



Food and Drug Administration
Rockville MD 20857

ADMINISTRATIVE STAFF

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Dear Ms. Davidson:

This letter concerns the citizen petition dated March 16, 1981, that was submitted jointly by Dow Chemical Co., Burroughs-Wellcome Co., and Schering Corp., to support a change in the dosage schedule for pseudoephedrine for use as an oral nasal decongestant from 60 mg every 6 hours, not to exceed 240 mg in 24 hours, to 60 mg every 4 to 6 hours, not to exceed 240 mg in 24 hours. (A copy of this material is coded CP, Docket No. 76N-052N, and is on file in the Dockets Management Branch.)

The Bureau of Drugs has reviewed the data submitted in support of a dosage schedule of every 4 to 6 hours. The data include information on the pharmacokinetic behavior of pseudoephedrine and a review of adverse drug reactions related to pseudoephedrine. The submission contains a computer simulation of steady-state pseudoephedrine concentration profiles as a function of the dosage interval (i.e., every 4 hours vs. every 6 hours with a 240-mg maximum daily dose). The results show that the major determinant of the half-life of pseudoephedrine is urinary pH and that the half-life varies from 4 to 8 hours in normal individuals who are representative of the population at large. Based on the pharmacokinetic data, the Bureau concludes that 60 mg of pseudoephedrine given every 4 to 6 hours is permissible and more reflective of the achievable blood levels than a fixed dosage given every 6 hours.

In addition, eight studies were included in the petition. The Bureau notes that, the results of 6 of the studies are not relevant to the issue of whether the frequency of administration of pseudoephedrine is a factor in the incidence of side effects. However, two studies are supportive. The Kuntzman study demonstrates the influence of urine pH on the half-life of pseudoephedrine. When urinary pH is decreased, plasma half-life of pseudoephedrine is decreased markedly. In

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