

NOTE OF CELGENE'S SUBMISSIONS ON HUMAN RIGHTS (GROUND 3.3)

Introduction

1. This note sets out the submissions of Celgene Limited on why the Appraisal Committee has exceeded its powers by making a recommendation in the FAD in breach of human rights. The note also responds to the Memorandum dated 14 May 2010 from [REDACTED], Beachcroft, to the Appeal Panel, setting out his advice on the human rights issues ("the Memo").
2. The note refers to a number of legal cases and other authorities. So as not to burden the Appeal Panel unduly (and following the approach taken in the Memo), Celgene is not submitting a full set of the authorities referred to. However, copies of the materials can of course be provided if that would assist.
3. There can be no doubt that as a public body NICE is bound in its appraisals to take account of human rights legislation. There are numerous references to this obligation in NICE guidance: see, for example, to the NICE Guide to Methods of Technology Appraisals at §§ 1.4.3, 6.1.3 and 6.2.20; see also the Social Value Judgments principles at § 3.1 on page 9, and § 9 on page 29. The obligation to comply with the Human Rights Act 1998, and hence with the European Convention on Human Rights ("the Convention") which is scheduled to it, appears to be accepted in the Memo.
4. Four Articles of the Convention are in play in this appeal: Article 2 (the right to life); Article 3 (the right not to be subject to inhuman or degrading treatment); Article 8 (the right to private and family life); and Article 14 (the right not to be discriminated against in the enjoyment of other Convention rights). Celgene will address in turn why each of these Articles is infringed by the decision not to recommend azacitidine.
5. Before turning to the four Articles of the Convention, it is important to note that the human rights context of this appeal also impacts upon the approach which the Panel should take to ground 2, perversity. This is because the more substantial is the interference with human rights, the more is required by way of justification before the Appeal Panel should accept that the decision is a reasonable rather than a perverse one. This approach is now well established in the case law: see, in particular, *R v Ministry of Defence, ex p. Smith* [1996] QB 517, 554 per Sir Thomas Bingham MR; see also in a healthcare context *R (Rogers) v Swindon NHS Primary Care Trust* [2006]

1 WLR 2649, § 56 "... the case is concerned with a decision which may be a life or death decision for the claimant. In these circumstances it is appropriate for the court to subject the decision to refuse funding for the treatment (and thus in practice the treatment) to rigorous scrutiny."

Article 2

6. The right to life is engaged by the decision of the Appraisal Committee. Its effect is to deprive MDS patients of an effective treatment which on average extends life by almost 10 months.
7. Article 2 does not only oblige the State to refrain from depriving persons of life intentionally, but also imposes a positive obligation to take adequate measures to protect life. For example, in *Vo v France* (2005) 40 EHRR 12 the Grand Chamber of the European Court of Human Rights¹ held:

88 The Court reiterates that the first sentence of Art.2, which ranks as one of the most fundamental provisions in the Convention and also enshrines one of the basic values of the democratic societies making up the Council of Europe, requires the State not only to refrain from the "intentional" taking of life, but also to take appropriate steps to safeguard the lives of those within its jurisdiction.

89 Those principles apply in the public health sphere too. The positive obligations require states to make regulations compelling hospitals, whether private or public, to adopt appropriate measures for the protection of patients' lives. ..." [footnotes omitted]

A similar observation was made by the European Commission of Human Rights² in the *Scialacqua* case cited at §5 of the memo. Furthermore, as the Memo acknowledges, the Commission was prepared to assume that Article 2 imposes on States "... the obligation to cover the costs of certain medical treatments or medicines that are essential in order to save lives...". The reason why the Commission rejected the application was that the herbal remedies in question, unlike azacitidine, were not approved as officially recognised medicines.

8. The domestic courts have recognised that the right of patients to treatment which will prolong life engages Article 2. For example, in *Simms v Simms; A v A (A Child)* and

¹ The Memo refers to the 'ECJ', which is shorthand for the European Court of Justice (§§ 17, 20, 21). The European Court of Justice is the court of the European Union in Luxembourg. The court which decided the cases referred to in the Memo and in this Note is the European Court of Human Rights in Strasbourg, an institution of the Council of Europe. The ECJ has no relevance to the human rights issues which the Appeal Panel must decide.

² The European Commission of Human Rights previously provided first tier rulings on cases brought under the Convention. Cases which were declared admissible would then proceed to the European Court of Human Rights. Following procedural reforms, all cases now go directly to the European Court of Human Rights.

Another [2003] Fam 83, a case concerning innovative treatment for variant CJD, the President of the Family Division held at § 61:

"There is, from the medical evidence, a possibility of arresting the disease temporarily, and the possibility of prolonging the life of these two patients to some extent, although whether that be in weeks, months or years is impossible to tell. **Each patient is entitled under article 2 of the Convention for the Protection of Human Rights and Fundamental Freedoms to the right to life. Article 8 gives to each patient the right to respect for his family life.** Is a prolongation of life as it is led worthwhile for JS and JA? The parents of each say emphatically yes. There is undoubtedly evidence that there is some value to their lives. A reduced enjoyment of life even at quite a low level is to be respected and protected. Each patient is at present within a devoted and wonderfully caring family and is being provided with the best life possible in these tragic circumstances. I consider that even the prospect of a slightly longer life is a benefit worth having for each of these two patients. There is sufficient possibility of unquantifiable benefit for me to find that it would be in their best interests to have the operations and the treatment subject to an assessment of the risks. There is no alternative treatment available."

Accordingly, the court was recognising that Article 2 (and Article 8) are engaged by a decision whether or not to approve life-prolonging treatment. The suggestion in the Memo (§6) that Article 2 is not engaged must therefore be rejected.

9. Celgene recognises, of course, that there are limits on public resources, and that Article 2 does not impose an untrammelled obligation on the state to provide unlimited resources for life-prolonging treatment. However, in the exceptional circumstances of the present case, given the extent to which azacitidine prolongs life, the quality of the prolonged life, and the small number of patients who would potentially benefit from the treatment (and hence the total cost in issue), it is unjustified and hence contrary to Article 2 for the Appraisal Committee to refuse to recommend azacitidine.³
10. In this regard, it is relevant that azacitidine is currently available in a number of specialist centres in the UK treating MDS, and has reimbursement in all but four other Member States of the EU. Thus, to deny azacitidine to MDS patients in the UK would be to refuse them a life-prolonging and potentially life-saving treatment⁴ which is available to the general public in most of the EU. Such a decision would be contrary to Article 2 of the Convention.

³ Reference to other decided cases is necessarily of only limited assistance in the intensely fact-sensitive question of whether an interference with Article 2 is or is not made out. This is recognised by the European Court of Human Rights in a number of the cases cited in the Memo. For example, in *Nitecki v Poland* (App. 65653/01, 21.3.02) the Court stressed that its decision that there was no violation of Article 2 in Poland only paying for 70% of a particular drug was taken "... in the special circumstances of the present case...".

⁴ The Memo proceeds on the assumption that the only issue is "... the rate of progression towards death" (§6). This overlooks the fact that in some (admittedly exceptional) cases, treatment with azacitidine has had such a significant effect on a patient that they become a candidate for stem-cell transplantation, a potentially curative treatment which was previously unavailable to them.

11. Further or alternatively, the failure to take appropriate steps to adapt the appraisal system for the special position of ultra-orphan drugs such as azacitidine is contrary to the procedural obligation contained in Article 2. Where it is likely that a situation presents a real risk to an individual's health, then a State is under a duty to take appropriate steps to safeguard the lives of those within their jurisdiction: see, for example, *LCB v UK* (1998) 27 EHRR 212, § 38.⁵
12. The FAD records at §4.12 that there are approximately 700 patients in England and Wales with MDS who could be eligible for azacitidine. Accordingly, azacitidine is an ultra-orphan drug, as that term has been defined by NICE in its Social Value Judgements publication (2nd ed., p. 36: 1 in 50,000, i.e. less than 1,000 in the UK). NICE has recognised that the result of an appraisal of an ultra-orphan drug under conventional criteria will invariably give rise to values which would be considered cost ineffective: Guide to Appraising Orphan Drugs, March 2006 (Draft) (§4.6); see also NICE Citizens Council Report, November 2004, pp. 4 & 6; and evidence of ██████████, Chair of NICE, to the House of Commons Health Committee, May 2007, referring to the need for 'special rules' for ultra-orphan drugs.
13. If, contrary to Celgene's primary submission, the Appraisal Committee is not obliged to take account of the approach set out in the draft NICE guidance, then the absence of any appropriate mechanism by which to appraise ultra-orphan drugs means that they will inevitably be ruled cost ineffective. In the case of a life-extending drug such as azacitidine, this is contrary to the procedural obligation under Article 2 on a State to take appropriate steps to safeguard the lives of those within their jurisdiction. By failing to take proper account of the ultra-orphan status of azacitidine in the appraisal, the Appraisal Committee therefore failed to do what was required of it to protect life under Article 2.

Article 3

14. The European Court of Human Rights has held that where an applicant was in the advanced state of a terminal and incurable illness, the withdrawal of sophisticated medical treatment (which would be consequent upon the applicant's deportation to his

⁵ That case concerned the risk of a child developing childhood leukaemia, following her father's exposure to excess radiation while serving in the Royal Air Force during nuclear tests on Christmas Island. The Court found no violation of Article 2 in that case, because there was no convincing evidence that the father had been exposed to excessive levels of radiation. However, the result of that case, which turned on the strength of the evidence of the health risk, does not undermine the general principle that Article 2 includes a procedural obligation. In the case of MDS/azacitidine, of course, there is no dispute about the existence of a real health risk.

home country of St Kitt's) would amount to inhuman treatment in violation of Article 3 of the Convention: *D v UK* (1997) 24 EHRR 423, §§ 52 - 53. In view of the Court's conclusion on that issue, it did not consider it necessary to consider the issues which arose under Article 2 (§ 59) or Article 8 (§ 64). The Court stressed the exceptional circumstances of the case, and took account of the critical stage which the applicant's fatal illness had reached.

15. Celgene submits that patients suffering from MDS are in a similarly exceptional situation, and are tragically suffering from a terminal illness. Accordingly, to refuse to accord them treatment which can significantly prolong and improve the quality of their final months of life amounts to inhuman treatment contrary to Article 3.
16. It is recognised that Article 3 does not routinely apply to a failure to provide healthcare, since such failure will not usually reach the minimum level of severity required to constitute inhuman or degrading treatment. However, the present case falls into the exceptional group of cases where the benefits of the treatment are sufficiently established, and the effects of denying treatment so severe, that Article 3 is engaged and is violated.
17. The Memo overlooks the important case of *D v UK*, and refers instead to *Pretty v UK* (2002) 35 EHRR 1. *Pretty* concerned the quite different issue of facilitating assisted suicide, which raises particular ethical issues. The *Pretty* case does not assist in determining the present appeal.
18. The Memo suggests (§9) that Article 3 of the Convention may require some sort of process akin to NICE technology appraisals. Such a broad contention is no part of Celgene's case, and is not an issue which the Appeal Panel needs to determine. Furthermore, this argument suggests an approach to the issues which is not that which would be taken by the courts when determining whether there has been a breach of Article 3. Rather, the court would focus on the particular case before it, and consider whether in the particular circumstances of that case the absence of treatment would cause suffering which reaches the level of severity required to constitute inhuman or degrading treatment. For the reasons set out above, in the case of high risk MDS the severity threshold is met, and the decision not to recommend azacitidine constitutes a breach of Article 3 of the Convention.

Article 8

19. Even if, contrary to the submissions set out above, the Panel does not accept that the effects of the decision are sufficiently severe to constitute a violation of Article 2 and/or 3, it constitutes an interference with the private and family life of MDS patients contrary to Article 8. The text of Article 8 of the Convention is set out at §11 of the Memo.
20. By denying patients on average 9.6 additional months of life, the decision will terminate the family life of patients. Furthermore, it will render the patient's final months of life more painful and difficult, with a likelihood of an increased risk of physically invasive blood transfusions. Article 8 protects not only private and family life, but also the wider concept of physical and moral integrity: see, for example, *Bensaid v UK* 2001-I, § 47, where mental health was regarded as a crucial part of moral integrity and the preservation of mental health a vital precondition to the effective enjoyment of private life. Accordingly, Celgene submits that denying patients access to azacitidine constitutes an interference with private and family life contrary to Article 8(1) of the Convention.
21. The Memo includes consideration of a number of cases decided by the European Court of Human Rights under Article 8 (§§13 – 17). Celgene does not accept the relevance of all of those cases or of some of the analysis put forward. However, since the Memo correctly reaches the conclusion that Article 8 should be taken to apply, and that failure to provide treatment with azacitidine could amount to an infringement of Article 8(1), it is not necessary to burden the Appeal Panel with a detailed rebuttal. It is common ground that denying patients access to azacitidine constitutes (or, at least, should be taken to constitute) an interference with private and family life contrary to Article 8(1) of the Convention.
22. An interference with private and family life may be justified in accordance with the requirements of Article 8(2). Celgene accepts that the appraisal pursues a legitimate aim since it seeks to protect the health of other patients by fairly allocating resources. However, for an interference to be justified under Article 8(2), it must be 'necessary in a democratic society', which has been interpreted by the European Court of Human Rights to mean that it must be proportionate.
23. The Memo rightly accepts that the question of necessity is a question of fact, which the Appeal Panel must determine having regard to the specific features of this case (§22). Celgene disagrees with the contradictory suggestion at § 23 of the Memo that the

Panel should speculate as to the possible outcome of other, hypothetical, cases. What is required under Article 8 is for the Appeal Panel to determine whether this particular interference with the rights of high risk MDS patients is justified under Article 8(2).

24. Celgene also disagrees with the apparent suggestion at § 21 of the Memo that the Panel should allow a “margin of appreciation” to the decision of the Appraisal Committee not to recommend azacitidine. The doctrine of margin of appreciation concerns the reluctance of an international court (the European Court of Human Rights) to substitute its judgment for that of the domestic authorities.⁶ It is not relevant when a national body is making an expert determination as to whether a particular decision is proportionate. This is acknowledged at least to some degree by § 24 of the Memo, which recognises that the Appeal Panel must form its own view of necessity/proportionality, rather than simply reviewing the Appraisal Committee’s decision on grounds of perversity.
25. The decision is disproportionate for all of the reasons set out above. In particular, given the extent to which azacitidine prolongs life, the quality of the prolonged life, the small number of patients who would potentially benefit from the treatment, the total sums at issue, and the fact that the ICER is relatively close to the standard cost effectiveness threshold, it is disproportionate for the Appraisal Committee to refuse to recommend azacitidine. Accordingly, the decision is in breach of Article 8.

Article 14

26. Article 14 prohibits discrimination in the enjoyment of other Convention rights. Accordingly, for Article 14 to be engaged, one of the other Convention rights must be applicable (although not necessarily infringed). For the reasons set out above, each of Articles 2, 3 and 8 are engaged, such that Article 14 applies. The Memo rightly accepts that this is the case (§26).
27. MDS is overwhelmingly a disease of old age. Over 90% of patients with MDS are over 60 at the time of diagnosis, and the median age at diagnosis is 75. Accordingly, by refusing to recommend azacitidine, the Appraisal Committee has taken a decision which will disproportionately affect older patients. The decision therefore constitutes indirect discrimination against older patients. The Memo only appears to consider the possibility of direct discrimination, between two groups of MDS patients (§27).

⁶ See, for example, “Human Rights Law and Practice” (2nd ed.) Lester & Pannick, § 3.18.

However, Article 14 also prohibits indirect discrimination, that is an apparently age-neutral provision (such as the decision not to recommend azacitidine), which as a matter of fact has a disproportionate and unjustified impact on members of a particular group (older persons).⁷

28. Furthermore the majority of older MDS patients are precisely the group who are ineligible for stem-cell transplants, such that azacitidine represents their best and only real hope for survival. As the MDS UK patient support group stated in its submission to NICE: "Please do not consider these patients as a group of older patients (they are for the most part) who DO NOT deserve this therapy and deny them the chance to live better and longer lives". Therefore contrary to the assumption in the Memo (§27), the decision not to recommend azacitidine is discriminatory as between high-risk MDS patients, as it will impact particularly badly on older patients who are ineligible for stem-cell transplantation.
29. Difference of treatment on a prohibited ground (such as age) may be objectively justified. The courts approach the question of objective justification under Article 14 in the same way as that described in relation to Article 8(2) above. Accordingly, and for the same reasons as set out above, the difference of treatment is disproportionate in its impact on older MDS patients, and hence violates Article 14.

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Brick Court Chambers

⁷ In *Thilimmenos v Greece* (2000) 31 EHRR 411 the ECtHR held that there was discrimination contrary to Article 14 where a rule prohibiting persons from becoming a chartered accountant if they had a conviction for a felony impacted disproportionately on a Jehovah's Witness who had a conviction for refusing to enlist in the army for religious reasons.