

## **FDA MISCONCEPTIONS REGARDING MYOTROPHIN/INCRELEX (“FREE IGF-1”) VS IPLEX (IGF-1/IGFbp-3)**

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Myotrophin or Increlex is Free IGF-1 (it is unbound). Myotrophin is refrigerated and is injected SQ 2x per day (total dose for children = .24mg/kg per day). Myotrophin is FDA approved for Short Growth Stature and Myotrophin/Increlex has FDA Orphan Drug status for ALS and is currently available for FDA approved off-label use by ALS patients.

Iplex is BOUND IGF-1 = rIGF1BP3. Iplex is FROZEN and is injected SQ 1x per day (total dose for children = 2mg/kg) Due to the binding protein in Iplex, they are very different drugs, as you can see in its formulation, storage, delivery, and dosing. Iplex is believed to have a better half life in the body, can be administered at higher doses and has a better safety profile than Myotrophin or Increlex. Iplex is FDA approved for Short Growth Stature - but due to a patent settlement dispute - Iplex marketing status has been discontinued. Iplex is approved in Europe for Premature Retinopathy (Infants). Iplex has FDA Orphan Drug Status for Myotonic Dystrophy and has just completed Phase II clinical trials for MD. Iplex (formerly SomatoKine) has been tested in a variety of clinical settings in over 300 patients from infant to 92 years of age - with no serious adverse side effects. Iplex has been used for over 2 years in Italy for the indication of ALS. Well over 150 Italian ALS patients have been given the privilege and the right to take Iplex to fight off the ravages of ALS. This number of Italian patients continues to grow.

In FDA denials of the right to Iplex, Dr. Katz compares Iplex to Myotrophin and in a most contradictory fashion. Dr. Katz questions the safety of Myotrophin. Yet, In 1996, in the FDA transcripts reviewing the first 2 Myotrophin trials (Study 1200 & Study 1202), Dr. Katz himself, Dr. Temple and other FDA representatives unanimously agreed that "Myotrophin was safe" for ALS.

See link – page 306: [www.fda.gov/ohrms/dockets/ac/96/transcript/3183t2.rtf](http://www.fda.gov/ohrms/dockets/ac/96/transcript/3183t2.rtf) They also noted that there was statistically significant improvement in ALS symptoms in the higher dose (.1mg/kg) arm of the trial. There is a wealth of information in these transcripts and this 1996 FDA approval led to a third Myotrophin trial (10 years later). Dr. Katz is questioning the safety of Myotrophin -- yet it was unanimously approved by him and others as safe -- and the FDA followed by allowing another 330 ALS patients to be exposed to Myotrophin. And they continue to allow Myotrophin to be used off-label by ALS patients. Sadly, the 2006 Myotrophin ALS trial was conducted at the low dose (.05mg/kg) -- the same dose that was found statistically insignificant by everyone in the 1996 transcript. Please note this dose is almost 5x less than the dosage prescribed for and FDA approved for children.

Regarding our right to take Iplex interfering with the success of “unknown, unplanned, possible” future clinical trials: There is not a single USA pharmaceutical trial that the vast majority of ALS patients qualify for at this time (due to time of symptom onset, feeding tube, bi-pap, ventilation, etc). Those applying for the emergency IND for Iplex are “throw away” patients. No clinical trial would want them -- their limited survival potential and their severe disease symptoms would throw off the potential of clinical trials which are usually designed for early stage patients. Iplex is not in clinical trial for ALS. Insmed cannot afford another clinical trial. MDA has invested its limited resources in the Myotonic Dystrophy/Iplex trial. If there were a future “Iplex for ALS” trial -- this trial will be for ALS patients of the future. Today's patients do not have the luxury of time-- the 3rd Myotrophin trial took 10 years to initiate. It is woefully unfair for the FDA to try to keep Iplex from us based on “unknown, unplanned, possible clinical trials”, but it is our opinion that the best way to promote the future of a clinical trial of Iplex for ALS is to allow these “throw away” patients, to be given their legal right to Iplex. Because if the results are as we believe then patients and physicians will push for an Iplex trial. Also, in another contradiction, FDA allowed ALS patients to take Myotrophin off-label before the Myotrophin trial, during the trial and are continuing to allow ALS patients to take it (under the brand name Increlex).

**ALS WORLDWIDE is a non-profit organization that provides support to ALS families internationally through scientific research interpretation, individual patient advocacy and community activism.**

Italian ALS patients have been given the privilege and the right to access Iplex -- an American drug. In an act of protecting its terminally ill citizens, the Italian Ministry of Health is spending millions of dollars to purchase Iplex on behalf of their ALS patients. In Insmmed's February 12 phonecast (see directions below) - Insmmed announces the growing number of Italian ALS patients taking Iplex and the fact that Iplex will be available throughout Europe in the beginning of the 2nd quarter of 2009. **In other words -- all the world's ALS patients - except Americans -- will have the right to take Iplex to help stop the death and devastation of ALS.** How can the FDA do this to us? Do terminally ill Americans with ALS deserve less than the other citizens of the world?

We must have the right to Iplex and we ask that you help us with this, for which thousands of ALS families will be eternally grateful. Although the first formal Appeal has been filed in response to the initial denials of IND usage, we have already been forewarned by FDA that our Appeals will be denied. We are therefore taking this to the media, our government representatives and the judiciary. There is no compelling reason to keep Iplex from American ALS patients who, with the support of their physicians, will follow the proper regulatory guidelines for an Emergency IND. This drug, Iplex, that is FDA approved for children and used successfully for premature infants, the most fragile population of all, cannot be as or more dangerous than the horrific effects and guaranteed 100% mortality of ALS.