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NOTE OF BMS'S SUBMISSIONS ON HUMAN RIGHTS (GROUND 3.1)

Introduction

1. This note sets out the submissions of Bristol-Myers Squibb Pharmaceuticals Limited ("BMS") on why the Appraisal Committee has exceeded its powers by making a recommendation in the FAD in breach of human rights.

2. The note refers to a number of legal cases and other authorities. So as not to burden the Appeal Panel unduly, BMS 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.[1] 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, was accepted by the Appeal Panel in its Decision in "Azacitidine for the treatment of myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia" ("the Azacitidine Decision").

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 respect for private and family life); and Article 14 (the right not to be discriminated against in the enjoyment of other Convention rights). BMS will address in turn why each of these Articles is infringed by the decision not to recommend dasatinib for the treatment of blast-phase CML patients.

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

[1] See, for example, 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.

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."

6. It is, with respect, very important for the Appeal Panel to keep this need for rigorous/anxious scrutiny in mind when considering all aspects of the appeal, and in particular the perversity grounds. For example, the decision not to apply the End-of-Life Criteria to blast-phase patients is challenged under ground 2.3, and this submission needs to be considered on a rigorous/anxious scrutiny basis. The End-of-Life Criteria were applied in the Azacitidine Decision, and this is a material distinction between that case and the present one.[2] Once the decision not to apply the End-of-Life Criteria is viewed through the lens of rigorous/anxious scrutiny, the perversity of the decision is particularly apparent.

Article 2

7. The right to life is engaged by the decision of the Appraisal Committee. Its effect is to deprive blast-phase CML patients of an effective treatment which increases median overall survival from 3-6 months to 8-11 months (see the SPC for dasatinib, cited in the Grounds of Appeal at ground 2.3). In other words, treatment with dasatinib is on average capable of extending life by up to 8 months.

8. 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 Rights held:

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2 Of course, where the End-of-Life Criteria are applied, this may result in NICE recommending treatments with materially higher ICERs. See, e.g. TA169, Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma, March 2009, where the ICER was between £49,300 and £54,400.

"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 Rights[3] in *Scialacqua v Italy* DR 81, 35. Furthermore, 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 dasatinib, were not approved as officially recognised medicines.

9. 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 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. Any suggestion that Article 2 is not engaged should therefore be rejected.

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3 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.

10. In the Azacitidine Decision, the Appeal Panel was strongly influenced in its approach to Article 2 (and Article 3, considered further below), by the fact that the rights are absolute rather than qualified (§54). However, with respect this concern misunderstands the way in which an absolute Convention right such as Article 2 works. Article 2 contains an in-built balance, such that it will not be engaged or breached where the situation is not sufficiently serious. Accordingly, it is only in genuinely life-threatening situations, such as the present, and which can be remedied in a proportionate manner that Article 2 will be in play. If the Appeal Panel's approach in the Azacitidine Decision were the correct one, then the European Court of Human Rights would have taken that very different approach in its judgments in analogous cases.[4] Furthermore, for the reasons set out in the section on Article 3 below, the Panel in the Azacitidine Decision was wrong to reject the appellant's reliance on the case of *D v UK*.

11. BMS 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 dasatinib prolongs life, the quality of the prolonged life,[5] and the relatively 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 dasatinib.[6]

12. In this regard, it is relevant that dasatinib is currently available in a number of specialist centres in the UK treating CML, and has reimbursement in all other Member States of the EU as well as other developed states including Australia and New Zealand. Thus, to deny dasatinib to blast-phase CML patients in the

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4 For example, in *Nitecki v Poland* (App. 65653/01, 21.3.02) discussed at footnote 6 below.

5 The specialist who responded to the ACD on behalf of Healthcare improvement Scotland noted that following treatment with dasatinib or nilotinib "I cannot think of a single working patient in our large CML practice (60-80 patients) who has stopped work for disease or treatment related reasons".

6 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. 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... ".

UK would be to refuse them a life-prolonging treatment which is available to the general public in other comparable States throughout the world. Such a decision would be contrary to Article 2 of the Convention.

13. Further or alternatively, the failure to take appropriate steps to adapt the appraisal system for the special position of ultra-orphan drugs such as dasatinib 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.[7]

14. The perversity appeal point put forward by BMS concerning the ultra-orphan status of dasatinib was not accepted as valid.[8] Accordingly, it is particularly important that the Appeal Panel should take account of the status of dasatinib as an ultra-orphan drug in the context of this human rights ground of appeal.

15. Dasatinib 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 Prof Rawlins, Chair of NICE, to the House of Commons Health Committee, May 2007, referring to the need for 'special rules' for ultra-orphan drugs.

16. The fact that the draft NICE guidance is only in draft, and does not constitute NICE policy, does nothing to undermine this submission. With respect, the Appeal Panel in the Azacitidine Decision did not take adequate account of the

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7 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 CML/dasatinib, of course, there is no dispute about the existence of a real health risk.

8 Ground 2.5. See letter from [redacted] ated 30 September 2011.

ultra-orphan submissions in the context of the quite separate human rights ground of appeal.[9] Since the Azacitidine Decision holds that the Appraisal Committee is not obliged to take account of the approach set out in the draft NICE guidance, the absence of any appropriate mechanism by which to appraise ultra-orphan drugs means that they will inevitably be ruled cost ineffective. The factual reasons why this submission was rejected in the Azacitidine Decision (§44) do not apply in the present case.

17. Accordingly, in the case of a life-extending drug such as dasatinib, the failure to apply a special approach (of the sort set out in the draft NICE Guide) 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 dasatinib in the appraisal, the Appraisal Committee therefore failed to do what was required of it to protect life under Article 2.

Article 3

18. 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 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.

19. BMS submits that patients suffering from blast-phase CML 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.

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9 The ultra-orphan submission was only dealt with, and rejected, as a perversity ground, in particular at §42.

20. 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. That is why the concerns which the Appeal Panel expressed in the Azacitidine Decision about the absolute nature of Article 3 are, with respect, misplaced. 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.

21. The Azacitidine Decision sought to distinguish the situation before the Panel in that case from *D v UK* on the basis that the patient in *D* was actively moved to a situation where treatment would not be provided. However, BMS submits that this distinction does not, on analysis, withstand scrutiny. If the FAD were adopted, all blast-phase CML patients (for which no other similarly effective treatment is licensed) who are not already being treated with dasatinib would be moved to a situation where treatment would not be provided. The fact that the movement is by reason of policy/treatment, rather than geographical (as it was in *D*) , makes no difference at this level of the analysis.

Article 8

22. 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 right to respect for private and family life of blast-phase CML patients contrary to Article 8.

23. By denying blast-phase patients on average up to 8 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. 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, BMS submits that denying patients access to dasatinib constitutes

an interference with private and family life contrary to Article 8(1) of the Convention.[10]

24. An interference with private and family life may be justified in accordance with the requirements of Article 8(2). BMS 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.

25. The question of necessity is a question of fact, which the Appeal Panel must determine having regard to the specific features of this case. What is required under Article 8 is for the Appeal Panel to determine whether this particular interference with the rights of blast-phase CML patients is justified under Article 8(2).

26. In the Azacitidine Decision the Panel was, with respect, wrong to hold that Article 8(1) was not engaged on the basis that the high threshold was not met (§55). In any event, in the present case, and in relation to the blast-phase of the disease, the failure to recommend dasatinib denies CML patients in their final months of life access to the only effective and life-prolonging treatment (nilotinib is not authorised for the blast-phase). The situation could not be more serious for those patients' lives. Furthermore, the Panel will wish to be aware that the Grand Chamber of the European Court of Human Rights has recently stressed that the "margin of appreciation" (or discretion) which a state enjoys in relation to Article 8 and medical treatment is "not unlimited" (*A, B and C v Ireland*, 16.12.10 §238). In finding a breach of Article 8 in relation to one of the applicants in that case, the Court referred back to its earlier case law holding that states are under a positive obligation to secure to their citizens their right to effective respect for their physical and psychological integrity (§245), and held

10 The recent judgment of the Supreme Court in *R (McDonald) v Kensington and Chelsea* [2011] PTSR 1266, [2011] UKSC 33 does not undermine this submission. That case raised different issues concerning dignity rather than life expectancy (the use of incontinence pads rather than a commode during the night time). Lord Brown, with whom Lords Walker, Kerr and Dyson JJSC agreed in this respect, stressed that there is "... of course, a positive obligation under article 8 to respect a person's private life" (§19). In that case no breach of Article 8 was found because, to put it crudely, the claimant's suffering was not sufficiently severe. By contrast, the present case unquestionably concerns suffering at the end of a terminal illness.

that the applicant who had a rare form of cancer (§250),[11] had suffered a violation of her right to effective respect for her private life.

27. The decision not to recommend dasatinib is disproportionate for all of the reasons set out above. In particular, given the extent to which dasatinib prolongs life, the quality of the prolonged life, the relatively small number of patients who would potentially benefit from the treatment, the total sums at issue, and the fact that on some calculations the ICER is relatively close to the standard cost effectiveness threshold, it is disproportionate for the Appraisal Committee to refuse to recommend dasatinib for the treatment of blast-phase CML patients. Accordingly, the decision is in breach of Article 8.

Article 14

28. 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. In the Azacitidine Decision, the Panel accepted that Article 14 was engaged (§57).

29. There are two respects in which the recommendation in the FAD is indirectly discriminatory: race and age.

30. First, the decision denies any treatment other than best supportive care to patients with blast-phase CML who are unable to be treated with stem cell transplantation due to their ethnicity. It is well-established that there is a marked shortage of suitable donors for patients from ethnic minorities. This means that those patients will suffer more harm from the non-recommendation of dasatinib than other groups of patients, since they are much less likely to be able to benefit from stem cell transplantation.

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11 The applicant feared for her life as she believed that her pregnancy increased the risk of her cancer returning and that she would not obtain treatment for that cancer in Ireland while pregnant (§250). The case is of course a different one, as it concerned abortion, but the observations of the Court relied on here are nonetheless applicable to the present case.

31. Second, CML is overwhelmingly a disease of old age. The median age at the time of diagnosis is 65.[12] Accordingly, by refusing to recommend dasatinib, the Appraisal Committee has taken a decision which will disproportionately affect older patients. Even though nilotinib has been recommended with certain conditions, it is not licensed for the most serious blast-phase of the disease.

32. The decision therefore constitutes indirect discrimination against older patients and patients from ethnic minorities. Article 14 prohibits indirect as well as direct discrimination, that is an apparently age- and race- neutral provision (such as the decision not to recommend dasatinib), which as a matter of fact has a disproportionate and unjustified impact on members of a particular group (those from ethnic minorities, older persons).[13]

33. In the Azacitidine Decision the Panel held that the putative right in play was the right to access the treatment in question, not the right to access treatment for the disease in question (§58). This approach is contrary to the approach generally taken in discrimination cases, and would deprive the prohibition on indirect discrimination of all meaning. If the Panel were correct, it would never be possible to establish that refusal to recommend a treatment was indirectly discriminatory, since the treatment would always apparently be available to all patients on equal terms. The Panel should therefore, with respect, reconsider the approach suggested in the Azacitidine Decision.

34. Difference of treatment on a prohibited ground (such as race or 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 and ethnic minority blast-phase CML patients, and hence violates Article 14.

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12 "Chronic myeloid leukaemia", Hehlmann, Hochhaus and Baccarani: Lancet 2007; 370; 342-50 at 342, l.h. column.

13 In *Thlimmenos 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.

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35. Furthermore, BMS notes that the summary of the Response to comments on the ACD refers (p. 4) to the publication of an equality impact assessment report on the NICE website. So far as BMS is aware, any equality impact assessment which has been conducted has not yet been published. Pending sight of any such document, and given the very summary treatment of the equality obligations at §4.3.31 of the FAD, BMS expressly reserves its position in relation to whether there has been a breach of the public sector equality duty provided for under the Equality Act 2010.

3rd October 2011

Brick Court Chambers