

were treated with prussian blue for nonradioactive thallium poisoning. Prussian blue treatment reduced the mean serum biologic half-life of thallium from 8 days to 3 days (see Barbier, 1974; De Groot, 1985; Van Kesteren, 1980; and Vrij, 1995).

The primary adverse effects of prussian blue are constipation and nonspecific gastrointestinal distress. These side effects are more troublesome at high doses and respond to treatment with orally administered fiber (see Farina, 1991). Other rare adverse events are discussed in the published literature and in the draft labeling we have prepared.

B. Labeling for Prussian Blue

We have prepared draft labeling for orally administered drug products containing 500-mg prussian blue capsules. You can submit this draft labeling as part of an application for 500-mg prussian blue capsules that relies on our findings of safety and effectiveness. The draft labeling reflects our conclusion on the potential safety and effectiveness of 500-mg prussian blue drug products for the treatment of internal contamination with radioactive thallium, nonradioactive thallium, or radioactive cesium. If you wish to change the labeling to include a different or broader indication, different dosage, or make any other significant changes to the draft labeling, you should provide, as part of your application, additional literature or other studies to support your requested changes. If you submit an application for a prussian blue drug product that is not based on FDA's findings of safety and effectiveness of prussian blue, you may not use the draft labeling because it is based on our review of the published literature. If you submit such an application, your labeling must be based on the safety and effectiveness data contained in your NDA.

The draft labeling for applications based on this finding of safety and effectiveness is available on the Internet at <http://www.fda.gov/cder/foi/label/2003/ind51700lbl.pdf>. You may also contact the Center for Drug Evaluation and Research's Division of Medical Imaging and Radiopharmaceutical Drug Products for a copy of the draft labeling (see ADDRESSES).

III. Conclusions

We have determined that 500-mg prussian blue capsules can be safe and effective for the treatment of patients with known or suspected internal contamination with radioactive thallium, nonradioactive thallium, or radioactive cesium. We encourage the

submission of NDAs for prussian blue drug products. The requirement under 21 U.S.C. 355(b)(1) for full reports of investigations to support these NDAs may be met by citing the published literature we relied on in preparing this notice. A list of the published literature and reprints of the reports will be available for public inspection in the Dockets Management Branch (see ADDRESSES). It is unnecessary to submit copies and reprints of the reports from the listed published literature. We invite applicants to submit any other pertinent studies and literature of which they are aware.

IV. Availability of a Guidance

A. Notice of Availability

In this notice, we are also announcing the availability of a guidance for industry entitled, "Prussian Blue Drug Products—Submitting a New Drug Application." The guidance is intended to assist manufacturers who plan to submit NDAs for prussian blue.

This guidance is being issued as a level 1 guidance consistent with FDA's good guidance practices regulation (21 CFR 10.115). It is being implemented immediately without prior public comment because the agency believes it is in the interest of the public health to communicate this information to the public as quickly as possible. However, the agency welcomes comments on the guidance and, if comments are submitted, the agency will review them and revise the guidance if appropriate. The guidance represents the agency's current thinking on issues associated with the submission of NDAs for prussian blue. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

B. Comments

Interested persons may, at any time, submit written or electronic comments on the guidance to the Dockets Management Branch (see ADDRESSES). Two copies of any mailed comments are to be submitted except that individuals may submit one copy. Comments are to be identified with the docket number found in the brackets in the heading of this document. The document and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

C. Electronic Access

Persons with access to the Internet may obtain the guidance at either <http://www.fda.gov/cder/guidance/index.htm> or <http://www.fda.gov/ohrms/dockets/default.htm>.

V. Published Literature on the Safety and Effectiveness of Prussian Blue

The published literature we have relied on in making the determinations regarding prussian blue contained in this notice is listed in this section of this document. Copies of the published literature will be on display in the Dockets Management Branch (see ADDRESSES) and can be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Atsmon, J. et al., "Thallium Poisoning in Israel," *American Journal of the Medical Sciences*, 320:327–330, 2000.
2. Barbier, F., "Treatment of Thallium Poisoning," *Lancet*, 7886(II):965, 1974.
3. British Industrial Biological Research Association, "Short-Term Feeding Study of Sodium Ferrocyanide in Rats," *Food and Cosmetics Toxicology*, 7:409–410, 1969.
4. Brandao-Mello, C. E. et al., "Clinical Hematological Aspects of ¹³⁷Cs: The Goiania Radiation Accident," *Health Physics*, 60:31–39, 1991.
5. Buser, H. J. et al., "The Crystal Structure of Prussian Blue: Fe₄[Fe(CN)₆]₃•xH₂O," *Inorganic Chemistry*, 16:2704–2709, 1977.
6. Dresow, B. et al., "In Vivo Binding of Radiocesium by Two Forms of Prussian Blue and by Ammonium Iron Hexacyanoferrate (II)," *Clinical Toxicology*, 31:563–569, 1993.
7. De Groot, G. et al., "An Evaluation of the Efficacy of Charcoal Haemoperfusion in the Treatment of Three Cases of Acute Thallium Poisoning," *Archives of Toxicology*, 57:61–66, 1985.
8. De Groot, G., and A. N. P. Van Heijst, "Toxicokinetic Aspects of Thallium Poisoning. Methods of Treatment by Toxin Elimination," *The Science of the Total Environment*, 71:411–418, 1988.
9. Farina, R., C. E. Brandao-Mello, and A. R. Oliveira, "Medical Aspects of ¹³⁷Cs Decorporation: The Goiania Radiological Accident," *Health Physics*, 60:63–66, 1991.
10. Giambarresi, L., "Radioprotectants," in *Military Radiobiology*, Orlando, Academic Press, 1987.
11. Heydlauf, H., "Ferric-Cyanoferrate (II): An Effective Antidote in Thallium Poisoning," *European Journal of Pharmacology*, 6:340–344, 1969.
12. Hoffman, R. et al., "Comparative Efficacy of Thallium Absorption by Activated Charcoal, Prussian Blue, and Sodium Polystyrene," *Journal of Toxicology-Clinical Toxicology*, 37:833–837, 1999.
13. Hoffman, R., "The Toxic Emergency," *Emergency Medicine*, June:127–128, 1994.
14. International Atomic Energy Agency, *The Radiological Accident in Goiania*, Vienna, IAEA, 1988.
15. International Atomic Energy Agency, *Dosimetric and Medical Aspects of the Radiological Accident in Goiania in 1987*, Vienna, IAEA-TECDOC-1009, 1998.