CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022544Orig1s000

CHEMISTRY REVIEW(S)

NDA 22-544

Gralise (Gabapentin) Tablet

Abbott Products, Inc

Yong Hu, Ph.D.

Office of New Drug Quality Assessment

For

Division of Anesthesia and Analgesia Products

Table of Contents

Chemistry Review Data Sheet

1. NDA: 22-544

2. REVIEW #: 2

3. REVIEW DATE: 13-Jan-2011

4. REVIEWER: Yong Hu, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
CMC Review #1	03-Dec-2010
Biopharmaceutics Review #1	22-Nov-2010

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Quality/Response to Information Request	07-Dec-2010
Quality/Response to Information Request	29-Dec-2010
Quality/Response to Information Request	11-Jan-2011

7. NAME & ADDRESS OF APPLICANT:

Name:	Abbott Products, Inc
Address:	901 Sawyer Road, Marietta, GA 30062
Representative:	Michael F. Hare, Asst. Dir
Telephone:	770-578-5620

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Gralise Tablet
b) Non-Proprietary Name (USAN): Gabapentin Tablet
c) Code Name/# (ONDC only): DM-1796
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION:

505 b(2); The reference drug is the immediate-release product Neurontin (NDAs 20-129, 20-235, 20-882, 21-397, 21-423, and 21-424) from Pfizer.

10. PHARMACOL. CATEGORY and INDICATION:

Anticonvulsant/Analgesic; Treatment of postherpetic neuralgia (PHN).

11. DOSAGE FORM:

Tablet

12. STRENGTH/POTENCY:

300 and 600 mg

13. ROUTE OF ADMINISTRATION:

Oral

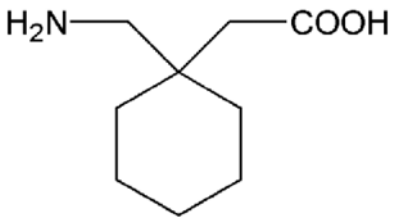
14. Rx/OTC DISPENSED: __x_Rx ___OTC

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

_____SPOTS product Form Completed

___x___Not a SPOTS product

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



Chemical name: 1-(Aminomethyl)cyclohexaneacetic acid
Molecular formula: $C_9H_{17}NO_2$
Molecular Weight: 171.24

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

Chemistry Review Data Sheet

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	Gabapentin drug substance	3	Adequate	21-Jun-2010	
	II		Gabapentin drug substance	1	Adequate	22-Nov-2010	
	IV		Hypromellose (b) (4)	4	N/A		
	IV		Microcrystalline cellulose (b) (4) (b) (4)	4	N/A		
	IV		Polyethylene oxide (b) (4)	4	N/A		
	IV		Opadry II white and beige	4	N/A		
	III		(b) (4)	4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	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:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	71,439	Gabapentin tablet sponsored by the applicant.

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	Not requested.		
EES	Acceptable.	26-May-2010	A. Inyard
Pharm/Tox	(b) (4) (b) (4) in the drug product is acceptable, based on the specification of Neurontin, the approved referenced product.	30-Nov-2010 (wrap-up meeting)	Armaghan Emami
Biopharm	The IVIVC model is not acceptable. The drug product should not be designated as an extended-release product taking into account the higher plasma concentration fluctuation index compared to Neurontin IR. The addition of a drug product manufacturing site post approval (subject of the compatibility protocol submitted) may require a bioequivalence study due to lack of IVIVC.	30-Nov-2010 (Wrap-up meeting) Biopharm review (dated 22-Nov-2010; signed off on 03-Dec-2010)	Sandra Suarez
LNC	N/A		
Methods Validation	Not requested for the conventional methods.		
OPDRA	N/A		
EA	Categorical exclusion acceptable.	03-Dec-2010	Yong Hu
Microbiology	N/A. Oral tablet.		

The Chemistry Review for NDA 22-544

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The NDA can be approved from CMC perspective.

The following comment should be communicated to the applicant in the Action Letter.

- The comparability protocol to support an alternate drug product manufacturer is insufficient. Addition of a drug product manufacturing site may require a bioequivalence study. You may discuss with the Agency and submit the alternate drug product manufacturing site and supporting data post-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(s) and Drug Substance(s)

The product is claimed to be an extended-release tablet, 300 and 600 mg, referred to by the applicant as G-ER. However, the Biopharmaceutics team recommends that the product should not be designated as an extended-release product based on the plasma concentration fluctuation index; (see the Biopharmaceutics review dated 22-Nov-2010 and signed off on 03-Dec-2010). Therefore, the drug product is to be designated as gabapentin tablet, with a "once-daily" dosing regimen. The tablets are intended for oral administration in the treatment of postherpetic neuralgia in adults at a dose of up to 1800 mg once-daily. The tablets are targeted to deliver approximately 90% of the total daily dose of gabapentin over approximately a 10 hour period to the upper gastrointestinal (GI) tract, where the drug is claimed to be most efficiently absorbed. Gastric retention of the tablets is said to be critical to delivering the drug to the upper GI tract over an extended period. Tablet swelling in gastric fluid and administration of the tablet with food are both necessary for gastric retention of the tablet. The "extended drug release" is claimed to be achieved by the diffusional control of the drug in the matrix of the polymers (b) (4) . The same polymers also control the swelling of the tablets. The tablet swelling is shown in the modified simulated gastric fluid in an in-vitro study. Regarding the safety of the swelled size, the clinical team informed that that there was no evidence that the size of the swelled tablets was problematic - in the clinical trials there were no instances of obstruction or sticking. In addition, a post marketing AERs search for GI AEs including

obstruction for similar formulations (Glumetza and Proquin XR) did not find any reports. The tablet is said to exit the stomach during Phase III of the migrating motor complex (housekeeper wave) in the fasting state and to transit through the GI tract and dissolve away. The applicant states that the same formulation technology has also been used in the approved NDA 21-744 (Proquin XR ciprofloxacin HCl) and NDA 21-748 (Glumetza ER Metformin HCl).

The 300 mg tablets are white to off-white, film-coated, 0.3937" X 0.6299" modified oval shaped tablets that are 714 mg in weight, and debossed with "SLV" on one side and with "300" on the other side.

The 600 mg tablets are beige, film-coated, 0.4330" x 0.7450" modified oval shaped tablets that are 1020 mg in weight, and debossed with "SLV" on one side and with "600" on the other side.

The 300 mg and 600 mg tablets are not compositionally proportional.

The excipients for the 300 and 600 mg tablets are polyethylene oxide, hypromellose, copovidone, magnesium stearate (b) (4), microcrystalline cellulose (300 mg), Opadry® II white (300 mg) and beige (600 mg). Opadry® II white contains polyvinyl alcohol, titanium dioxide, talc, polyethylene glycol 3350, and lecithin (soya). Opadry® II beige contains polyvinyl alcohol, titanium dioxide, talc, polyethylene glycol 3350, iron oxide yellow, and iron oxide red.

The commercial manufacturing site for the drug product is (b) (4) The manufacturing process involves (b) (4) The proposed commercial manufacturing scales are abou (b) (4) for 300 and 600 mg strengths, respectively. The phase 3/registration stability batches were manufactured at the proposed commercial site and ranged from (b) (4) in scale.

The Biopharmaceutics Review #1 determined that the tablet dissolution acceptance criteria and the IVIVC model were not acceptable. The applicant has since revised the tablet dissolution acceptance criteria in the product specification as requested by the Biopharmaceutics team. An in-vitro study showed that the drug release was decreased with increasing concentration of alcohol in the dissolution medium, suggesting a low risk of dose dumping in the presence of alcohol.

The phase 3/registration stability and commercial products differ in the deboss ("Depomed" vs "SLV") and coat color (white vs. beige) for 600 mg tablets and the deboss ("Depomed" vs "SLV") for 300 mg tablets. (b) (4) and there is no manufacturing process change from phase 3 to commercial manufacturing, the change in tablet dress is considered minor. The applicant provided long-term stability data for three registration batches of each strength in both bottle and blister packaging configurations. The registration batches were shown to be stable over 24 - 36 months at the long-term storage condition (25 ºC / 60%RH). The applicant also provided the stability data for one batch of 600 mg tablets with the commercial dress (deboss and color). The stability of the commercial 600 mg

tablets was comparable to the phase 3/registration batches over 3 months at long-term condition (25 ºC / 60%RH) and the accelerated condition (40 ºC / 75%RH).

The drug substance is freely soluble in water and the solubility is weakly dependently on the solution pH. The major degradation product is the (b) (4) (b) (4) (b) (4) . Particle size is said to be controlled by the primary supplier's internal specification. This reviewer also recommended, at the teleconference with the applicant on 20-Dec-2010, that the applicant establish an internal control of particle size of the drug substance from other suppliers.

The primary drug substance supplier is (b) (4) and the alternate supplier (b) (4) All phase 3/registration stability batches were manufactured using the (b) (4) gabapentin substance. The (b) (4) gabapentin substance has been shown to be comparable to the (b) (4) gabapentin substance when tested against the specifications. The drug products containing the (b) (4) and (b) (4) gabapentin substance are shown to be comparable when tested against the product specifications. Three months stability data at both long-term and accelerated conditions has been generated on one batch of the drug product containing the (b) (4) drug substance for each strength. The data shows no difference between the two suppliers so far.

The drug substance is stored at room temperature (b) (4)

The applicant submitted a Comparability Protocol to support post-approval addition of an alternate drug product manufacturing site. The applicant has not specified what changes will be involved and therefore this protocol was insufficient. A bioequivalence study will be required if a level 3 site change will take place, as the IVIVC has not been accepted by the Biopharmaceutics team. The applicant should submit the drug product alternate manufacturing site post approval.

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

The drug product is packaged in bottles and blister packs for pharmacy (trade) and physician (samples) distribution. The bottle container-closure system consists of tablets to be packaged in white opaque high density polyethylene (HDPE) bottles. The bottle and cap are induction sealed and do not contain a filler. The blister pack container-closure system consists of different configurations to be used as starter kits, titration kits, and unit dose packages. The blister material is (b) (4) and the backing material is aluminum foil with a heat-seal layer.

The drug product will be taken orally once daily with food (evening meal). The maximum daily dose of gabapentin is 1800 mg.

The applicant proposed a (b) (4) expiration dating period for the drug product. However, after reviewing the stability data, this reviewer recommends a 24-month expiration dating period for the tablets of both strengths packaged in either the bottle or blister packaging configurations. The tablets are to be stored at 25ºC (77ºF); excursions permitted to 15° to 30ºC (59° to 86ºF) [see USP Controlled Room Temperature].

C. Basis for Approvability or Not-Approval Recommendation

The applicant has satisfactorily provided the information requested based on the CMC Review #1. The applicant has revised the tablet dissolution acceptance criteria in the product specification as requested by the Biopharmaceutics team. The NDA has provided adequate scientific information to support the identity, purity, strength, and quality of the drug product.

The manufacturing facilities have been deemed acceptable by the Office of Compliance.

The following comment should be communicated to the applicant in the Action Letter.

- The comparability protocol to support an alternate drug product manufacturer is insufficient. Addition of a drug product manufacturing site may require a bioequivalence study. You may discuss with the Agency and submit the alternate drug product manufacturing site and supporting data post-approval.

III. Administrative

A. Reviewer's Signature

See DARRTS.

B. Endorsement Block

See DARRTS.

C. CC Block

See DARRTS.

14 Pages have been Withheld in Full as b4 (CCI/TS) immediately following this page.

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

/s/

YONG HU
01/13/2011
The NDA can be approved from CMC perspective.

PRASAD PERI
01/13/2011
I concur

NDA 22-544

Gabapentin Extended-Release Tablet

Abbott Products, Inc

Yong Hu, Ph.D.

Office of New Drug Quality Assessment

For

Division of Anesthesia and Analgesia Products

Table of Contents

Chemistry Review Data Sheet

1. NDA: 22-544

2. REVIEW #: 1

3. REVIEW DATE: 03-Dec-2010

4. REVIEWER: Yong Hu, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
N/A	

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original submission	30-Mar-2010
Amendment (Establishment information)	20-Apr-2010
Amendment (Response to 74-day letter)	06-Aug-2010
Amendment (Response to CMC IR)	19-Aug-2010
Amendment (Response to CMC IR)	23-Aug-2010
Amendment (Comparability protocol)	28-Oct-2010
Amendment (Response to CMC IR)	12-Nov-2010
Emailed Response to CMC IR	23-Nov-2010

7. NAME & ADDRESS OF APPLICANT:

Name:	Abbott Products, Inc
Address:	901 Sawyer Road, Marietta, GA 30062
Representative:	Michael F. Hare, Asst. Dir
Telephone:	770-578-5620

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Gralise extended-release tablet
b) Non-Proprietary Name (USAN): Gabapentin extended-release tablet
c) Code Name/# (ONDC only): DM-1796

d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION:

505 b(2); The RLD is the immediate-release product Neurontin (NDAs 20-129, 20-235, 20-882, 21-397, 21-423, and 21-424) from Pfizer.

10. PHARMACOL. CATEGORY and INDICATION:

Anticonvulsant/Analgesic; Treatment of postherpetic neuralgia (PHN).

11. DOSAGE FORM:

Extended-release tablet

12. STRENGTH/POTENCY:

300 and 600 mg

13. ROUTE OF ADMINISTRATION:

Oral

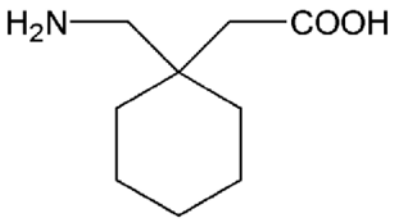
14. Rx/OTC DISPENSED: __x_Rx ___OTC

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

_____SPOTS product Form Completed

___x___Not a SPOTS product

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



Chemical name: 1-(Aminomethyl)cyclohexaneacetic acid
Molecular formula: $C_9H_{17}NO_2$
Molecular Weight: 171.24

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	Gabapentin drug substance	3	Adequate	21-Jun-2010	
	II		Gabapentin drug substance	1	Adequate	22-Nov-2010	
	IV		Hypromellose (b) (4)	4	N/A		
	IV		Microcrystalline cellulose (b) (4) (b) (4)	4	N/A		
	IV		Polyethylene oxide (b) (4)	4	N/A		
	IV		Opadry II white and beige	4	N/A		
	III		(b) (4)	4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	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:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	71,439	Gabapentin extended-release tablet sponsored by the applicant.

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	Not requested.		
EES	Acceptable.	26-May-2010	A. Inyard
Pharm/Tox	(b) (4) (b) (4) in the drug product is acceptable, based on the specification of Neurontin, the RLD.	30-Nov-2010 (wrap-up meeting)	Armaghan Emami
Biopharm	Tablet dissolution specification and IVIVC model are not acceptable. (b) (4) The drug product should not be classified as an extended-release product taking into account the higher plasma concentration fluctuation index compared to Neurontin IR. The comparability protocol for the addition of a drug product manufacturing site post approval is pending.	30-Nov-2010 (Wrap-up meeting) Biopharm review (dated 22-Nov-2010; signed off on 03-Dec-2010)	Sandra Suarez
LNC	N/A		
Methods Validation	Not requested for the conventional methods.		
OPDRA	N/A		
EA	Categorical exclusion granted.	03-Dec-2010	Yong Hu
Microbiology	N/A. Oral tablet.		

The Chemistry Review for NDA 22-544

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The NDA is approvable from CMC perspective. The manufacturing facilities have been deemed acceptable by the Office of Compliance.

The final "Approval" recommendation is pending until

1. The applicant revises the drug product dissolution specification as requested by the Biopharm team.
2. The applicant provides an adequate response to the requested information described at the end of this review;

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

None at this time.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The product is an extended-release tablet, 300 mg and 600 mg, referred to by the applicant as G-ER (Note: the Biopharm team recommend that the product should not be classified as an extended-release product based on the plasma concentration fluctuation index; see the Biopharm review dated 22-Nov-2010 and signed off on 03-Dec-2010). The tablets are intended for oral administration in the treatment of postherpetic neuralgia in adults at a dose of up to 1800 mg once-daily. The tablets are targeted to deliver approximately 90% of the total daily dose of gabapentin over approximately a 10 hour period to the upper gastrointestinal (GI) tract, where the drug is claimed to be most efficiently absorbed. Gastric retention of the tablets is critical to delivering the drug to the upper GI tract over an extended period. When administered with a meal, the tablet is said to swell to the size which promotes gastric retention. The extended drug release is claimed to be achieved by the diffusional control of the drug in the matrix of the polymers (b) (4). The same polymers also control the swelling of the tablets. The tablet swelling is indicated by the significant weight gain in mSGF from an in-vitro study, however, no data has been provided regarding the swelled tablet size. The tablet is said to exit the stomach during Phase III of the migrating motor complex (housekeeper wave) in the fasting state and to transit through the GI tract and dissolve away. The applicant states that the same formulation technology has also been used in the approved NDA 21-744 (Proquin XR ciprofloxacin HCl) and NDA 21-748 (Glumetza ER Metformin HCl).

The 300 mg tablets are white to off-white, film-coated, 0.3937" X 0.6299" modified oval shaped tablets that are 714 mg in weight, and debossed with "SLV" on one side and with "300" on the other side.

The 600 mg tablets are beige, film-coated, 0.4330" x 0.7450" modified oval shaped tablets that are 1020 mg in weight, and debossed with "SLV" on one side and with "600" on the other side.

The excipients for the 300 and 600 mg tablets are polyethylene oxide, hypromellose, copovidone, magnesium stearate (b) (4), microcrystalline cellulose (300 mg), Opadry® II white (300 mg) and beige (600 mg).

The commercial manufacturing site for the drug product is (b) (4) The manufacture process involves (b) (4) The proposed commercial manufacturing scales are abou (b) (4) for 300 and 600 mg strengths, respectively. The phase 3/registration stability batches were manufactured at the proposed commercial site and ranged from (b) (4) in scale.

The Biopharm review determined that the tablet dissolution acceptance criteria and the IVIVC model are not acceptable. An in-vitro study showed that the drug release is decreased with increasing concentration of alcohol in the dissolution medium, suggesting a low risk of dose dumping in the presence of alcohol.

The phase 3/registration stability and commercial products differ in the deboss ("Depomed" vs "SLV") and coat color (white vs. beige) for 600 mg tablets and the deboss ("Depomed" vs "SLV") for 300 mg tablets. (b) (4) and there is no manufacturing process change from phase 3 to commercial manufacturing, the change in tablet dress is considered minor. The applicant provided long-term stability data for three registration batches of each strength in both bottle and blister packaging configurations. The registration batches were shown to be stable over 24 - 36 months at the long-term storage condition (25 ºC / 60%RH). The applicant also provided the stability data for one batch of 600 mg tablets with the commercial dress (deboss and color). The stability of the commercial 600 mg tablets was comparable to the phase 3/registration batches over 3 months at long-term condition (25 ºC / 60%RH) and the accelerated condition (40 ºC / 75%RH).

The drug substance is freely soluble in water and the solubility is weakly dependently on the solution pH. The major degradation product is the USP gabapentin-related compound A ((b) (4) (b) (4) (b) (4), thus, particle size specification has not been proposed for the drug substance. Particle size is said to be controlled by the supplier's internal specification. No data in the NDA supports the applicant's claim (b) (4). The applicant will need to include particle size specification for the drug substance.

The primary drug substance supplier is (b) (4) and the alternate supplier (b) (4). All phase 3/registration stability batches were manufactured using the (b) (4) gabapentin substance. The (b) (4) gabapentin substance has been shown to be comparable to the (b) (4) gabapentin substance when tested against the specifications, however, the applicant has not provided a comparison of the particle size distribution for the drug substances from both suppliers. This information will be requested to assess the risk of bioequivalence of the alternate source drug substance. In addition, as mentioned above, the applicant will need to include particles size specification for the drug substance. The drug products containing the (b) (4) and (b) (4) gabapentin substance are shown to be comparable when tested against the product specifications. Three months stability data at both long-term and accelerated conditions has been generated on one batch of the drug product containing the (b) (4) drug substance for each strength. The data shows no difference between the two suppliers so far.

The drug substance is stored at room temperature (b) (4)

The applicant submitted a Comparability Protocol to support post-approval addition of an alternate drug product manufacturing site. The protocol will be evaluated in the next review. Biopharm input will also be necessary to determine the adequacy of the protocol.

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

The drug product is packaged in bottles and blister packs for pharmacy (trade) and physician (samples) distribution. The bottle container-closure system consists of tablets to be packaged in white opaque high density polyethylene (HDPE) bottles. The bottle and cap are induction sealed and do not contain a filler. The blister pack container-closure system consists of different configurations to be used as starter kits, titration kits, and unit dose packages. The blister material is (b) (4) and the backing material is aluminum foil with a heat-seal layer.

The drug product will be taken orally once daily with food (evening meal). The maximum daily dose of gabapentin is 1800 mg.

A 24-month expiration dating period is recommended for the tablets of both strengths packaged in either the bottle or blister packaging configurations. The tablets are to be stored at 25ºC (77ºF); excursions permitted to 15° to 30ºC (59° to 86ºF) [see USP Controlled Room Temperature].

C. Basis for Approvability or Not-Approval Recommendation

The Biopharmaceutics review has determined that the drug product dissolution acceptance criterion is not acceptable. The applicant will need to revise the acceptance criteria for dissolution as requested by the Biopharm team.

The acceptance criterion for the total impurities in the drug product should be tightened to reflect the batch stability data and also to be in line with the USP specification for gabapentin tablets.

The applicant has not provided adequate data to justify the omission of particle size specification for the drug substance. Particle size control should be implemented to mitigate the risk of bioequivalence for drug substance from different suppliers.

The applicant has not provided an adequate post-approval stability protocol.

See the details of the comments/information request at the end of the review. The applicant should be able to address the comments during the review cycle.

The alternate supplier (b) (4) for the drug substance will not be approved until the applicant shows comparable particles size data of the alternate source drug substance with that of the primary source drug substance or otherwise justified with data.

The Comparability Protocol for the post-approval addition of an alternate drug product manufacturer is being reviewed. However, the decision on the protocol will not affect the approvability of the NDA.

III. Administrative

A. Reviewer's Signature

See DARRTS.

B. Endorsement Block

See DARRTS.

C. CC Block

See DARRTS.

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

/s/

YONG HU
12/03/2010
The NDA is approvable. The CMC comments/information request should be sent to the applicant.

PRASAD PERI
12/03/2010
I concur