CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208401Orig1s000

SUMMARY REVIEW

DIVISION OF CARDIOVASCULAR AND RENAL PRODUCTS

Divisional Memo

NDA: 208401 Lisinopril solution (Qbrelis) for hypertension, heart failure, and acute myocardial infarction.

Sponsor: Silvergate Pharmaceuticals

Review date: 20 July 2016

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

This memo conveys the Division's decision to approve this application.

This application has been the subject of reviews of CMC (Wilson-Lee et al., 23 March 2016), pharmacology/toxicology (Hausner; 10 February 2016), and clinical pharmacology (Madabushi, 24 March 2016). There is also a CDTL memo (Thompson; 17 July 2016), with which I am in complete agreement.

This is a 505(b)(2) application relying upon safety and effectiveness of Zestril. There are no remaining product quality issues. The facility inspections are complete.

There are no new nonclinical studies. There are no new findings in the literature. Recognized excipients were used at levels considered safe.

The sponsor performed two bioequivalence studies, single-dose crossover studies at 10 mg, one in the fasted state and one in the fed state. Both studies met conventional bioequivalence criteria.

I question whether either study was necessary. Lisinopril is freely soluble under acid conditions, yet it has a Tmax around 6 hours. This suggests that it is transport across the gut that is rate-limiting. Barring some excipient that further impeded transport, it is hard to see how the solution could fail to be bioequivalent to the tablet.

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/s/

NORMAN L STOCKBRIDGE
07/20/2016