registered charity: 1114037

[redacted]
Chair, Appeal Committee
National Institute for Health and Clinical Excellence
MidCity Place
71 High Holborn
London WC1V 6NA

29th August, 2011

Dear [redacted],

Re: Appeal against the Final Appraisal Determination (FAD): *Dasatinib, high dose imatinib and nilotinib for the treatment of imatinib-resistant chronic myeloid leukaemia (CML) (part review of NICE technology appraisal guidance 70), and dasatinib and nilotinib for people with CML for whom treatment with imatinib has failed because of intolerance.*

The CML Support Group is writing to you to appeal against the above FAD on Grounds 1 and 2 of the appeal process.

Ground 1: The Institute has failed to act fairly.

1. Our objection is that the Appraisal Committee have failed to follow the NICE procedures set out in the 2008 NICE "Guide to the methods of technology appraisals" in the selection of a comparator, in this case hydroxycarbamide (HU).

1.2. Section 2.2.4. of the Guide is the basis for our opinion that HU should not have been selected to be an appropriate comparator because it is not used in current clinical practice by specialist clinicians for the treatment of patients resistant or intolerant to the current standard first line therapy for chronic stage CML.

1.3. Compliance with Section 2.2.4. of the Guide would involve the only appropriate comparator for the treatment of patients showing resistance being, in the first instance, an escalation of the dose of the current standard first line therapy followed by one of the other available inhibitors for which there is a relevant marketing authorization. This represents current best practice and existing widespread use in the NHS.

1.4. Compliance with Section 2.2.4. of the Guide would involve the only comparator for the treatment of patients showing intolerance being an inhibitor for which there is a relevant marketing authorization other than imatinib. This represents both current best practice and existing widespread use in the NHS.

1.5. With reference to Section 5.2.5. of the Guide; we consider that HU is not a justifiable technology because, as a chemotherapy intervention, it does not promote any cytogenetic response in patients with imatinib failure and is rather, in very few cases only, used as a palliative therapy. Its selection is therefore not justified in relation to the definition of the decision problem.

Ground 2. The Institute has formulated guidance which cannot be reasonably justified in the light of the evidence submitted

2.1. FAD Section 4.3.3. The Committee's conclusion is flawed. Relevant inhibitor technologies, including standard dose imatinib, are available and are proven to be able to induce cytogenetic responses at high rates in patient populations resistant or intolerant to standard dose imatinib. HU, on an in principle basis, cannot do so, interferon has minor efficacy and low tolerability and stem cell transplantation (STC) is available only to a minority. Current European Leukaemia Network CML treatment guidelines, part of the evidence submitted, make no mention of HU or interferon with STC to be considered only after inhibitor failure and subject to donor availability.

2.1.1. The use of a "non-availability of therapies" argument in FAD 4.3.3. logically permits infinite regression over an unlimited time span. Reductio ad absurdum prevails with specialist clinicians being invited to imagine scenarios that are based on historical practice rather than offer evidence based on contemporary NHS practice. This degrades the evidence based rationale of the appraisal process.

2.2. FAD Sections 4.3.7, 4.3.8. & 4.3.9. Professor Apperley, in her comment on the Appraisal Consultation Document (ACD) that discussed the trial mentioned in FAD section 4.3.7. stated the evidence as to the clinical effectiveness of the technologies was "excellent" going on to say "There is not a single CML expert in the world that would argue these drugs are ineffective". Her evidence

and that of other leading clinicians rebuts the claims made of “poor quality of the evidence base” (4.3.8) and “the limited evidence base” (4.3.9.).

Conclusion:

Taken together we feel our Ground 1 & 2 objections demonstrate that the decision taken at the scoping stage to include HU as an (inexpensive) comparator was entirely inappropriate but, once taken, resulted in a cascade of events the outcome of which were very high QALY values. These in turn were fundamental to the Committee’s decision to make a negative recommendation regarding dasatinib and high dose imatinib. The positive recommendation for nilotinib which is subject to a formal offer by the company to the DH of a patient access scheme effectively removes this from the appeal process.

We wish to this appeal to proceed as an oral appeal.

Yours faithfully,

XXXXXXXXXX

Director and on behalf of

The CML Support Group

The CML Support Group, PO Box 56213, London N4 4WF, UK.
[redacted] . www.cmlsupport.org.uk . cmlsupportgroup@gmail.com