

**APPEAL AGAINST THE FINAL EVALUATION DETERMINATION FOR
SEBELIPASE ALFA FOR THE TREATMENT OF LYSOSOMAL ACID LIPASE
DEFICIENCY**

**Legal Submissions in Support of Appeal Point 1.8: The Committee has Failed to
Consider the Status of Children with Juvenile-Onset Lysosomal Acid Lipase Deficiency
in Accordance With the Provisions of the Human Rights Act 1998**

Lysosomal acid lipase deficiency (LAL-D) is predominantly a childhood condition that can rapidly progress with serious complications occurring at an early age. Infants presenting with LAL-D represent a medical emergency as they experience a rapidly progressive condition generally leading to death within the first year of life. Estimates suggest that approximately 50% of children and adults with LAL Deficiency progress to fibrosis, cirrhosis, and liver transplant within 3 years from clinical manifestation onset.

In the above circumstances Alexion submits that the Evaluation Committee is required to give particular consideration to the situation of those patients with juvenile-onset LAL-D as children, in accordance with the requirements of the Human Rights Act 1998 (the HRA).

Legislation

Alexion refers the Panel in particular to the following provisions of the HRA:

Section 6(1) of the HRA states:

“It is unlawful for a public authority to act in a way which is incompatible with a Convention right”.

The European Convention on Human Rights (the Convention) is provided at Schedule 1 to the HRA and includes the following fundamental rights:

Article 2: the right to life, which commences at Article 2(1) with the statement: “Everyone’s right to life shall be protected by law”.

Article 3: the prohibition of torture, which states: “No one shall be subjected to torture or to inhuman or degrading treatment or punishment.”

Article 8: the right to respect for private and family life, which states at Article 8(1): “Everyone has the right to respect for his private and family life, his home and his correspondence.”

Article 14: prohibition of discrimination, which states: “The enjoyment of the rights and freedoms set forth in this Convention shall be secured without discrimination on any ground such as sex, race, colour, language, religion, political or other opinion, national or social origin, association with a national minority, property, birth or other status.”

Case Law

Following the decision of the Appeal Panel who considered the appeal in relation to the appraisal of dinutuximab, the fact that Articles 2, 8 and 14 are engaged in the context of the evaluation of sebelipase alfa is established. However the following authorities illustrate the practical implications of those Articles and, in the case of Article 3, confirm that it is engaged by the evaluation process.

Article 2

Article 2 does not only require a state to refrain from intentionally depriving persons of life, it also includes a positive obligation to save life. Therefore, in Scialacqua v Italy DR 81, 35, the European Commission on Human Rights suggested that Article 2 might impose on States

“...the obligation to cover the costs of certain medical treatments or medicines that are essential in order to save lives.”

While the application in Scialacqua was dismissed on other grounds it confirms the requirement to consider the application of Article 2 in these circumstances.

The English Courts have also reached similar conclusions.

Even before the HRA came into effect, the English Courts have recognised the value of human life in the context of life-saving treatment. Therefore in R v Cambridge Health Authority, ex parte B [1995] 1WLR 898, Lord Bingham stated:

‘Our society is one which a very high value is put on human life. No decision affecting human life is one that can be regarded with other than the greatest seriousness.’

While ex parte B involved treatment that had such a small risk of success that it could be considered experimental. In cases where the treatment has a high likelihood of saving the patient’s life, the courts will no doubt require a higher degree of justification for the refusal of the treatment.

In NHS Trust A v M and NHS Trust B v H [2001] Fam 348, a hospital sought permission to withdraw artificial hydration and nutrition from a person diagnosed as being in a permanent vegetative state. The Court in that case, noted that Article 2 imposed a positive obligation to give treatment where that is in the best interests of the patient. While treatment in the case under consideration would have been futile and therefore discontinuing treatment would not be an intentional deprivation of life under Article 2, the Court commented that any withdrawal of treatment would need to be in line with a respected body of medical opinion and that the patient should be unaware and not suffering, in order to ensure that there was no inhuman or degrading treatment for the purposes of Article 3. Clearly this case involved standard treatment, rather than the introduction of a new therapy, again the case provides authority for the proposition that failure to provide necessary medical treatment requires consideration of the implications in the context of Article 2.

In R (Burke) v General Medical Council [2005] EWCA 1003, the Court noted:

“There is a very strong presumption in favour of taking all steps to prolong life and, save in exceptional circumstances or where the patient is dying, the best interests of the patient will normally require such steps to be taken. In case of doubt, that doubt falls to be resolved in favour of the preservation of life.”

Article 3

The deprivation of vital medical treatment may amount to inhuman and degrading treatment in breach of Article 3. In D v United Kingdom (1997) 24 EHRR 43, ECtHR, the European Court of Human Rights considered the proposed expulsion of a convicted drug trafficker with advanced AIDS to a country where it was accepted that the absence of vital medical treatment would rapidly accelerate his death. The Court concluded that such treatment would constitute a violation of Article 3, in the context of the particular circumstances of the case.

Mental suffering, such as that experienced by a parent, is sufficient to fall within the definition of inhuman and degrading treatment for the purposes of Article 3.

In Kurt v Turkey (1998) 27 ECRR 373, ECtHR, the Court held that a mother who suffered anguish as a result of the disappearance of her son following his detention by the authorities, was herself to be regarded as a victim under Article 3.

Osmanoglu v Turkey Application 48804/99 (2008) ECtHR involved the failure by the authorities to investigate the disappearance of the applicant's son. Again the failure was found to constitute a breach of Article 3.

In considering whether mental anguish is sufficient to bring a case within the scope of Article 3, key factors will be the proximity of a family tie, the closeness of the relationship with a person who has suffered harm, the extent to which the harm was witnessed and the actions of the authorities. These factors are directly impacted in the case of a parent who witnesses a child suffer pain, disability and potentially death in circumstances where an effective treatment is available but the State refuses to make it available.

Article 8

The construction of Article 8 under the Convention is broad and covers a wide range of personal interests, including physical or bodily integrity, family life, the home and the home environment.

The European Court of Human Rights, accepted in Pentiacova v Moldova (2005) 40 EHRR SE 23 that Article 8 requires consideration of access to medical treatment.

Article 14

The convention also includes a prohibition on discrimination, based on the substantive rights and freedoms set out in other articles. In the context of the evaluation of sebelipase alfa, the fact that children with HPP are deprived a treatment, constitutes, in the submissions of Alexion, discrimination based on grounds of age.

The decision of the Appeal Panel who considered the Final Appraisal Determination for dinutuximab for treating high-risk neuroblastoma

The appellant, Solving Kids Cancer (SKC), in the appeal against the final appraisal determination for dinutuximab for treating high-risk neuroblastoma, challenged the conclusions of the Appraisal Committee in that case, on the basis that “there [had] been a breach of section 11 of the Children Act 2004, Article 3 of the United Nations Convention on the Rights of the Child and human rights legislation”. Neuroblastoma is a malignancy that predominantly affects children. SKC argued that there was no evidence in the committee papers that the Committee had considered the special position of children or treated their best interests as a primary concern. In response to these concerns, the Chairman of the Appraisal Committee stated that the Committee had been prepared to consider the appraisal flexibly; they recognised that the benefit of a response in children could be greater than in adults, that an extension to life could be valued more highly in that group and had considered the stress and anxiety caused to parents and the impact of bereavement on parents. The Chairman stated that the Committee would have accepted a higher ICER for this population than it would have done for an adult population.

The Appeal Panel in that case concluded:

- They were not persuaded that the UN Convention on the Rights of the Child applied to the work of the Appraisal Committee;
- They were not persuaded that there was as such a requirement to document a specific consideration of what was in the interests of children;
- The Panel agreed that articles 2, 8 and 14 of the European Convention on Human Rights were engaged by the decision;
- The Panel recognised that the status of patients as children could be relevant purely on ordinary public law principles and it noted the Public Sector Equality Duty;
- In the context of the appraisal of dinutuximab, “the Panel was not satisfied, given the lack of specific evidence in the FAD that sufficient consideration had been given to the position of the patients as children”. The Panel stated that while “the law did not require that status to have a paramount or even a primary weight”, it “did consider that it was a relevant issue and one that had to rank as one among the many important considerations that the Committee had to deal with”. The Panel was “not satisfied that the Committee’s treatment of the issue met that requirement”.

The particular features of the Appraisal Committee’s appraisal of dinutuximab, which resulted in that conclusion by the Panel were:

- i. There was no written evidence in the FAD that the particular status of patients as children had been taken into account by the Committee (while written consideration was not a requirement in itself, in the absence of contemporaneous documents, the Panel concluded that it should be cautious about accepting later evidence);
- ii. There was no evidence that any explicit discussion regarding the status of patients as children had taken place;

- iii. The Panel referred specifically to the End of Life Policy and the fact that, while the Committee had understood that NICE's guidance could be departed from, it had failed to consider the policy in relation to dinutuximab, because the extent of the departure that would have been needed was substantially larger than that considered in other cases involving treatment of adults; this however assumed that the End of Life Policy would apply to children in the same way as it would apply to adults.
- iv. Even if the Committee had not been given quantifiable data as regards important factors that may differ as between adult and child patients (e.g. quality of life and bereavement of parents) a discussion of the issues by the whole Committee was still a requirement and should be documented in the FAD.

For these reasons, the Panel concluded that the Appraisal Committee's consideration of the dinutuximab appraisal had been inadequate and upheld the appeal on this point.

The evaluation of sebelipase alfa for the treatment of juvenile-onset lysosomal acid lipase deficiency

Consistent with the legislation and case law described above and the decision of the Appeal Panel which considered the dinutuximab appeal, the HRA is engaged by the current evaluation of sebelipase alfa. The requirements of the Act have however been breached in relation to the conduct of the evaluation for the treatment of juvenile-onset LAL-D in children:

- The recommendations of the Evaluation Committee as set out in the FED will potentially deprive infants and children with LAL-D of life (and, based on current evidence, normal life), contrary to Article 2 of the European Convention on Human Rights (ECHR).
- Refusing to recommend effective, potentially life-saving treatment with sebelipase alfa to children with LAL-D, a serious disorder, constitutes inhuman and degrading treatment to both children and their parents contrary to Article 3 ECHR.
- Refusing to recommend effective treatment with sebelipase alfa to infants and children with LAL-D, a serious disorder, constitutes a denial of the right to family life and privacy, contrary to Article 8 ECHR.
- The Evaluation Committee's refusal to recommend treatment with sebelipase alfa, principally affects children and is therefore discriminatory based on age, contrary to Article 14 ECHR.

Alexion does not suggest that the Evaluation Committee was not aware, in general terms, that patients eligible for treatment with sebelipase alfa are children, but simply that the Committee has failed adequately to consider the particular situation of children in the course of its evaluation or the requirement to protect the welfare of children. This is demonstrated by the following matters:

- a) the FED documents no discussion or consideration of the particular situation of patients affected by the evaluation in the context of their status as children;

- b) the summary tabulation at the end of the FED confirms that, while the Committee considered whether there was any objection to considering patients with early and late-onset LAL-D (a determination based on age at diagnosis) separately as two distinct populations, the Committee gave no other consideration to the implications of its evaluation or recommendations in the context of its equalities obligations;
- c) there is no indication that the Committee gave any consideration to whether the evaluation should be modified to reflect end of life considerations in certain groups of patients with LAL-D (e.g. infants with rapidly progressive disease);
- d) there is no indication that the Committee took into account the impact of bereavement on parents of infants with LAL-D when making its recommendations;
- e) there is no indication that the Committee took into account the suffering of parents as a result of the deprivation of available, potentially life-saving treatment from their children when making its recommendations; and
- f) to the extent that the Committee was not provided with specific evidence on these matters, it was, nevertheless not prevented from discussing them and recording those discussions.

Consistent with the decision of the Appeal Panel in the dinutuximab case, Alexion does not suggest that the human rights considerations set out above are paramount. However the fact that they have not been considered in this case represents a deficiency in the process. We refer to the conclusion of the Panel in dinutuximab:

“Provided the Committee asks itself whether its approach should change to reflect the fact that the population targeted for this technology are children, and gives a reasoned answer, it will have corrected the error identified by the Panel. What it should then do will be a matter for its judgement and will depend on whether or not it considers a different approach is needed and the evidence available to it”

While the Evaluation Committee has referred to budgetary constraints as providing justification for a refusal to recommend use of sebelipase alfa, in circumstances where the consequences of that decision are extreme - children with LAL-D will die - the Committee is required to demonstrate that a balancing of national priorities and individual human rights has been conducted and is clearly evidenced in the decision-making process.

We therefore respectfully submit that this evaluation should be returned to the Evaluation Committee for further consideration of the implications of human rights legislation in the context of the status of patients eligible for sebelipase alfa therapy as children.