

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

**APPLICATION NUMBER: 21-515/S-007**

**ADMINISTRATIVE DOCUMENTS**

**REGULATORY PROJECT MANAGER  
LABELING REVIEW**

Date: May 21, 2004  
 DRUG/NDA: Wellbutrin (bupropion HCl) Immediate Release Tablets (NDA 18-644)  
 and Wellbutrin SR (bupropion HCl) Sustained Release Tablets (NDA 20-358)  
 Sponsor: GlaxoSmithKline  
 Indication: Major Depressive Disorder (MDD)  
 Supplements:

<b>NDA</b>	<b>Supplement</b>	<b>Dated</b>	<b>Action</b>
<b>Wellbutrin (bupropion HCl) Immediate Release Tablets (NDA 18-644)</b>			
18-644	SLR-026	4-22-04	AP Letter Dated 10-22-02
18-644	SLR-027	4-28-04	OPEN
18-644	SLR-028	5-11-04	OPEN
<b>Wellbutrin SR (bupropion HCl) Sustained Release Tablets (NDA 20-358)</b>			
20-358	SLR-030	3-10-04	AP Letter Dated 4-26-04
20-358	SLR-031	4-28-04	OPEN
20-358	SLR-032	5-11-04	OPEN
<b>Wellbutrin XL (bupropion HCl) Extended Release Tablets (NDA 21-515)</b>			
21-515	Original NDA	8-26-02	AP Letter Dated 8-28-03
21-515	SLR-006	4-28-04	OPEN
21-515	SLR-007	5-11-04	OPEN

**Review**

- As part of a class labeling initiative, all sponsors of the current antidepressants were requested to revise their labeling to incorporate the following changes regarding suicide risk:
  1. The addition of a new subsection under **WARNINGS** entitled **Clinical Worsening and Suicide Risk**.
  2. Revisions to the **PRECAUTIONS-Information for Patients** section.
  3. Delete the section in **PRECAUTIONS-General** entitled "Suicide".

4. Add a reference to the **WARNINGS** section at the end of the **PRECAUTIONS-Pediatric Use** section, i.e., (see **WARNINGS-Clinical Worsening and Suicide Risk**).
- GSK also proposed revisions to their ~~\_\_\_\_\_~~ labeling. This was submitted in their supplements dated ~~\_\_\_\_\_~~.
  - It was decided, at the Division level, that it was unclear what language needed to be added to the PPI. Therefore, we requested that GSK separate the changes made to the prescriber labeling to those made to the PPI. These changes were submitted by GSK in supplements dated 5-11-04 and 5-12-04.
  - The changes to the prescriber labeling, submitted on 5-11-04, are identical to the changes as requested in our 3-19-04 supplement request letter which was subsequently amended and conveyed in an e-mail to the sponsor on 4-19-04.

## CONCLUSIONS

1. The above labeling supplements only provide for those revisions as requested by the Division.
2. I recommend that supplemental applications 18-644/S-027, 20-358/S-031, and 21-515/SLR-006 be administratively closed since these were superseded by the submissions dated 5-11-04 and 5-12-04.
3. I recommend that supplemental applications 18-644/S-028, 20-358/S-032, and 21-515/SLR-007 dated 5-11-04 be approved.
4. At this point in time, we are unable to take an action on supplemental applications ~~\_\_\_\_\_~~ ~~\_\_\_\_\_~~ if a decision has been made on how to globally address what changes need to be made to the PPIs.

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Paul David, R.Ph.,  
Senior Regulatory Health Project Manager

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/s/

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Paul David  
5/27/04 09:25:38 AM  
CSO