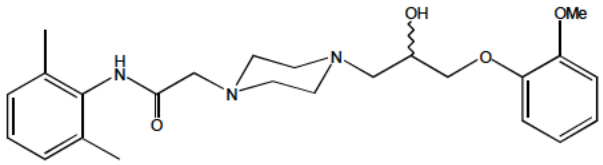
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-526/S004

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW #1

1. ORGANIZATION ONDQA		2. NDA NUMBER 21-526	
3. NAME AND ADDRESS OF APPLICANT (*City and State*) CV Therapeutics, Inc. 3172 Porter Drive Palo Alto, CA 94304.		4. AF NUMBER	
		5. SUPPLEMENT (S) NUMBER(S) DATES(S)	
6. NAME OF DRUG Ranexa	7. NONPROPRIETARY NAME Ranolazine	SE1-004	09-27-2007
8. SUPPLEMENT PROVIDES FOR: First line therapy for the long-term treatment of chronic angina.		9. AMENDMENTS DATES	
10. PHARMACOLOGICAL CATEGORY Treatment of chronic angina	11. HOW DISPENSED RX ✓ OTC	12. RELATED IND/NDA/DMF	
13. DOSAGE FORM(S) Extended-Release Tablets	14. POTENCY 500 mg and 1000 mg		
15. CHEMICAL NAME, STRUCTURE, MOLECULAR FORMULA AND MOLECULAR WEIGHT 1-Piperazineacetamide, N-(2,6-dimethylphenyl)-4-[2-hydroxy-3-(2-methoxyphenoxy)propyl]-, (+)-; $C_{24}H_{33}N_3O_4$ 427.54  		16. RECORDS AND REPORTS CURRENT YES__ NO REVIEWED YES__ NO	

17. COMMENTS

This drug is currently approved for the treatment of chronic angina. This application is submitted to seek approval for first line therapy for the long-term treatment of chronic angina. No new CMC information was submitted in this application. Minor changes are proposed to the "Description" and "How Supplied" sections of labeling. The reviewer recommended the following changes to "Description" section of labeling: Ranexa (ranolazine) is available as a film-coated, extended-release tablet for oral administration.

The applicant has submitted a claim for categorical exclusion under 21 CFR 25.31 (b). Based on applicant's calculation for the expanded indication and also based on production volume of drug substance, the amount of active moiety that is expected to enter into the aquatic environment is slightly greater than 1 ppb. However, the applicant has further indicated that based on metabolism and excretion of pharmacologically active ingredient, the actual amount of pharmacologically active material with potential for environmental impact would be approximately (b) (4). Owing to the above difference in EIC, a consult to evaluate the EA document was sent to OPS. Dr. Raanan Bloom in an e-mail dated 06/06/2008 indicated his acceptance of applicant's calculation accounting for metabolites and their claim under 21 CFR 25.31 (b). Based on the above, the applicant's claim is found to be acceptable.

18. CONCLUSIONS AND RECOMMENDATIONS

This supplement is recommended for approval from the standpoint of chemistry, manufacturing and controls.

19. CHEMIST

NAME	SIGNATURE	DATE COMPLETED
Nallaperumal Chidambaram, Ph.D.		25-06-2008

DISTRIBUTION	ORIGINAL NDA	DIVISION FILE	Chemist: N. Chidambaram Ph.D.	CSO: J. David HFD-110	Branch Chief: J. Vidra Ph.D.

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/s/

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