

Dear Sir/Madam
REF: Docket No. 2006N-0062
REF: RIN 0910-AF14

I am providing comment on these proposed guidelines.

I work for The Life Raft Group, an internet-based support group for patients with Gastrointestinal Stromal Tumors (GIST). We provide support and information to patients and family members around the world.

We have had a number of occasions in the past few years to work with patients trying to obtain drugs on a compassionate use (expanded access) basis. Recently Novartis, the maker of AMN107 (nilotinib) expressed a willingness to provide AMN107 via expanded access for individual patients with GIST after failing Gleevec and Sutent.

AMN107 is a promising agent that is in phase II trials for Chronic Myelogenous Leukemia (CML) (and other leukemia's). It is also in phase I/II trials for GIST, but this trial has not been accruing patients for the last 6 months or more (accrual has been hit or miss for longer than that, with frequent starts and stops). Expansion to phase III is not expected until April, 2007.

During this interim period, about a half-dozen of our members have tried to access AMN107 via expanded access for individual patients. The results have been very disappointing. The two major problems that we have encountered are:

1. Patients report that their doctors are unwilling to participate in this process citing that it takes months to accomplish and many hours of their time.
2. Patients and doctors report that the Institutional Review Board (IRB) process is very slow, tedious and cumbersome.

One doctor reported spending about 6 hours of her own time (not staff time) trying to access AMN107 through expanded use. Even with a template supplied by the drug manufacturer (supporting the rationale and safety), she still was unable to access the drug for her patient.

- o This process took around two months.
- o Here is the message from the oncologist: "I am saddened to report that Mark passed away Christmas morning. He never received the medication. He knew it was coming but slipped into a coma the day it arrived. I am appreciative of all of your help. Many people will miss Mark. Please pass the news on to those who knew him."

One patient upon receiving the contracts for access, noted that it was unlikely that he would be able to proceed noting the very frequent monitoring requirements (EKGs and monthly CT scans) citing that it would cost tens of thousands of dollars (assuming insurance would not cover expenses beyond normal monitoring; e.g. CT scans every 3 months, etc).

Even patients trying to access expanded use through major treatment centers, such as Dana-Farber cancer center (the principal site for the AMN107 phase I/II trial), have generally been unable to access the drug through expanded use.

Your proposed changes seem to be aimed at reimbursement for drug manufacturers. While this may be a problem in some cases, our own experience with a manufacture willing to provide access, suggests that the major problems with the program are complexity, unwillingness for doctors to participate and a cumbersome IRB process. The problems with IRBs extend to major institutions as well.

To summarize; even in extreme, life-threatening circumstances, with a willing drug manufacture, a fairly proven drug, a strong treatment rational and no ongoing access through clinical trials, it is *very difficult* to access the drug via expanded use for individuals. Some specific suggestions:

1. Streamline the process.
 - a. Guidance should be provided in a document that is specific for the intended use. A user should not have to pick through an 83 page document and try to find the relevant sections that pertain to individual access. While the document you have is fine for an overview of the whole program, each individual portion should be broken out into its own document.
 - b. Forms should be specific to their intended function. From reading your document, it is not clear if a doctor needs to fill out form 1571. Form 1571 appears to be a generic form, primarily used by investigators for a new drug. It is not appropriate for an individual doctor to try to fill out this form and try to fit his intended use to a form that was designed for something else. Provide a specific form for use with each intended function, e.g. a specific form for individual expanded access.
2. Some type of centralized IRB may be needed for small to medium sized access programs.
3. Access will not improve until the doctor/IRB barrier is broken.
 - a. Doctor paperwork time must be drastically minimized.
 - b. The IRB barrier must be broken.
 - c. Education and attitudes of doctors about the process must be improved.
 - d. Doctors are not familiar with the IRB process.
 - e. Access for individuals at major centers is no better than going through a local IRB (at least in our experience).
4. The process is so far skewed toward “protecting the patient from an unproved drug” that dying patients, with no other options, find it *extremely difficult* to access drugs through this program.

Sincerely,

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