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APPLICATION NUMBER: NDA 20375/S002

CHEMISTRY REVIEW(S)

FEB 22 1995

CHEMIST'S REVIEW

1. ORGANIZATION DMEDP, HFD-510 2. NDA NUMBER 20-375

3. NAME AND ADDRESS OF APPLICANT 3M Pharmaceuticals 3M Center, Bldg. 270-3A-01 Saint Paul, Minnesota 55144-1000 4. SUPPLEMENT NUMBER, DATE Supplement S002 1-26-95 6. NAME OF THE DRUG Climara 7. NONPROPRIETARY NAME Estradiol Trans-dermal System

ORIGINAL

9. AMENDMENTS/REPORTS, DATE

8. SUPPLEMENT PROVIDES FOR: Addition of as a manufacturer of estradiol drug substance

10. PHARMACOLOGICAL CATEGORY Estrogen replacement 11. HOW DISPENSED RX OTC X 10. RELATED IND/NDA/DMF DMF

13. DOSAGE FORM Transdermal patch 14. POTENCY 3.9 and 7.8 mg/patch

15. CHEMICAL NAME AND STRUCTURE C18H24O2 MW = 272.39 Estra-1,3,5(10)-triene-3,17-diol, (17beta)-

16. COMMENTS This Supplement provides for addition of as a manufacturer of estradiol drug substance. was listed as a drug substance manufacturer in the original NDA submission, before the application was approved (on 22-Dec-94). The withdrawal was the result of notification to the Division (by telephone) by the Office of Compliance that the compliance status of a facility was not acceptable. The original EER was then returned (14-Dec-94) showing that all remaining facilities were acceptable. It is stated in the DMF that estradiol drug substance is synthesized in their (continued on page 2)

17. CONCLUSIONS AND RECOMMENDATIONS The compliance status of the facility used to manufacture the drug substance supplied to 3M Pharmaceuticals is Acceptable. The Supplement can be approved.

18. REVIEWER NAME Helen W. Davies, Ph.D. SIGNATURE /S/ DATE COMPLETED 2/22/95

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R/D initialed by: N20375S2 ipchee 2/22/95

Remarks - continued

facility and micronized in their facility. The firm has stated in the Supplement that estradiol used by 3M Pharmaceuticals is not micronized. A new EER was submitted (07-Feb-95) for evaluation of only the facility. This EER was returned on 10-Feb-95 and reports that this facility is acceptable. The Supplement can therefore be approved. The completed EER is attached.