Dragon, Karen E. (CDC/NIOSH/EID)

From: Uriel Cadsap [Uriel.Cadsap@tercica.com]
Sent: Wednesday, September 26, 2007 5:05 PM
To: NIOSH Docket Office (CDC)
Subject: 105 - HazDrug Update Comments
Attachments: Copy of PublicReviewForm2006-05-01-07.xls

Please consider the comments for Increlex. The review form is attached and our comments why Increlex shouldn't be classified as hazardous can also be found at the lower part of this email.

Thank you.

<<Copy of PublicReviewForm2006-05-01-07.xls>>

Uriel Cadsap

Associate Director, Quality Compliance

Tercica

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Brisbane, CA 94005

650-238-1535

The active ingredient of Increlex is mecasermin which is a recombinant version of the human hormone insulin-like growth factor 1 (IGF-1). It is a polypeptide consisting of 70 amino acids. IGF-1 is present in the blood and many tissues of all normal humans in highly variable concentrations. Unless bound to specific binding proteins, its half-life is short (less than an hour). As a polypeptide, its oral bioavailability is low.

IGF-1 has a strong structural homology to insulin and that insulin and IGF-1 have similar pharmacologic and toxicologic activities in animal studies, including in toxicology studies such as carcinogenicity studies where insulin and IGF-1 show similar effects.

Increlex is approved for the long-term treatment of children with growth failure due severe Primary IGF-1 deficiency. In this indication, it is administered per subcutaneous injection twice a day. The quantities typically administered are in a similar order of magnitude as those that would be produced by a normal individual. The typical duration of treatment is several years; it usually ends when linear growth ends with the fusion of the growth plates.

Significant inadvertent exposure to Increlex in the workplace is conceivable only through accidental injection, since other contact to the product would not lead to significant absorption. Accidental injection, however, would be expected to occur only in isolated instances or at most occasionally, but not on a chronic basis. The most notable expected acute effect of IGF-1 injections is a decrease of the blood glucose concentration. However, a substantial quantity would have to be injected to lead to hypoglycemia in an adult. Since variations in IGF-1 blood levels are part of normal human physiology, occasional short-lived increases in IGF-1 exposure are unlikely to have any significant lasting effect, particularly not with respect to carcinogenicity, reproductive toxicity, genotoxicity, or organ toxicity. Therefore, Tercica believes that Increlex should be removed from the NIOSH list of hazardous drugs.

Drugs to Review 2006 Docket #NIOSH-105

Reviewer : Gary Neumann

Affiliation : Tercica

Proprietary Name	Established Name	Should this Drug be Included in the NIOSH Hazardous Drugs List ? yes	no	Comments
New FDA Drugs and Warnings Fitting NIOSH Criteria For Hazardous Drugs				
Increlex	mecasermin (rDNA origin)		X	IGF-1 has a strong structural homology to insulin and that insulin and IGF-1 have similar pharmacologic and toxicologic activities in animal studies, including in toxicology studies such as carcinogenicity studies where insulin and IGF-1 show similar effects.
				The active ingredient of Increlex is mecasermin which is a recombinant version of the human hormone insulin-like growth factor 1 (IGF-1). It is a polypeptide consisting of 70 amino acids. IGF-1 is present in the blood and many tissues of all normal humans in highly variable concentrations. Unless bound to specific binding proteins, its half-life is short (less than an hour). As a polypeptide, its oral bioavailability is low.
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Drugs to Review 2006 Docket #NIOSH-105				Send reviews to: niocindocket@cdc.gov
Reviewer : Gary Neumann				
Affiliation : Tercica				
Proprietary Name	Established Name	Should this Drug be Included in the NIOSH Hazardous Drugs List ? yes	no	Comments
New FDA Drugs and Warnings Fitting NIOSH Criteria For Hazardous Drugs				
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ADDITIONAL COMMENTS				