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Public Citizen's Health Research Group's Comments On: Schedules of Controlled Substances: Proposed Placement of Butorphanol into Schedule IV [DEA No. 166P]

Submitted - August 11, 1997

Public Citizen's Health Research Group appreciates the opportunity it has been given to comment on the classification of butorphanol (Stadol and Stadol Nasal Spray) as a controlled substance.

Since 1972, Public Citizen's Health Research Group has been promoting research-based, system-wide changes in health care policy as well as advocating for the appropriate prescribing and use of prescription drugs. The Health Research Group testifies before Congress and petitions the Food and Drug Administration (FDA) on issues such as banning or relabeling of drugs and the misleading advertising of prescription and non-prescription drugs by their manufacturers. Our publications help consumers make informed decisions about the health care they receive and the drugs they are prescribed.

Public Citizen strongly supports this action by the Drug Enforcement Agency (DEA) to regulate all forms of the potent opioid pain reliever butorphanol as a controlled substance. Butorphanol's classification under the Controlled Substance Act (CSA) will finally inform doctors and consumers of this drug's potential addicting properties. Most importantly, it will allow consumers to make informed decisions, with their doctors, about accepting the risks of taking a drug that can cause physical and psychological dependence.

However, this action by the DEA is 19 years too late for many consumers who were not warned of butorphanol's addictive properties and were unwittingly made dependent on this drug while it was being heavily promoted to doctors as non-addicting by its producer Bristol Laboratories now Bristol-Myers Squibb of Princeton New Jersey. Many consumers would have been warned about butorphanol if the FDA had heeded the recommendation of its own Drug Abuse Advisory Committee to control butorphanol when it was first approved in 1978. At the same time that butorphanol was being

Ralph Nader, Founder
1600 20th Street NW • Washington, DC 20009-1001 • (202) 588-1000

approved, the FDA also disregarded the dependence caused by pentazocine (Talwin), another potent pain reliever, and chemical cousin to butorphanol. Experts predicted that pentazocine, like butorphanol, would cause dependence, but pentazocine was approved without control in 1967 and was marketed for 12 years as a non-addicting pain reliever before being regulated as a controlled substance in 1979, shortly after the approval of butorphanol in 1978.

Unfortunately there is a well established pattern in the United States of drugs that should have been initially regulated as controlled substances, which were then heavily promoted to doctors as safe and nonaddicting by their manufacturers after their approval without controls, then were uncritically accepted by the medical profession as breakthrough drugs, and ultimately unsuspecting consumers became dependent on them. This pattern is now being repeated with another pain reliever, tramadol (Ultram), a drug that was known to be addictive before it was approved, but was approved in 1995 without controls and remains uncontrolled today. Dependence with butorphanol, pentazocine and tramadol was predictable. Considerable harm could have been prevented if these drugs had been initially been regulated as controlled substance, thus warning consumers of their of their addictive properties. However, as long as regulatory authorities continue a policy of not controlling a drug until a significant public health problem has emerged and large numbers of consumers have been injured this pattern will continue to be repeated. Butorphanol, pentazocine and now tramadol raise serious questions about the effectiveness of controlled substance regulatory policy in protecting the public's health.

The CSA [21 USC 811(b)] requires the following factors be considered in determining the classification of a drug as a controlled substance:

(1) Its actual or relative potential for abuse.

(2) Scientific evidence of its pharmacological effect, if known.

(3) The state of current scientific knowledge regarding the drug or other substance.

(4) Its history and current pattern of abuse.

(5) The scope, duration, and significance of abuse.

(6) What, if any, risk there is to the public health.

(7) Its psychic or physiological dependence liability.

(8) Whether the substance is an immediate precursor of a substance already

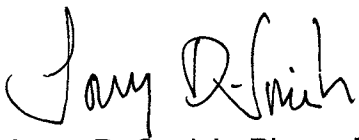
controlled under this subchapter.

These factors rely heavily on a large number of consumers being harmed before a drug is controlled. Factors (1), (4), and (5), can only be ascertained after a drug is approved for marketing and many unsuspecting consumers are injured. Pursuing a policy that requires this information before regulating a drug under the CSA in effect makes the American public subjects in a large uncontrolled experiment in which the participants have not been fully informed of the risk of dependence with the drug. Factors (2) and (3) are vague and this type of information may be presented by companies seeking approval of their new drugs as innovative, breakthrough products which are safe and nonaddictive based on animal studies or abuse liability studies in former addicts. This was the case with butorphanol, pentazocine and tramadol. Factors (6) and (7) can be assessed for new drugs by their chemical and pharmacological similarities to drugs already known to cause physical and psychological dependence. To quantify the risks in Factors (6) and (7) studies would have to be done after a drug is approved for marketing. Factor (8) is known before a drug is approved and is self explanatory.

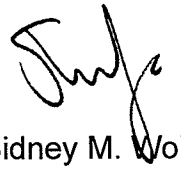
Controlled substance regulation, as exemplified by butorphanol, pentazocine and tramadol, strongly favors protecting the marketing potential of a new drug and the economic interests of drug companies at the expense of consumers unknowingly becoming drug dependent. These three drugs were predicted to cause physical and psychological dependence based on their chemical similarities to morphine and their ability to interact with the same brain receptors as morphine. Public Citizen believes that chemical structure and brain receptor characteristics must be strongly considered in initially classifying a new drug as a controlled substance. The burden of proof must rest with drug companies to show that new potentially addicting drugs, based on their similarities to drugs known to cause dependence, in fact, do not injure consumers in valid post-marketing studies.

Public Citizen strongly urges the DEA and the FDA to examine their policies on regulating new drugs that can potentially cause physical and psychological as controlled substances and to error on the side of consumer safety.

Sincerely,



Larry D. Sasich, Pharm.D., M.P.H., FASHP
Research Analyst,
Public Citizen's Health Research Group



Sidney M. Wolfe, M.D.
Director,
Public Citizen's Health Research Group