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Expanded Access to Investigational Drugs for Treatment Use

Geisinger Health Plan welcomes the opportunity to provide comment to the FDA on the proposed amendment of its regulations on access to investigational drugs for the treatment of patients. The Food and Drug Administration Modernization Act of 1997 allows for access to investigational drugs according to specific criteria. The FDA is proposing this amendment in order to increase awareness of expanded access programs, and to make clear the procedures for obtaining investigational drugs. As stated by The Assistant Commissioner for Policy, Dr. Jeffrey Shuren, this expansion of access to drugs to individuals, intermediate sized groups and to larger populations under a treatment IND or treatment protocol must be balanced with the FDA's statutory responsibility to ensure that drugs are safe.

The current regulations that inform FDA determinations regarding expanded access for treatment use (Section 312.34) allow for access to investigational drugs under a treatment IND or treatment protocol. The conditions that must be met have been clearly specified. The criteria are:

1. The drug is intended to treat a serious or immediately life-threatening disease;
2. There is no comparable or satisfactory alternative drug or other therapy to treat that stage of the disease in the intended patient population;
3. The drug is under investigation in a controlled clinical trial under an IND in effect for the trial, or all clinical trials have been completed; and
4. The sponsor of the controlled clinical trial is actively pursuing marketing approval of the investigational drug with due diligence.

Section 312.34 specifies that for serious disease, data from phase 3 trials or, when appropriate, phase 2 trials would be needed before approval for expansion to a broad population. The standard for immediately life-threatening conditions is that there is reasonable evidence that the drug may be effective and would not expose the patient to additional risk of illness or injury. According to the background information provided, the FDA seeks to further specify criteria used in their decisions on individual patient treatment use and other treatment use programs. It is stated that part of what motivates this is a response to criticism that access to investigational drugs for treatment use has focused on patients with HIV or cancer. Furthermore, it is stated that patients outside of academic medical centers are less likely to have access to investigational drugs for treatment purposes. The document is noteworthy for a lack of information about differences in outcomes for patients who have obtained access to investigational drugs under these criteria compared with those who have not. Nor is there mention of health outcomes comparing these patients who have been treated with investigational drugs in

academic medical centers compared to those who have not. This is relevant because one goal of this proposal is to expand access. It would be important to learn what the experience has been comparing patients treated within clinical trials to those individuals who were treated with investigational drugs as a result of Section 312.34. If patients are more likely to receive investigational drugs at academic medical centers, there is no language in the existing policy that dictates this. The proposal stated that it has to do with increased familiarity of FDA regulations within academic centers. If this is true, one might ask why this is so. If it is because these centers are more likely to treat patients with life-threatening disease who have exhausted available conventional treatment options, it is also possible that it is in the public interest that this trend continues. It may not always be true that greater numbers and experience leads to better outcomes but there are enough examples of this to place the burden of evidence on those who claim that this is not the case. As is stated in the proposal, access to investigational drugs can pose risks to patients. The level of evidence FDA requires for individual patients is less than for larger groups. It is stated that for individual patients there may not even be Phase 1 data available. Determinations to expand coverage for an individual patient may be based upon preclinical data or on mechanism of action. This significant relaxation of the standards of evidence required before expanded access is granted would likely magnify the risk while offering an unknown benefit.

Another concern that was raised was whether the expansion of access to investigational drugs for treatment would adversely impact the ability of sponsors to enroll sufficient numbers of patients in clinical trials. This may be particularly true for certain areas of the country such as rural communities. Even if sufficient numbers of patients are enrolled from urban areas, an unintended consequence could be the skewing of demographics of those who participate in clinical trials.

Geisinger Health Plan looks to the FDA for guidance in ensuring that treatments offered to our members promote health and limit risk of harm. We trust that the FDA will give careful consideration to the proposal to expand the availability of investigational drugs to the most vulnerable of our society, those with life-threatening disease.

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