FYI

The New and Generic Drug Manufacturing Team in the Division of Manufacturing and Product Quality has completed its review and evaluation of the final TB-EER for Savient's STN 125293. Please see the attached form for individual site compliance statuses. There are no pending or ongoing compliance actions that prevent approval of this BLA.

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1.12.14. ENVIRONMENTAL ASSESSMENT OR CATEGORICAL EXCLUSION

1.12.14.1 Biological Identification

Puricase® is a colorless, clear, sterile solution containing 8 mg/mL uricase protein conjugated to methoxypolyethylene glycol (mPEG) in phosphate buffered saline.

1.12.14.2 Categorical Exclusion Justification

The greatest annual production of uricase (active moiety of the Drug Substance) in the finished product is expected to be (b) (4) for the five year marketing period (2009-2013) following anticipated approval of submission in 2009.

The expected introduction concentration (EIC) of an active moiety into the aquatic environment should be calculated as follows:

EIC-Aquatic (ppb) = A x B x C x D

Where
A = kg/year produced for direct use (as active moiety)
B = 1/liters per day entering POTWs*
C = year/365 days
D = 10⁹ µg/kg (conversion factor)

* 1.214 x 10¹¹ liters per day entering publicly owned treatment works (POTWs), or

EIC = (b) (4) x (1/1.214 x 10¹¹ liters per day) x (year/365 days) x 10⁹ µg/kg = (b) (4)

Based on this calculation Biologics License Application for Puricase® meets the criteria for categorical exclusion under 21 CFR Section 25.31(b). Section 25.31(b) provides for a categorical exclusion regarding an action on this BLA, if the action increases the use of the active moiety, but the estimated concentration of the substance at the point of entry into the aquatic environment will be below 1 part per billion.