CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-304

CHEMISTRY REVIEW(S)

DIVISION OF ANTIVIRAL DRUG PRODUCTS
Review of Chemistry, Manufacturing and Controls

NDA #: **21-304**

CHEMISTRY REVIEW #: 1 **DATE REVIEWED:** 3/16/2001

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	CONTENT
Original	9 29/2000	10/2/2000	CMC
Amendment	11/16/2000	11/17/2000	Master batch record
Amendment	3/8/2001	3/9/2001	Stability data
Amendment	3/14/2001	3/15/2001	CMC response
Amendment	3/20/2001	3/21/2001	CMC response

NAME / ADDRESS OF APPLICANT: Roche Global Development
A Division of Syntex (U.S.A.) LLC
3401 Hillview Avenue
Palo Alto, CA 94304

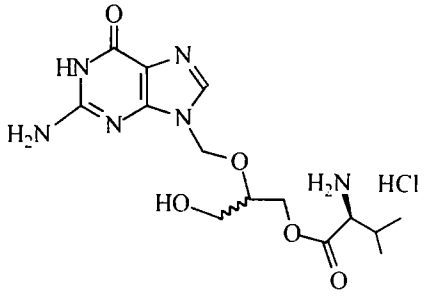
DRUG PRODUCT NAME
Proprietary: VALCYTE™
Nonproprietary: Valganciclovir Hydrochloride, Ganciclovir Valinate Hydrochloride
Code Name/#: 107-9070/194, RS-79070-194
CAS Registry#: 175865-59-5 (hydrochloride), 175865-60-8 (free base)

PHARMACOLOGICAL CATEGORY: Antiviral
INDICATION: Treatment of cytomegalovirus (CMV) retinitis
DOSAGE FORM/STRENGTH: Tablet/450 mg (free base)
ROUTE OF ADMINISTRATION: Oral

SPOTS: No

CHEMICAL NAME / STRUCTURAL FORMULA:
L-Valine, 2-[(amino-1,6-dihydro-6-oxo-9H-purin-9-yl)methoxy]-3-hydroxypropyl ester, monohydrochloride

9-[[2-Hydroxy-1-(hydroxymethyl)ethoxy]methyl]-guanine monoester with L-valine, monohydrochloride



Molecular formula: $C_{14}H_{22}N_6O_5 \cdot HCl$
Relative molecular mass: 390.83

RELATED/SUPPORTING DOCUMENTS:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	19-661	Cytovene®-IV (ganciclovir sodium) Sterile Powder
NDA	20-460	Cytovene® (ganciclovir capsules)

IND	[redacted]
IND	
IND	

RELATED DMF DOCUMENTS:

DMF Number	DMF Type	HOLDER	ITEM REF	CODE*	ACTION
[redacted]					

* Action Codes for DMF Table:

1. DMF Reviewed. Other codes indicate why the DMF was not reviewed, as follows:
2. Type I DMF
3. Reviewed previously and no revision since review
4. Sufficient information in application
5. Authority to reference not granted
6. DMF not available
7. Other (explain under "Comments")

STATUS OF CONSULTS AND OTHER REVIEWS:

ITEM	RECOMMENDATION	DATE	REVIEWER'S NAME
Trademark: [redacted]	Not recommended*	1/5/2001	OPDRA

*The Division proposed Valcyte as trademark, which is accepted by the applicant.

FAX COMMUNICATION TO THE APPLICANT

DATE	CONTENT
3/5/2001	Recommendations to revise the limit for individual impurity in drug substance and to revise the bottle label for drug product
3/16/2001	Request clarifications on proposed drug product specifications

CONCLUSIONS & RECOMMENDATIONS:

The NDA submission provides adequate information on the chemistry, manufacturing and controls to assure the identity, quality, purity and strength for VALCYTE™ tablets. The inspections of the ———and———manufacturing facilities have been completed and both were judged to have acceptable cGMP status. Therefore, NDA 21-304 for VALCYTE™ (Valganciclovir HCl tablets), as amended, is recommended for approval from the chemistry perspective.

{Signed Electronically}
Zi-Qiang Gu, Ph.D.
Review Chemist

Concurrence:
HFD-530: Stephen P. Miller, Ph.D.*{Signed Electronically}*
Chemistry Team Leader

APPEARS THIS WAY
ON ORIGINAL

59 Pages have been redacted in full from this document

Reason:

_____ b(2) 'low'
__✓__ b(4) CCI
__✓__ b(4) TS
_____ b(5) Deliberative Process:
Attorney Client and Attorney Work Product Privilege
_____ b(6) Personal Privacy
_____ b(7) Law Enforcement Records

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