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# Client Alert


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## FDA Grants "Compassionate Use" Access to Drug for ALS Patients: An Overview of the Issues Surrounding Expanded Access to Experimental Drugs

On March 10, 2009, the Food and Drug Administration reversed course and announced it will now grant patients suffering from ALS (Amyotrophic Lateral Sclerosis, or "Lou Gehrig's Disease) access to Iplex on a compassionate use basis. ALS is a fatal neurodegenerative disease for which there is no known cure. Iplex is currently approved by the FDA only for the treatment of growth failure in children with severe primary IGF-1 deficiency or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH. While Iplex's efficacy for ALS has not been established by any well-controlled clinical studies, there is substantial anecdotal evidence that the drug has been helpful when administered to ALS patients in Italy.

Over the past several months several dozen ALS patients and their physicians have filed applications requesting access to Iplex for "compassionate use" treatment of named patients under single-patient INDs. In a series of letters in January, FDA's Division of Neurology rejected the INDs on the ground that there was insufficient evidence of Iplex's safety and efficacy in treating ALS. In addition, although it was not a basis for the denial, FDA noted that the only way to determine if Iplex was beneficial or harmful in the treatment of ALS was to conduct a controlled clinical trial. Several patients objected to the denial and argued that the denials violated FDA's own regulations which contemplate that in most instances Treatment INDs will be granted to patients with life-threatening illnesses who lack other effective treatment options.

The FDA's reversal was prompted in part by assurances from Italian officials monitoring the use of Iplex that no major safety concerns had arisen among doctors who were administering the drug to their ALS patients. FDA's decision to allow access to Iplex for patients with ALS will occur in two ways under an IND:

- The agency will approve Treatment IND applications for all ALS patients who filed for "compassionate use" access by March 6, 2009; and
- The remaining supply of Iplex, which is very limited, will be use to conduct a clinical trial under an IND in which other patients with ALS who are interested in receiving Iplex treatment will be randomly selected to participate through a lottery system.

Furthermore, FDA will require all patients under either a single-patient IND or in the clinical trial to be adequately informed by their treating physician of the possible benefits and risks of treatment. To facilitate that informed consent, FDA will make available relevant documents concerning the drug.

The controversy over Iplex illustrates the complex issues surrounding expanded access to investigational drugs. Nothwithstanding the availability of accelerated approval procedures at the FDA, drugs that show promise for serious diseases are often not available to patients until many years after the

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drug's potential benefits have been identified. This situation has long created pressure on both FDA and the pharmaceutical industry to make promising experimental drugs available to patients other than those enrolled in clinical trials for the drug. This is especially the case when those patients have immediately life-threatening diseases for which no comparable or satisfactory alternative therapy is available. The current regulatory system has not resulted in clinical trials of sufficient scope and geographic distribution to provide reasonable options for the majority of patients suffering from life-threatening diseases with unmet needs.

Private sector participation in compassionate use and expanded access programs, although a response to this issue, has been too limited and uncertain to fill the gap, and as a result it has been argued that the FDA drug approval process fails to serve thousands of Americans each year. And as a result, over the past few years lawsuits have been filed seeking to establish a constitutional right for terminally ill patients to have access to unapproved drugs that might save their lives. A brief summary of the expanded access programs of FDA and the current legal issues surrounding these programs will place these developments in perspective.

**What expanded use programs exist for patients who are not able to enroll in a clinical trial?**

Drugs that are being clinically tested, but whose safety and efficacy have not yet been approved by the FDA are called "investigational drugs" and are tested in humans pursuant to an investigational new drug application (IND) approved by the FDA. Access to an investigational drug, when you are not enrolled in a clinical trial pursuant to an IND can occur in two main ways: (1) expanded access programs (EAP) or (2) single-patient access.

Since 1987 the "treatment IND" mechanism has been available to allow an experimental drug to be provided outside a controlled clinical trial to treat patients with serious or immediately life-threatening diseases for which no alternative treatment exists. The treatment IND program has been viewed as inadequate and underutilized, however, largely because the parameters to qualify are limited and the drug companies are not allowed to make any profit at all from such use. In light of these drawbacks, the FDA in 2006 proposed new regulations to allow easier access to investigational drugs prior to approval. The revised criteria for allowing treatment access to experimental drugs are: (1) the drug is intended to treat a "serious or immediately life-threatening disease or condition" for which there is "no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition"; (2) the potential benefit outweighs the potential risks; and (3) providing the drug for treatment uses will not interfere with the clinical investigations that could support marketing approval.

In addition to the Treatment IND and expanded access programs, FDA may also give permission for physicians to receive and administer an investigational drug to an individual patient outside the confines of a clinical trial program. These INDs are know as "single-patient INDs", or depending on the context, either "compassionate use" or "emergency use" INDs. To qualify under these programs, the identified patient must have an advanced serious disease that has not responded to available treatment options and must not be eligible to participate in a clinical trial that meets the patient's need. Also, the patient's doctor must have determined that there is no comparable or satisfactory alternative therapy and that the probable risk from the drug is less than the probable risk of the disease itself.

**Is there a constitutional right to access to experimental drugs?**

Despite these expanded access programs and single-patient INDS, the boundaries between new drug development and the desire of seriously ill patients for life-saving treatments remain uncertain. The decision about whether an individual patient should be allowed compassionate use can be difficult because the


drugs in question are experimental and in many cases, there is limited information about whether they are effective, or even safe. In the face of a life-threatening disease, it is often easy for patients and their families to be too easily oversold on the benefits of a potential treatment and in turn, the drug companies engaged in the clinical trials may also embrace the hype because they long for the blockbuster drug.

The issue of expanded access has led to recent litigation. Under the Fifth Amendment's guarantee that "No person shall be deprived of life, liberty, or property without due process of law," advocates on behalf of critically ill patients recently sued FDA to argue these patients should have access to unapproved drugs that may save their lives so long as they agree to bear the risks involved. Essentially the plaintiffs sought to overturn the FDA's ability to prohibit access to new drugs before they have been approved. The argument was simple and powerful—if we are willing to take the risk and we have no other options, we should be able to gain access to a drug that may help us because our lives are at stake. The argument was also advanced that since the constitution affords adults the right to refuse life-saving therapy, how can it not also extend its protection to people seeking to save their own lives.

These claims led to an initial 2-1 decision by the United States Court of Appeals for the D.C. Circuit finding a constitutional right to access to unapproved investigational drugs. The court noted that "where there are no alternative government-approved treatment options, a terminally ill, mentally competent adult patient's informed access to a potentially life-saving investigational new drug determined by the FDA after Phase I trials to be sufficiently safe for expanded human trials, warrants protection under the Due Process Clause." *Abigail Alliance for Better Access to Developmental Drugs v. Eschenbach*, 445 F.3d 470, 486 (D.C. Cir. 2007). FDA sought an en banc reconsideration of this decision, and on August 7, 2007, the full court rejected the panel's constitutional analysis and ruled that "there is no fundamental right… of access to experimental drugs for the terminally ill." Id. At 697. The full court found no justification for a constitutional right that would interfere with the collective judgment of the scientific and medical communities derived from the Congressionally mandated FDA approval process for new drugs. The Supreme Court declined to review the case.

Even without a constitutional right on which to base their case, some terminally ill patients in FDA-approved clinical trials have sued manufacturers demanding that they continue supplying them with experimental drugs after the manufacturer has made the decision not to continue with the trial. For example, in *Abney v. Amgen*, Inc., 443 F.3d 540 (6th Cir. 2006), such claims were rejected because the court found that nothing in the informed consent forms signed by the plaintiffs or in the study materials they received amounted to a binding contract to keep giving them the medication after the manufacturer decided not to continue with the study. The court also held that the manufacturer had done nothing that amounted to a promissory estoppel ( a legal term for a promise that fails to meet the standards for a contract, but that the court decides to enforce nevertheless) and also had no fiduciary relationship with the study subjects.

Undoubtedly, arguments concerning this emotionally charged issue will continue and new litigation strategies will be advanced. However, as the recent decision by FDA to allow patients with ALS to gain access to Iplex demonstrates, compassionate use petitions for patients who have exhausted all other treatment options remain a viable option.