Solving Kids' Cancer Response to NICE's Legal Advisor's Submissions on Human Rights and the Rights of the Child (Ground 1b)

Introduction

1. This note sets out Solving Kids' Cancer's response to the Memorandum dated September 2016 from the legal representative to the Appeal Panel (, DAC Beachcroft) in respect of our submissions on human rights and the rights of the child in this appeal (the Memo).

2. There can be no doubt that NICE, as a public body, is bound in its appraisals to take account of human rights legislation, including that relating to the rights of the child. The Memo acknowledges and accepts that NICE is obliged to comply with the European Convention on Human Rights (the ECHR). The Memo also rightly accepts that Articles 2, 8 and 14 of the ECHR are engaged by NICE's appraisal of dinutuximab. However, with respect, we disagree that the UN Convention on the Rights of the Child (the UN Convention) does not apply to NICE and that Article 3 of the ECHR is not engaged in this appeal.

3. Solving Kids' Cancer will address below why the UN Convention applies to this appeal and provide in turn its comments on the legal submissions in the Memo concerning Articles 2, 3, 8 and 14 of the ECHR.

UN Convention

4. The Memo concludes at § 9 in respect of the UN Convention *"that it does not as such impose any obligations on NICE."* The reasons provided are that the *"UN Convention does not have direct effect in UK law"* (§ 6) and that *"none of the legislative provisions that establish NICE make reference to children as a special case. Whether or not that is compatible with the UK's international obligations would not be relevant to the question of whether NICE itself has acted lawfully. The Panel should be wary about applying the UN Convention directly to NICE..."* (§ 8).

5. Solving Kids' Cancer disagrees that NICE is not obliged to comply with the UN Convention. The UK became a State Party to the UN Convention in 1991. As the Memo points out, the UN Convention has not been directly implemented into domestic law, the UK Supreme Court has confirmed that the 'spirit' if not the letter of the UN Convention is binding in relation to decisions concerning children. For example, in the case *ZH (Tanzania) v Secretary of State for the Home Department* [2011] UKSC 4, the Court held at §§ 23-25 that:

> *"[Article 3(1) of the UN Convention] is a binding obligation in international law, and the spirit, if not the precise language, has also been translated into our national law.*
> *[....]*

Further, it is clear from the recent jurisprudence that the Strasbourg Court will expect national authorities to apply article 3(1) of UNCRC and treat the best interests of a child as "a primary consideration.""

6. Additionally, all human rights are universal, indivisible, interdependent and interrelated. For example, in *Neulinger v Switzerland* (2010) ECHR 1053, at § 131, the European Court for Human Rights (ECtHR) observed that:

> *"the [UN] Convention cannot be interpreted in a vacuum but must be interpreted in harmony with the general principles of international law. Account should be taken ... of 'any relevant rules of international law applicable in the relations between the parties' and in particular the rules concerning the international protection of human rights."*

The ECtHR went on to note, at § 135 that:

> *"there is currently a broad consensus – including in international law – in support of the idea that in all decisions concerning children, their best interests must be paramount."*

7. Lady Hale quoted with approval the above observation of the ECtHR in *ZH (Tanzania)* that *"the Convention cannot be interpreted in a vacuum but must be interpreted in harmony with the general principles of international law" (ZH (Tanzania) at §21).* More recently the Supreme Court observed that *"the Convention rights protected in our domestic law by the Human Rights Act can also be interpreted in the light of international treaties, such as the [UN Convention on the Rights of the Child] UNCRC, that are applicable in the particular sphere" (see SG v Secretary of State for Work and Pensions* [2015] UKSC 16 at § 83). The Supreme Court, therefore, has affirmed that the UN Convention is binding in domestic law where an ECHR right is engaged, as is the case in this appeal.

8. NICE as a public body accepts that it is bound in its appraisals to take account of human rights legislation. For the reasons set out above, Solving Kids' Cancer submits that NICE's obligation extends to complying with the provisions of the UN Convention.

9. Further, in the cases of *SG v Secretary of State for Work and Pensions* [2015] UKSC 16 at § 106 and *Mathieson v Secretary of State for Work and Pensions* [2015] UKSC 47 at § 39, the Supreme Court adopted the UN Committee on the Rights of the Child's meaning of "best interests," which provides that Article 3(1) is directly applicable:

> *"... the child's best interests is a threefold concept:*
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> *(a) A substantive right: The right of the child to have his or her best interests assessed and taken as a primary consideration when different interests are being considered in order to reach a decision on the issue at stake, and the guarantee that this right will be implemented whenever a decision is to be made concerning a child, a group of identified or unidentified children or children in general.* ***Article 3, paragraph 1, creates an intrinsic obligation for***

States, is directly applicable (self-executing) and can be invoked before a court.

(b) *A fundamental, interpretative legal principle: If a legal provision is open to more than one interpretation, the interpretation which most effectively serves the child's best interests should be chosen. The rights enshrined in the Convention and its Optional Protocols provide the framework for interpretation.*

(c) ***A rule of procedure: Whenever a decision is to be made that will affect a specific child, an identified group of children or children in general, the decision-making process must include an evaluation of the possible impact (positive or negative) of the decision on the child or children concerned. Assessing and determining the best interests of the child require procedural guarantees. Furthermore, the justification of a decision must show that the right has been explicitly taken into account. In this regard, States parties shall explain how the right has been respected in the decision, that is, what has been considered to be in the child's best interests; what criteria it is based on; and how the child's interests have been weighed against other considerations, be they broad issues of policy or individual cases.***" (General Comment No 14 (2013), adopted by the UN Committee on the Rights of the Child at § 6, emphasis added).

10. Additionally, NICE may only exercise its functions relating to the provision of NHS services, public health services, or social care in England on the direction of the Secretary of State for Health and/or NHS England and subject to those directions (*see*, for example, Section 237 of the Health and Social Care Act 2012) and therefore there is a legitimate expectation that NICE is bound to take into account the State's obligation to protect the rights of the child in discharging its functions and to act in a manner consistent with the UK's international obligations. Indeed, absent a clear legislative or executive statement to the contrary, the national courts recognise a legitimate expectation that persons or bodies acting on behalf of a State or in exercise of governmental authority will comply with international treaty obligations (*see*, for example, *European Roma Rights Centre v Immigration Officer at Prague Airport (UN High Commissioner Intervening)* [2004] UKHL 55 where the House of Lords, referring to the International Covenant on Civil and Political Rights, found that UK immigration officers operating under the authority of the Home Secretary acted unlawfully).

11. Accordingly, Solving Kids' Cancer submits that the UN Convention applies to NICE. The suggestion in the Memo that the UN Convention is of no assistance and does not apply to NICE therefore must be rejected.

Article 24(1) of the UN Convention

12. The Memo acknowledges that Article 24(1) of the UN Convention requires that children should not be disadvantaged in decisions concerning what medicines should be made available (§ 12). This is consistent with the UN Committee on the Rights of the Child's

position that "[t]*he child's right to health (art. 24) and his or her health condition are central in assessing the child's best interest*" (see General Comment No 14 (2013), adopted by the UN Committee on the Rights of the Child at § 77). The Memo goes on to say that in order to comply with this obligation, the Appeal Panel must decide *"whether all material issues relating to the patient group have been considered in this case and whether NICE's procedures might systematically disadvantage children's treatments"* (§ 12).

13. Solving Kids' Cancer submits that the Appraisal Committee did not consider the material characteristics of the paediatric population nor the impact of its decision on this vulnerable group during the appraisal of dinutuximab. Instead, NICE rigidly applied its inflexible standard methodologies and cost effective thresholds, which were not designed for evaluating novel paediatric drugs for rare conditions. Nor did it consider whether the interests of children should been weighed against other considerations and whether this requires the exercise of appropriate discretion. Rather, dinutuximab was simply appraised in a manner that was likely to result in a finding that it was "cost ineffective," as the incremental cost-effectiveness ratios generated for orphan drugs are almost always outside the cost-effectiveness thresholds acceptable to NICE when appraising such drugs on its standard technology process.

14. In fact none of NICE's appraisal processes or procedures make reference to children as a special case nor take into account the material characteristics of this group. For example, NICE imposes an arbitrary 2-year life-expectancy threshold for its special end-of-life criteria. This does not take into account that children live longer after cancer diagnosis than adults (80% versus 66% survive 5 years after diagnosis).[1] Moreover, the implications of increased life expectancy for a child is not the same as those for an adult patient and therefore it is inappropriate and unreasonable to apply the same metrics for assessing interventions in adults as in children.

15. In the present case, even on the Appraisal Committee's preferred assumptions, dinutuximab extends the life of the child on average up to 2.81 life years compared to isotretinion alone (Final Appraisal Determination at § 4.22). That is, on average patients could expect to live for nearly 3 years longer if treated with anti-GD2-based immunotherapy rather than retinoic acid maintenance alone. However, as the median life expectancy of paediatric patients with neuroblastoma exceeds NICE's 2-year life-expectancy threshold for its special end-of-life criteria, the Appraisal Committee could not use its discretion and apply these special criteria (Final Appraisal Determination at § 4.21). Perversely, dinutuximab failed on the criterion for shortened life expectancy, that is, paediatric patients' life expectancy was not short enough. However, as noted by the international paediatric cancer research community, *"while a life expectancy of 4 years may be considered too long for a 73-year old, it is beyond difficult to consider it too long when applied to a 3-year-old."*[2] Further, as noted by a parent advocate *"the current*

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[1] See Howlader N, Noone AM, Krapcho M, *et al.* (eds). SEER Cancer Statistics Review, 1975-2011, National Cancer Institute. Bethesda, MD (http://seer.cancer.gov/csr/1975_2011/) based on November 2013 SEER data submission, posted to the SEER web site, April 2014; available at: http://seer.cancer.gov/archive/csr/1975_2011/results_merged/topic_survival.pdf

[2] Adamson PC, Park JR, Pearson AD. *When Life Expectancy is Not Short Enough: A Perspective on the National Institute for Health and Care Excellence (NICE) Preliminary Guidance for Dinutuximab.* Pediatric Blood & Cancer. 2016 Jan 6.

NICE approach uses a single definition for short life expectancy, implying that a toddler who might survive 4 years after diagnosis is less deserving of special consideration than a senior citizen who has been told that he/she will live only for another 18 months."[3] Accordingly, NICE's rigid inflexible policies are unfair and biased towards children and disadvantage life-extending paediatric treatments for rare conditions.

16. Further, NICE's use of its standard criteria for appraising novel paediatric treatments not only systematically disadvantages current children's treatments, but has far reaching implications for future treatments. Anti-GD2-based immunotherapy is of considerable importance in the context of high-risk neuroblastoma in children, a highly-aggressive cancer with poor long-term overall survival and limited therapeutic options. Over the past two decades, only approximately 50% of patients with newly diagnosed high-risk neuroblastoma, and well less than 10% of patients whose disease recurs, will survive.[4] In the UK, neuroblastoma accounts for approximately 10% of all deaths from childhood cancer.[5] Further, due to the *ultra*-rare orphan disease status of high-risk neuroblastoma, affecting only 350 children per year in the US (population 315 million), industry has traditionally been reluctant to invest in the development of novel therapies for the condition. Indeed, dinutuximab was not developed by industry, but rather by US government funding through the US National Cancer Institute over the course of 25 years before industry became involved.[6]

17. Treatment of high-risk neuroblastoma is one of the most intense medical interventions for cancer, and is extraordinarily toxic. Anti-GD2-based immunotherapy, used to stimulate the immune system to permanently kill microscopic traces of disease that can cause relapse, is the least toxic and does not create additional late effects to damage children. Consequently, dinutuximab, which has demonstrated efficacy, is now considered as part of the standard of care for children with high-risk neuroblastoma in Europe and the US.[7]

18. Further, many European centres, including those in the UK, are currently investigating dinutuximab-beta (APN311), another anti-GD2 monoclonal antibody, as a part of an ongoing International Society of Paediatric Oncology Europe Neuroblastoma Group trial for children with neuroblastoma. The study is critically important, as *"it is exploring the role of IL-2, a drug that contributes substantially to the toxicity of the regimen developed by the COG, in combination with antibody."*[8]

19. If NICE maintains its current position and policies, there is very little prospect of an Appraisal Committee positively recommending other anti-GD2 monoclonal antibodies for high-risk neuroblastoma, such as dinutuximab-beta. The implication of the Appraisal

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[3] Bernstein J. *Restricting Access to Hope: A Parent's Perspective on the National Institute for Health and Care Excellence (NICE) Preliminary Guidance for Dinutuximab.* Pediatric Blood & Cancer. 2016 Jan 6.
[4] *Ibid.*
[5] See Cancer Research UK's children's cancer statistics; available at: http://www.cancerresearchuk.org/health-professional/cancer-statistics/childrens-cancers/mortality%20-%20heading-One
[6] *Supra* Note 2.
[7] *Ibid* and Statement from CCLG in response to decision by NICE not to recommend Dinutuximab for treatment of high-risk neuroblastoma, dated 15 July 2016; available at: http://www.cclg.org.uk/news/statement-from-cclg-in-response-to-decision-by-nice-not-to-recommend-dinutuximab-for-treatment-of-high-risk-neuroblastoma
[8] *Supra* Note 2.

Committee's non-recommendation of dinutuximab, therefore, means that patients in the UK are not only denied access to the sole approved drug specifically developed for the treatment of neuroblastoma, but also will likely be denied access to other anti-GD2 antibodies in development. The lack of anti-GD2 monoclonal antibody for therapeutic use in the UK will have a significant impact on paediatric patients and is of serious concern to clinicians and the international research community.[9]

20. For the reasons set out above, NICE's appraisal of dinutuximab is in breach of Article 24 of the UN Convention, coupled with a breach of Article 3(1) of the UN Convention, as discussed below.

Article 3(1) of the UN Convention

21. For the reasons set out above, the UN Convention applies to NICE. Even if the Appeal Panel were to follow the advice in the Memo, Article 3(1) of the UN Convention, unlike the other Articles of the Convention, is not specifically addressed to the State Parties. Rather Article 3 is broader in scope and imposes an obligation on public bodies to act in the best interests of the child. Specifically, Article 3(1) of the UN Convention provides that:

> *"**In all actions concerning children**, whether **undertaken by public** or private **social welfare institutions**, courts of law, administrative authorities or legislative bodies, **the best interests of the child shall be a primary consideration**."* (Emphasis added)

22. The UN Committee on the Rights of the Child has clarified that the term "*public or private social welfare institutions*" should not be narrowly construed or limited to social institutions *stricto sensu*, but should be understood to mean all institutions whose work and decisions impact on children and the realisation of their rights, including amongst others, *"those related to economic, social and cultural rights (e.g. care, **health**, environment, education, business, leisure and play, etc.)"* (General Comment No 14 (2013), adopted by the UN Committee on the Rights of the Child at § 26, emphasis added). We submit that NICE, as a public health care body, is obliged to take into account the best interests of the child during technology appraisals.

23. The Memo suggests that Article 3(1) requires *"the best interests of the child to be a primary consideration. It does not rule out other considerations and it does not require paramountcy"* (§ 13).

24. Firstly, Solving Kids' Cancer has from the outset acknowledged that NICE has difficult decisions to make about the allocation of resources, which requires the balancing of different needs and considerations. However, any decision about whether to recommend a technology must be taken lawfully and rationally in accordance with NICE's obligations as a public body.

25. Secondly, there is no evidence that the Appraisal Committee took into account the best interests of the child, let alone that it was a primary consideration, in the appraisal of

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[9] *Supra* Note 7.

dinutuximab. Thirdly, although the best interests of the child is not a factor that will prevail over all others, *"it is a factor that must rank higher than any other. It is not merely one consideration that weighs in the balance alongside other competing factors"* (see *ZH (Tanzania)* [2011] UKSC 4 at § 46).

26. In the case of *ZH (Tanzania)*, the Supreme Court set out the proper approach to reaching decisions that will affect a child, stating that as a starting point decision-makers should take into consideration the best interests of the child and then assess whether their best interests are outweighed by the strength of any other considerations. Lady Hale went onto to cite two Australian cases, as illustrative examples of the correct approach:

> *"... As Mason CJ and Deane J put it in the case of Minister for Immigration and Ethnic Affairs v Teoh [1995] HCA 20, (1995) 183 CLR 273, 292 in the High Court of Australia:*
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> > *"A decision-maker with an eye to the principle enshrined in the Convention would be looking to the best interests of the children as a primary consideration, asking whether the force of any other consideration outweighed it."*
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> *As the Federal Court of Australia further explained in Wan v Minister for Immigration and Multi-cultural Affairs [2001] FCA 568, para 32,*
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> > *"[The Tribunal] was required to identify what the best interests of Mr Wan's children required with respect to the exercise of its discretion and then to assess whether the strength of any other consideration, or the cumulative effect of other considerations, outweighed the consideration of the best interests of the children understood as a primary consideration."*
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> *This did not mean (as it would do in other contexts) that identifying their best interests would lead inexorably to a decision in conformity with those interests.* ***Provided that the Tribunal did not treat any other consideration as inherently more significant than the best interests of the children, it could conclude that the strength of the other considerations outweighed them. The important thing, therefore, is to consider those best interests first. That seems, with respect, to be the correct approach to these decisions in this country as well as in Australia."*** (emphasis added)

Lord Kerr agreed with Lady Hale's judgment above and went on to say that:

> *"It is a universal theme of the various international and domestic instruments to which Lady Hale has referred that, in reaching decisions that will affect a child, a primacy of importance must be accorded to his or her best interests. This is not, it is agreed, a factor of limitless importance in the sense that it will prevail over all other considerations. It is a factor, however, that must rank higher than any other.*

> *It is not merely one consideration that weighs in the balance alongside other competing factors.* ***Where the best interests of the child clearly favour a certain course, that course should be followed unless countervailing reasons of considerable force displace them.*** *It is not necessary to express this in terms of a presumption but* ***the primacy of this consideration needs to be made clear in emphatic terms.*** *What is determined to be in a child's best interests should customarily dictate the outcome of cases such as the present, therefore, and it will require considerations of substantial moment to permit a different result."* (emphasis added)

27. Further, the decision-maker must explicitly demonstrate that they have taken the right into consideration following the Supreme Court's adoption of the UN Committee on the Rights of the Child's meaning of "best interests." For example, in *Mathieson v Secretary of State for Work and Pensions* at § 39 the Supreme Court held that:

> *"The first aspect of the concept is the child's substantive right to have his best interests assessed as a primary consideration whenever a decision is made concerning him. The second is an interpretative principle that, where a legal provision is open to more than one interpretation, that which more effectively serves his best interests should be adopted. The third is a "rule of procedure", described as follows:*
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> > *"Whenever a decision is to be made that will affect a specific child, an identified group of children or children in general, the decision-making process must include an evaluation of the possible impact (positive or negative) of the decision on the child or children concerned ...* ***Furthermore, the justification of a decision must show that the right has been explicitly taken into account"*** (emphasis added)

28. Procedurally, this requires that the decision-maker *"shall explain how the right has been respected in the decision, that is, what has been considered to be in the child's best interests; what criteria it is based on; and how the child's interests have been weighed against other considerations, be they broad issues of policy or individual cases"* (General Comment No 14 (2013), adopted by the UN Committee on the Rights of the Child at § 6).

29. NICE's appraisal of dinutuximab did not explicitly, nor even in substance, consider the best interests of the child and therefore is in breach of Article 3(1) of the UN Convention.

Article 2 of the ECHR

30. The Memo considers the cases of *Scialacqua v Italy* DR 81, 35 and *NHS Trust A v M* [2001] Fam 348 in relation to Article 2. Solving Kids' Cancer does not accept some of the analysis put forward, in particular that the Commission's rejection of the application in *Scialacqua* due to the treatment in question being a herbal remedy not an officially recognised medicine (unlike dinutuximab) is in principle the same as enabling the State decide which life-saving treatments it provides. However, as the Memo correctly accepts that Article 2 is engaged (§ 28) and concludes that in respect of NICE's appraisal of dinutuximab, Article 2 requires *"a fair balance to have been struck between the needs of*

these patients, and the needs of patients at large" (§ 28), it is unnecessary to burden the Appeal Panel with a detailed rebuttal.

31. Solving Kids' Cancer recognises that public resources are finite, and that Article 2 does not impose an obligation on the State to provide unlimited resources for medical treatment. Rather, in exceptional life-saving situations, as in this case, it is unjustified and hence contrary to Article 2 for NICE not to recommend dinutuximab.

32. Reference to decided cases is of limited assistance in determining whether an interference with Article 2 is justified. This is a fact-sensitive question that the Appeal Panel must decide taking into consideration the circumstances of each case. In the present case, dinutuximab is a life-saving treatment and (even on its preferred assumptions) the Appraisal Committee accepted that for those patients that it does not represent a cure, dinutuximab extends the life of the child on average up to 2.81 life years compared to isotretinion alone (Final Appraisal Determination at § 4.22). In the context of the paediatric population the extension of life provided by dinutuximab of nearly 3 years is even more acute given the median life expectancy for children with high-risk neuroblastoma is 4 years. Further, dinutuximab represents the least toxic therapeutic option for high-risk neuroblastoma and the only product specifically developed and approved for this condition. NICE's non-recommendation of dinutuximab means paediatric patients in the UK are denied this standard of care and the significant increased life expectancy associated with the product, even though dinutuximab is considered as part of the standard of care for children with high-risk neuroblastoma in Europe and the US.[10] Families will be faced with the difficult decision to either self-fund dinutuximab treatment or access other investigative anti-GD2-based immunotherapies through clinical trials. This is illustrated by a parent advocates response to NICE's decision not to recommend dinutuximab that *"[h]ad we known that such an option existed but was out of reach, my wife and I would have done everything in our power to remedy that situation."*[11]

33. The Memo suggests that the Appeal Panel has a "margin of appreciation" when conducting the above balancing exercise between the competing needs of paediatric patients with high-risk neuroblastoma and the needs of the population as a whole. The Memo refers to the case of *Pentiacova v Moldova* 14462/03 to support this submission. However, as the Memo points out "*Pentiacova concerned Article 8 (right to respect for private life) not Article 2. Important though Article 8 is, Article 2 must be considered more important still*" (§ 28).

34. Although Solving Kids' Cancer acknowledges that there is no limit "*a priori*" to the articles to which the margin of appreciation can be applied, the ECtHR traditionally has not used it in the assessment of absolute rights enshrined in the ECHR. Rather, the ECtHR has employed the margin of appreciation in respect of the qualified rights of the ECHR, which expressly acknowledge the possibility of limitations to the protected right.

35. Further, Solving Kids' Cancer disagrees, with respect, that the Appeal Panel has a margin of appreciation when conducting its balancing act. The doctrine is not relevant to the

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[10] *Supra* Note 7.
[11] *Supra* Note 3.

Appeal Panel, an expert national body, that was specifically established to assess the merits of Appraisal Committees' appraisal decisions. The Appeal Panel is the national competent body to make an expert determination whether a particular decision of an Appraisal Committee is proportionate and therefore, justified. Consequently, the Appeal Panel does not need to show the same deference to the recommendations of the Appraisal Committee as does a court. International and domestic case law cautioning the Courts from reviewing acts by public bodies within their power of appreciation are of no assistance.

36. For example, the case of *Pentiacova* illustrates the reluctance of an international court (the ECtHR) to substitute its judgment for that of the domestic court in the context of the allocation of health care resources. The ECtHR stated:

> *"...In view of their familiarity with the demands made on the health care system as well as with the funds available to meet those demands, the* ***national authorities are in a better position to carry out this assessment than an international court****"* (emphasis added)

37. For the reasons set out above, a margin of appreciation (*i.e.*, a measure of discretion) does not apply to the Panel.

Article 3 of the ECHR

38. The Memo advises the Panel that Article 3 is not engaged and refers to the case of *Pretty v UK* (2002) 35 EHRR 1 to support this conclusion. *Pretty* concerned the issue of facilitating assisted suicide, which raises particular ethical issues and does not assist in the determining the current appeal.

39. The Memo argues that Article 3 may *"require some sort of process akin to NICE technology appraisals, as the overall purpose is to maximise the health benefit from a given budget"* (§ 32). This argument suggests an analysis of Article 3 that is inconsistent with the courts approach to determining whether there has been a breach of the prohibition on inhuman or degrading treatment.

40. In respect of Article 3, the courts examine whether the minimum severity threshold for a breach is attained *"depend[ing] on the circumstances of the case, such as the duration of the treatment, its physical and mental effects and, in some cases, the sex, age and state of health of the victim, etc."* (see, for example, *Ireland and United Kingdom* (1978) 2 EHRR 25 at § 162).

41. For the reasons set out above under Article 2, and in our previous submissions on Article 3 of 26 August 2016, in the case of paediatric patients suffering from high-risk neuroblastoma the severity threshold is met and the decision not to recommend dinutuximab constitutes a breach of Article 3.

Article 8 of the ECHR

42. The Memo accepts that Article 8 is engaged by NICE's appraisal of dinutuximab (§ 37). Solving Kids' Cancer agrees with this advice and the Memo's recommendation that the

Appeal Panel must not take an unduly restrictive approach to the ambit of Article 8. As stated by the Court of Appeal in *R (Condiff) v North Staffordshire Primary Care Trust* [2011] EWCA Civ 910 *"[t]here is no universal yardstick for determining a state's positive obligations under Article 8."*

43. The question for the Panel, therefore, is whether NICE's negative recommendation for dinutuximab is a justified interference in accordance with the requirements of Article 8(2). That is, the interference must be "necessary", which the Memo correctly acknowledges is a question of fact bearing in mind the specific features of the present case and that what is "necessary" is a more than what is "desirable" or reasonable. However, Solving Kids' Cancer disagrees with the suggestion that the Panel has a margin of appreciation *i.e.*, a measure of discretion when applying the necessity test for the reasons set out above under Article 2.

44. In relation to the necessity test, the Memo refers to several cases (*Pentiacova v Moldova* (2005), *Sentges v Netherlands* (2003) and *R (on the application of McDonald) v Royal Borough of Kensington and Chelsea* [2011] UKSC 33) to support the submission that Article 8 is only likely to be breached where an applicant is denied access to a certain standard of treatment. However, in all the cited cases, the applicants already enjoyed a certain level of treatment and/or public financial assistance. For example, in *Pentiacova* the Moldovan State provided the applicants with two haemodialysis sessions a week, but in some instances patients had to fund a third session themselves. The ECtHR also noted that health care reform had significantly improved the applicants' situation and therefore held there was no breach of Article 8:

> *"Bearing in mind* ***the medical treatment and the facilities provided to the applicants and the fact that the applicants' situation has considerably improved after the implementation of the medical care system reform*** *in January 2004, the Court considers that the respondent State cannot be said, in the special circumstances of the present case, to have failed to discharge its positive obligations under Art. 8 of the Convention."* (emphasis added)

45. In *Sentges v Netherlands*, the ECtHR observed that whilst the applicant had been refused a robotic arm, he had *"access to the standard of health care offered to all persons.... It thus appears that he has been provided with an electric wheelchair with an adapted joystick."* That is, the State had provided the applicant with an alternative treatment. Similarly, in *R (on the application of McDonald) v Royal Borough of Kensington and Chelsea* [2011] UKSC 33) the applicant had access to a State funded alternative treatment (incontinence pads).

46. Further, *Nitecki v Poland* (App 65653/01) highlights the importance the ECtHR attaches to the fact that a State provides a certain level of financial assistance and concluded there was no breach of Article 8:

> *"Bearing in mind* ***the medical treatment and facilities provided to the applicant, including a refund of the greater part of the cost of the required drug****, the Court considers that the respondent State cannot be said, in the special circumstances of the present case, to have failed to discharge its*

obligations under Article 2 by not paying the remaining 30% of the drug price." emphasis added).

47. The circumstances of the present case are very different. There is no alternative treatment to dinutuximab for high-risk neuroblastoma paediatric patients and NICE's non-recommendation of the product ultimately means that patients in the UK will not benefit from any State support to fund their only treatment option. Families will be forced to look for clinical trials and to fundraise in order to afford the cost of the product either in the UK or alternatively, travel abroad to access dinutuximab where it is the standard of care. For example, Solving Kids' Cancer has been directly involved with 14 families who raised approximately £3.5 million and each spent 6 months abroad disrupting their employment and family life. The current treatment costs are now approximately double the costs when patients were accessing the pivotal COG trial prior to 2010.

48. Solving Kids' Cancer submits that the Appraisal Committee's decision not to recommend dinutuximab is therefore not necessary, that is, it is disproportionate for all the reasons set out above. In particular, given dinutuximab is a life-saving or at the least a significant life-extending drug, the duration and quality of a treated paediatric patient's life, the absence of an alternative treatment, and the use of standard NICE methodologies and cost effective thresholds to appraise the paediatric orphan drug.

49. In relation to the latter, the Memo advises that *"[t]he Appeal Panel needs to look at necessity in the round, with the fact that the drug is above the usual threshold (and the degree by which it exceeds the threshold) being one factor to weigh in the balance"* (§ 48). We consider, with respect, that this is a misnomer and overlooks the key issue that NICE failed to consider the clinical and cost effectiveness of dinutuximab, in light of the special needs of the paediatric population and that it is an orphan drug. Instead, NICE rigidly applied its standard methodologies and cost effective thresholds. Consequently, dinutuximab was likely to be "cost ineffective," as the incremental cost-effectiveness ratios generated for orphan drugs are almost always outside the cost-effectiveness thresholds acceptable to NICE when appraising such drugs on its standard technology process.

50. Further, NICE's rigid application of its standard criteria to novel paediatric cancer treatments means that there is very little prospect of an Appraisal Committee positively recommending other anti-GD2 monoclonal antibodies for high-risk neuroblastoma, such as dinutuximab-beta. The implication of the Appraisal Committee's non-recommendation of dinutuximab therefore means that patients in the UK are not only denied access to the sole approved drug for the treatment of high-risk neuroblastoma, but also will likely be denied access to other anti-GD2 antibodies in development.

51. Accordingly, the Appraisal Committee's non-recommendation of dinutuximab is disproportionate and in breach of Article 8.

Article 14 of the ECHR

52. The Memo accepts that Article 14 is engaged, as NICE's appraisal of dinutuximab is within the ambit of Article 2 and 8 of the ECHR. Additionally, the Memo concludes that NICE must ensure that it has complied with its duty under section 149 of the Equality Act 2010 to have due regard to eliminate discrimination.

53. The Memo summarises that *"indirect discrimination occurs where the same policy is applied to all, but a certain group is particularly disadvantaged"* (§ 53). There can be no doubt that the rigid application of NICE's standard technology appraisal methodologies to the paediatric orphan drug, dinutuximab, and the subsequent non-recommendation of the product, specifically disadvantages children.

54. The key question for the Panel, therefore, is whether NICE's negative recommendation for dinutuximab, which indirectly discriminates against children, is objectively justified. The courts approach the question of objective justification under Article 14 in the same manner as that described in relation to Article 8(2) above. Accordingly, and for the same reasons as set out above, the Appraisal Committee's non-recommendation of dinutuximab is disproportionate and has an unreasonable impact on paediatric patients with high-risk neuroblastoma. Further, NICE failed to have due regard to the need to eliminate discrimination and to minimise the detrimental impact of its decision on the vulnerable paediatric population during the appraisal process for the reasons set out above.

55. Accordingly, Solving Kids' Cancer submits that NICE's non-recommendation of dinutuximab is in breach of Article 14 and section 149 of the Equality Act 2010.

56. Further, the right to act in the best interests of the child is linked to the right to non-discrimination under Article 2 of the UN Convention (see General Comment No 14 (2013), adopted by the UN Committee on the Rights of the Child at § 41). For the reasons set out above, NICE's appraisal of dinutuximab was discriminatory and therefore in breach of Articles 3(1) and 2 of the UN Convention.

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Covington & Burling LLP

23 September 2016