Health Canada Santé Canada

Scientific Advisory Committee on Oncology Therapies (SAC-OT)
Arsenic Trioxide - Consultation *via* Email
August/September 2011

Final Compilation of Recommendations

Participating Committee Members: Alexander Paterson (Chair), Rick Abbott, Charles A. Butts, Diana M. Ermel, Stan Z. Gertler, Kong E. Khoo, Kara E. Laing, Ronald E. MacCormick, Wojciech Morzycki, Lynne Nakashima, Scott A. North, Lesley K. Seymour, Douglas Stewart, Ian F. Tannock, Maureen E. Trudeau.

Health Canada Representatives: Theresa Burke, Caroline Hunt, Thea Mueller, Eric Ormsby

Health Canada solicited expert opinion whereby SAC-OT members provided recommendations through an email consultation process.

The SAC-OT members were consulted on an issue regarding arsenic trioxide and its use, in conjunction with other chemotherapeutic agents, to treat acute promyelocytic/myeloid leukaemia (APL). Specifically, the question posed to the committee revolved around section C.01.040 (b) of the *Food and Drug Regulations* that prohibits the sale of a drug for human use that contains arsenic, its salts or its derivatives as an ingredient.

Question Posed to the Committee

Health Canada posed the following question to the committee for their considered opinion:

1. *While clinical trials using prohibited substances (including arsenic) are permitted in Canada provided there is a potential benefit to humans, the sale of such products remains prohibited. Health Canada is proposing that the regulation prohibiting the use of arsenic as an ingredient in drugs sold for human use be amended to allow a more flexible regulatory mechanism under specified circumstances.*

   In order to repeal the original prohibition decision, Health Canada is asking the SAC-OT whether or not they support the revocation of the regulation section C.01.040(b) prohibiting the sale of drugs for human use that contain arsenic, its salts or derivatives in drugs.

A Brief Overview of the Regulatory Background of Arsenic

In 1979, an external advisory committee convened by the Health Protection Branch concluded that there was no longer any rationale for the use of arsenic in human medication. In 1981, a final recommendation was issued stating that arsenic and its salts or derivatives be prohibited in

drugs for human use. The *Food and Drug Regulations* were subsequently amended to prohibit the sale of a drug for human use that contained arsenic as an ingredient; these regulations came into force in January 1990.

Since then, results of clinical trials have demonstrated that arsenic trioxide can be effective in the treatment of acute promyelocytic leukaemia. Based on this supportive evidence, arsenic trioxide has been approved for use in chemotherapeutic treatment regiments by other regulatory agencies [The Australian Therapeutic Goods Administration, The United States Food and Drug Administration (FDA), and the European Medicines Agency].

Committee's Recommendation

Members who participated in the email consultation stipulated that arsenic trioxide is still considered a useful and well tolerated agent to treat relapsed acute promyelocytic/myeloid leukaemia (APL), and promising data from front-line studies are emerging. As such, the members supported the revocation of the *Food and Drugs Regulation* section C.01.040(b) that prohibits the sale of drugs for human use that contain arsenic, its salts or derivatives in drugs.

The Chair noted that the consensus among SAC-OT members was to amend the *Food and Drug Regulations* to allow the sale of arsenic trioxide. He noted that the repeal of this regulation would allow submissions containing this potentially useful anti-leukemic agent to be reviewed with no legal concerns.

It was emphasized that through this recommendation, the committee is not endorsing the approval of drug submissions containing arsenic trioxide, its salts or derivatives.

Health Canada would like to thank all committee members for their time and effort in participating in this recommendation request.

References:

1. United States Food and Drug Administration. Drug Approval Package. Trisenox (Arsenic Trioxide) Injection Company: Cell Therapeutics, Inc. Application No.: 21-248, Approval Date: 9-25-2000
2. *Food and Drugs Act. Food and Drug Regulations*, Amendment. Regulatory Amendment to Prohibit Arsenic. P.C. 1989-719, April 28, 1989.