CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-387

SUMMARY REVIEW

DIVISION OF CARDIO-RENAL DRUG PRODUCTS

Divisional Memo

NDA: 22-387 (inhaled treprostinil for pulmonary hypertension)

Sponsor: United Therapeutics

Review date: 28 July 2009

Reviewer: N. Stockbridge, M.D., Ph.D., HFD-110

Distribution: NDA 22-387
HFD-110/Brum/Karkowsky

This memo conveys the Division's recommendation to issue an approval letter for inhaled treprostinil for pulmonary arterial hypertension.

After my previous memo (25 April 2009), the application was given a 3-month extension. During this time, the sponsor provided biocompatibility data for the device and results of a human factors study.

Both responses are described in the CDRH review (signed 20 June 2009, DFSed 29 June 2009) by Sugato De and Ronald Kaye. The biocompatibility data were considered adequate. The human factors study and the device itself are not considered adequate. On this latter, all members of the review team appear to be in agreement.

The De-Kaye review concludes that a proper human factors study should be conducted with the next-generation device, but that these can be deferred to post-marketing commitments if the risks are considered small compared with the benefits. In this I agree, and, in consideration of the relatively benign safety profile of the experience with inhaled treprostinil and the less benign safety profile of its other approved routes of administration, I believe the current drug-device combination meets the test, and the review team seems adequately persuaded.

Other reviews completed in the interim include a second CMC review (Cooper; 23 July 2009) and a second CDTL memo (Karkowsky; 27 July 2009).

The sponsor appears to have a reasonable plan to evolve the device, probably in several stages, with the worst identified problems being resolved in the first round.

On this basis, I believe the product should now be approved. Labeling and post-marketing commitments and requirements have been negotiated.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

NORMAN L STOCKBRIDGE
07/28/2009