen J, Barton S, Nadebaum C, Anderson V, Catroppa C, et al. Altered cortical thickness following prenatal sodium valproate exposure. *Annals of Clinical and Translational Neurology*. 2014;1(7):497–501.

Acknowledgements

ACC would like to thank our partners for their assistance in producing this guide:

- Professor Amanda Wood – Neuropsychologist
- Denise Astill – FACS NZ
- Dr Greg Finucane – Neuropsychiatrist
- Jen Foulkes – FACS NZ
- Dr Kate Gibson – Geneticist
- Lisa Gallacher – Speech-Language therapist
- Dr Liza Edmonds – Paediatrician
- Megan Fowler – Neuropsychologist
- Dr Stephen Robertson – Geneticist
- Dr Warwick Smith – Paediatrician