

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-595

CHEMISTRY REVIEW(S)



NDA 21-595

Tradename: Sanctura

**Sponsor Name:
Indevus Pharmaceuticals**

**Chemistry Reviewer:
J. Salemme, Ph.D.
for Reproductive and Urologic Drug Products**

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2. REVIEW #: 1

21. REVIEW DATE: 4-May-2004

21. REVIEWER: J. Salemme, Ph.D.

21. PREVIOUS DOCUMENTS: None

21. SUBMISSIONS BEING REVIEWED:

<u>Submissions Reviewed</u>	<u>Document Date</u>
Original – electronic	28-Apr-2003
Amendment – electronic	28-May-2003
Amendment – paper	8-Aug-2003
Amendment – electronic	26-Aug-2003
Amendment – electronic	30-Sept-2003
Amendment – electronic	21-Nov-2003
Amendment – electronic	20-Jan-2004
Amendment – electronic	30-Jan-2004
Amendment – electronic	11-Feb-2004
Amendment – electronic	18-Feb-2004
Amendment – electronic	23-Mar-2004



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Amendment – electronic 5-May-2004

Amendment – electronic 20-May-2004

7. NAME & ADDRESS OF APPLICANT:

Name: Indevus Pharmaceuticals, Inc.
Address: 99 Hayden Avenue, Suite 200
Lexington, MA 02421-7966

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Sanctura
b) Non-Proprietary Name (USAN): Trospium Chloride
c) Code Name/# (ONDC only): None
d) Chem. Type/Submission Priority (ONDC only):
• Chem. Type: 1
• Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: N/A

10. PHARMACOL. CATEGORY: for the treatment of overactive bladder

11. DOSAGE FORM: Tablet

12. STRENGTH/POTENCY: 20 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: Rx OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product – Form Completed

Not a SPOTS product

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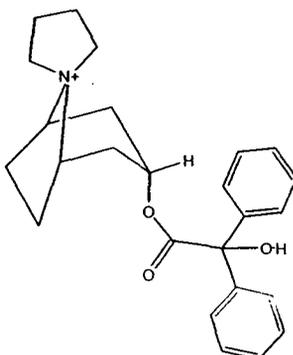
Chemistry Review Data Sheet

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Abstract Name: Spiro[8-azoniabicyclo[3.2.1]octane-8.1'-pyrrolidinium],3-[(hydroxydiphenylacetyl)-oxy], chloride, (1.alpha, 3.beta, 5.alpha)

Molecular formula: C₂₅H₃₀ClNO₃

Molecular weight: 427.97



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17. RELATED/SUPPORTING DOCUMENTS:

A. Drug Master Files (DMFs):

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
	II		i	1	Adequate	J. Salemme, Rev 2: 6-Feb-2004	
	III			4	N/A		
	III			3	Adequate	10-Feb-2003 Y. Lu	
	III			3	Adequate	15-Sept-2000 D. Klein	
	III			3	Adequate	22-Apr-2002 by R. Frankewich	
	III			3	Adequate	6-Aug-2002 by	

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					S. Zimmerman	
	III		3	Adequate	M. Heimann 24-Nov-2003	
	III		3	Adequate	L. Rocca 30- May-2003	
	III		3	Adequate	B. Ho, 23- May-2003	
	IV		4	N/A		

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: None

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	Overall Acceptable	11-Feb-2004	S. Adams
Pharm/Tox	N/A		
Biopharmaceutics	Acceptable	May 2004	L. Kenna
LNC	N/A		
Methods Validation	To be requested		
DMETS	Sanctura is acceptable.	15-Jan-2004	C. Holquist
EA	A categorical exclusion has been claimed and found to be acceptable.	26-Mar-2004	J. Salemme

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Microbiology	N/A		
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The Chemistry Review for NDA 21-595

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From a CMC perspective, this application is recommended for approval.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

None.

II. Summary of Chemistry Assessments

A. Description of the Drug Product and Drug Substance

The drug product, Sanctura (trospium chloride tablets) 20 mg, is a sugar-coated, immediate-release tablet containing 20 mg trospium chloride. The tablet is round, approximately 7 mm in diameter, brownish-yellow, and printed with a black ink. The manufacturer of the drug product for Indevus Pharmaceuticals, Inc., is Madaus AG, of Troisdorf, Germany.

The drug product is adequately controlled by the quality attributes of identification, assay, impurities, loss on drying, content uniformity, dissolution ($Q=100\%$ at 30 minutes), and microbiological purity.

Stability data up to 24 months were provided for unprinted tablets and up to 12 months for printed tablets in PVC blister packs, PVC Aclar blister packs, and _____ bottles justify a 24 month expiration date.

The drug substance, trospium chloride, is a new molecular entity manufactured by _____ The chemistry, manufacturing and controls are described in Drug Master File _____. The drug substance is colorless to slightly yellow crystalline powder, and is freely soluble in water _____. Trospium chloride has no chiral center and so does not exhibit optical activity. Additionally, only one crystal form exists.

The quality of the trospium chloride drug substance is adequately controlled by tests for identification, solubility, color, clarity, pH of solution, chromatographic impurities,



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Executive Summary Section for NDA 21-595

, residual solvents, water content, residue on ignition, assay by titration and assay by chromatography.

B. Description of How the Drug Product is Intended to be Used

The drug product is to be used daily for treatment of overactive bladder at a daily dose of 1 tablet (20 mg) twice daily.

C. Basis for Approvability or Not-Approval Recommendation

Deficiencies have been adequately addressed. The tradename, Santura, is acceptable to DMETS. The manufacturing sites have been recommended for approval by the Office of Compliance. The CMC information provided in the application is deemed adequate for demonstrating the identity, quality, purity, and potency of the drug substance and drug product.

III. Administrative

A. Reviewer's Signature

J. Salemme, Ph.D., 4-May-2004

B. Endorsement Block

ChemistryTeamLeaderName/Date
ProjectManagerName/Date

Moo-Jhong Rhee, Ph.D.
D. Cutright

C. CC Block

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

/s/

Jean Salemmé
5/26/04 01:20:09 PM
CHEMIST

Moo-Jhong Rhee
5/26/04 02:11:34 PM
CHEMIST
I concur

11 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

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