Sherman, Aaron

From: Norden, Janet M
Sent: Wednesday, July 16, 2008 12:59 PM
To: Sherman, Aaron
Subject: Print

From: Norden, Janet M
Sent: Friday, March 16, 2007 7:01 AM
To: Behrman, Rachel E; Locicero, Colleen L
Subject: FW: Waivers from PAS for Highlights

Hi Rachel,

This is fairly major. Don't you remember OCC agreeing with the waiver idea before the rule published? JN

From: Ray, Seth
Sent: Thursday, March 15, 2007 5:00 PM
To: Bernstein, Michael; Sadove, Elizabeth
Cc: Boocker, Nancy; Norden, Janet M; Colangelo, Kim M; Behrman, Rachel E; Bradshaw, Sheldon; Ray, Seth
Subject: RE: Waivers from PAS for Highlights

I spoke with Sheldon and OCC does not concur with OND's draft procedure/policy document that would allow sponsors to request a waiver from the review division such that important safety labeling changes to Highlights could be made via CBE supplements. The draft document is inconsistent with the amendments made to 314.70 as part of the PLR. Some of you might not be aware that these amendments were carefully crafted, in response to pending litigation, to ensure that changes to Highlights (other than minor changes) would only be made via prior approval supplements. If CDER managers feel differently, we should meet to discuss. Thanks for bringing this to our attention.

Seth

From: Bernstein, Michael
Sent: Thursday, March 08, 2007 3:41 PM
To: Sadove, Elizabeth; Ray, Seth
Cc: Boocker, Nancy
Subject: RE: Waivers from PAS for Highlights

Seth--

I just wanted to follow up on Liz's request on this. We really need to get a response from you on it and would greatly appreciate if you could take a look at it. Thanks!

Michael

From: Sadove, Elizabeth
Sent: Thursday, March 08, 2007 3:10 PM
To: Ray, Seth
Cc: Bernstein, Michael; Boocker, Nancy
Subject: FW: Waivers from PAS for Highlights

Seth- Please let me know whether you concur with OND's recommended procedures regarding waivers from prior approval supplements for Highlights. I think this is very straight forward and consistent with the discussions that we had when finalizing the PLR requirement.

Kim Colangelo needs a response as soon as possible.
Thanks, Liz Sadove

From: Sadove, Elizabeth
Sent: Monday, February 12, 2007 8:40 AM
To: Ray, Seth
Cc: Bernstein, Michael; Boocker, Nancy
Subject: Waivers from PAS for Highlights

Seth- I'm following up on the e-mail that I sent re: OND's proposed draft procedure for handling waiver requests. Kim would like to provide an update on this at a meeting tomorrow. Please let me know if you concur with the approach, or if you need any other information from me or Kim.
Thanks, Liz Sadove
<< File: PAS waiver procedures - clean ORP.doc >>

From: Sadove, Elizabeth
Sent: Tuesday, January 23, 2007 3:15 PM
To: Ray, Seth
Cc: Norden, Janet M; Behrman, Rachel E; Bernstein, Michael; Boocker, Nancy
Subject: FW: Question for ORP

Per Kim Colangelo's e-mail below, OND put together the attached draft procedures for handling waiver requests from the requirement that safety changes to Highlights must be submitted as Prior Approval Supplements. The stated policy appears consistent with PLR's intent that FDA have a chance to quickly review such changes before manufacturers implement them. Do you/OCC agree with this approach. Let me know if you think this needs a formal consult.
Thanks, Liz Sadove

<< File: PAS waiver procedures - clean ORP.doc >>

From: Colangelo, Kim M
Sent: Friday, January 05, 2007 4:25 PM
To: Boocker, Nancy; Bernstein, Michael
Subject: Question for ORP

Nancy and Michael,

We have a regulatory question for ORP, but I'm not certain to whom it should be directed.

In brief, the Physician's Labeling Rule dictates that any changes to the Highlights section of the label be submitted as a Prior Approval Supplement (PAS.) We also have regulations that allow certain important safety labeling changes to be made via a Changes Being Effected (CBE) supplement, allowing companies to get important safety information out quickly while the application is undergoing review.

Of course this creates a bit of a conflict when the important safety information requires a change in the Highlights section.

In order to allow for the intent of the CBE regulations to be upheld, we are proposing to allow companies to request a waiver from the review division for the prior approval supplement, allowing them to submit these changes (including changes to the Highlights) as a CBE supplement.

What we need to know is if ORP would find this plan acceptable (and/or does it require OCC input?)

How do I go about obtaining this input?

Have a great weekend!
Kim

Kim Colangelo
Associate Director for Regulatory Affairs
Office of New Drugs
CDER/FDA

301-796-0700 (OND IO main)
301-796-0140 (direct)
301-796-9856 (facsimile)

Kim.Colangelo@fda.hhs.gov

Locicero, Colleen L

From: Locicero, Colleen L
Sent: Wednesday, April 25, 2007 9:15 AM
To: Norden, Janet M
Subject: RE: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format

Thanks!

From: Norden, Janet M
Sent: Wednesday, April 25, 2007 9:04 AM
To: Locicero, Colleen L
Subject: FW: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format

FYI - JN

From: Jenkins, John K
Sent: Wednesday, April 25, 2007 8:58 AM
To: Axelrad, Jane A; Sadove, Elizabeth; Kweder, Sandra L; Colangelo, Kim M
Cc: Bernstein, Michael; Norden, Janet M; Jenkins, John K
Subject: RE: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format

Jane

Here are two examples, one recent and one a couple of years old where important safety information was added via a CBE and FDA needed much more time to review the underlying data to make a decision on the approved labeling. Another theoretical example would have been Vioxx. When we met with Merck in September 2004 they had preliminary results of the APPROVe trial that showed an increased risk of CV events. Has Merck not decided to voluntarily withdraw the product it would have been necessary for them to make labeling changes to add warnings about the new findings. We probably would not have issued an approval letter on the labeling changes since we would not have had access to the full study report for review so we could evaluate the actual data that would be added to the labeling. So, we probably would have agreed to interim labeling and asked Merck to submit it as a CBE and we would have made more official determinations later after we reviewed the full study report. The two attached examples, one in OAP and one DRUP are similar in that they led to addition of interim new important safety information the labeling, but without explicit FDA approval. In the DRUP case we later agreed to the labeling with minor revisions and in the OAP example we have not yet completed our review of the data from the new trial. While these two real world examples and the Vioxx hypothetical are related to new safety information from controlled trials, it is also possible that similar scenarios could arise from AERS reports where we want to do a more comprehensive analysis and allow the sponsor to add changes via CBE in advance. It is important to note that the CBE pathway does not mean we do not see and comment on the labeling before it is implemented. In many cases we do work with sponsors on the interim labeling to be added via CBE, but we do not approve it since our review is not yet complete. This is an important pathway to allow important new safety information to get to the labeling in a timely manner, and it is even more important today given our transmittal of new labeling to the NLM where it can be made available much more rapidly to prescribers and third party vendors. This is why most of our objected to the no CBE changes to the Highlights section of PLR and why we think it is important that we find a way to waive that requirement in appropriate cases.

John << Message: FW: Response to your CBE labeling question >> << Message: Response to your CBE labeling question >> << Message: Re: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format >>

John K. Jenkins, M.D.
Director, Office of New Drugs
10903 New Hampshire Avenue
Bldg #22, Room 6304
Silver Spring, MD 20993
301-796-0700
301-796-9856 (fax)
NOTE, New E-mail Address: john.jenkins@fda.hhs.gov

From: Axelrad, Jane A
Sent: Monday, April 23, 2007 4:50 PM
To: Sadove, Elizabeth; Kweder, Sandra L; Colangelo, Kim M; Jenkins, John K
Cc: Bernstein, Michael; Norden, Janet M
Subject: RE: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format

I would like concrete examples of safety changes that we thought were important that have been implemented through CBEs.

From: Sadove, Elizabeth
Sent: Monday, April 23, 2007 4:22 PM
To: Kweder, Sandra L; Colangelo, Kim M; Jenkins, John K
Cc: Axelrad, Jane A; Bernstein, Michael; Norden, Janet M
Subject: FW: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format
Importance: High

Jane and Seth spoke about this and Seth agreed to discuss this again with Sheldon if we could come up with very specific and narrow criteria for when a waiver would be applied. However, Jane thought that the case would be strongest if we first identify several compelling examples of important changes to safety information in Highlights that sponsors could not immediately distribute because of the PAS requirement. In other words, we need to articulate why this is such a big problem. It would help to have an explanation of how long it takes to review these labeling supplements and why.

If possible, we could use this ASAP... If Jane gets this information by Wednesday, she can brief Dr. Galson.

Thanks,
Liz Sadove

From: Axelrad, Jane A
Sent: Thursday, March 29, 2007 6:06 PM
To: Jenkins, John K
Cc: Kweder, Sandra L; Colangelo, Kim M; Sadove, Elizabeth
Subject: RE: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format

Liz is out this week, but I will discuss it with her early next week and get back to you. I have to refresh my recollection of how this was supposed to work and talk to Seth, who is also out this week. Then I'll get back with you with suggestions.

From: Jenkins, John K
Sent: Thursday, March 29, 2007 4:04 PM
To: Axelrad, Jane A
Cc: Jenkins, John K; Kweder, Sandra L; Colangelo, Kim M; Sadove, Elizabeth
Subject: FW: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format

Jane

Liz Sadove may have already made you aware of the issue that Kim documents below. This is not new of course since we had long discussions and specifically objected to this provision in the final PLR. We were over ruled. Now we face the problem of how to get important new safety information into the labeling in a timely manner, which runs up against the PLR requirement for a prior approval supplement. As you can see from Kim's summary below, we developed an approach that would allow us to waive the PAS requirement in appropriate circumstances and we sent that to ORP and OCC for comment. Seth Ray responded that this approach was not acceptable and that the PLR provisions were carefully crafted to address issues related to pre-emption (see attached e-mail string). I'm seeking your advice on where to take this. Requiring a PAS is really at odds with our goal to communicate safety information quickly and this is even more important as we are moving to the era of "real time" electronic labeling at NLM (i.e., the labeling changes can now be an effective rapid communication tool). It is often difficult, if not impossible, for us to specifically agree to the sponsor's proposed changes since we need to review the data, which in some cases can be voluminous and may not be available for some time after the early signal is detected (e.g., report from a new large study stopped by a Data Safety Monitoring Committee). The CBE mechanism provided the flexibility for us to provide some input and comment based on our preliminary review of

the data while reserving our final decision on the appropriate labeling language until we completed our review. Help!

John

John K. Jenkins, M.D.
Director, Office of New Drugs
10903 New Hampshire Avenue
Bldg #22, Room 6304
Silver Spring, MD 20993
301-796-0700
301-796-9856 (fax)
NOTE, New E-mail Address: john.jenkins@fda.hhs.gov

From: Colangelo, Kim M
Sent: Thursday, March 29, 2007 2:05 PM
To: Jenkins, John K; Kweder, Sandra L
Subject: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format

John and Sandy,

As requested during our discussion yesterday, here is a summary of the issue regarding the timely incorporation of important safety information in prescription drug labeling.

With the implementation of SPL and PLR, a centralized committee was established to evaluate waivers for either requirement, and to develop policy and procedures as experience was gained in these areas. The committee was chaired by me, and comprised of the six OND ADRAs, Armando Oliva, Laurie Burke and Lilliam Rosario from SEALD, and a representative from OGD (Koung Lee). Note: Armando stepped down from the committee a few months after its inception after the larger policy matters were sorted out.

One of the issues raised was not a novel concern: the inability for the sponsor to update product labeling with important new safety information via submission of a "Changes Being Effected" supplement. Under the new labeling rules, important safety changes would require changes to the Highlights, and any change to the Highlights of the label must be submitted for approval before implementation (thereby eliminating the use of CBE supplements for timely incorporation of new safety information.)

The SPL/PLR Waiver Committee developed a procedure (attached) that would allow a sponsor to formally request a waiver of the prior approval requirement and submit the changes as a CBE supplement. This proposal was sent to ORP for opinion and for consult to OCC. The response from OCC (through ORP) is attached, including a separate email from ORP to OCC expressing concerns with their decision.

I have subsequently had a conference call with ORP (Liz Sadove) and OMP (Janet Norden) on this matter and was informed that it would not be likely that a proposal involving the CBE mechanism for changes to Highlights would be found acceptable due to pre-emption concerns with the Highlights. If we wanted to pursue this, they recommended that we consider other mechanisms to get this type of safety information out in an expeditious manner, and to be ready to articulate those options along with strong justification and data to support our proposals. They also stressed that we would need the support of the Center Director to move this forward.

Please let me know if you have any questions, or if I can provide additional background/information on this matter. The SPL/PLR Waiver Committee meets again on April 10 and could begin work on alternative strategies at that time if desired.

Kim

<< File: PAS waiver procedures - clean ORP.doc >> << Message: FW: Waivers from PAS for Highlights >>

<< Message: RE: Waivers from PAS for Highlights >>

Kim Colangelo
Associate Director for Regulatory Affairs
Office of New Drugs, CDER, FDA
301-796-0700 (OND IO main)
301-796-0140 (direct)
301-796-9856 (facsimile)
Kim.Colangelo@fda.hhs.gov

Norden, Janet M

From: Hirsch, Mark S
Sent: Tuesday, April 24, 2007 3:15 PM
To: Jenkins, John K
Cc: Beitz, Julie G; Colangelo, Kim M
Subject: FW: Response to your CBE labeling question

Dr. Jenkins:

The CBE was submitted on September 24, 2003 (it was Serial 029 to NDA 20-180). As a CBE, it was in effect immediately. We took an "Approveable" action on March 25, 2004, suggesting minor changes to the Sponsor's proposal. The Sponsor responded fully and acceptably to the AE on April 13, 2004 and we approved the SLR on April 23, 2004.

Therefore, the changes were in effect for about 6 months before we finally approved the CBE supplement . And...we actually approved labeling that was a little different than the original Sponsor's proposal.

All of this is documented in DFS under NDA 20-180, including my fairly extensive medical officer's memo.

Let me know if I can be of any further assistance,
Mark

From: Beitz, Julie G
Sent: Tuesday, April 24, 2007 3:00 PM
To: Hirsch, Mark S
Subject: FW: Response to your CBE labeling question

Can you respond?

Julie

From: Jenkins, John K
Sent: Tuesday, April 24, 2007 2:05 PM
To: Beitz, Julie G
Cc: Colangelo, Kim M
Subject: RE: Response to your CBE labeling question

Julie

Can you clarify, when was the CBE submitted as compared to when we approved the labeling changes on 4/23/04? In other words, was the CBE in effect during the two review cycles noted in the 4/24/04 action letter?

John

John K. Jenkins, M.D.
Director, Office of New Drugs
10903 New Hampshire Avenue
Bldg #22, Room 6304
Silver Spring, MD 20993
301-796-0700
301-796-9856 (fax)
NOTE, New E-mail Address: john.jenkins@fda.hhs.gov

From: Beitz, Julie G
Sent: Tuesday, April 24, 2007 1:55 PM
To: Jenkins, John K
Cc: Colangelo, Kim M
Subject: Response to your CBE labeling question

John,

We believe this is an example (from DRUP) that responds to your question re: CBEs.

Julie

From: Hirsch, Mark S
Sent: Tuesday, April 24, 2007 1:40 PM
To: Beitz, Julie G
Cc: Monroe, Scott
Subject: CDataMy6.pdf

<< File: CDataMy6.pdf >> Julie:

I think this would be a good example of new labeling for an emerging safety issue via the CBE route with review of data to follow. It was the information about Proscar potentially increasing the risk of high-grade Gleason's prostate cancers derived from the Prostate Cancer Prevention Trial (Trial). I think this is the type of thing Dr. Jenkins was seeking.

Mark

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-180/S-029

Merck & Company
Attention: Vivian Fuh, M.D.
P.O. Box 2000
Mail Drop: RY 33-200
Rathway, NJ 07065

Dear Dr. Fuh:

Please refer to your supplemental new drug application dated September 24, 2003, received September 25, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for PROSCAR™ (finasteride 5 mg).

Your submission of April 13, 2004 constituted a complete response to our March 24, 2004 action letter.

This "Changes Being Effected" supplemental new drug application provides for proposed changes to the **ADVERSE REACTIONS** section of the label to include information from the Prostate Cancer Prevention Trial (PCPT), sponsored by the U.S. National Cancer Institute (NCI), and coordinated by the Southwest Oncology Group (SWOG) regarding prostate cancers with Gleason scores of 7 to 10, as reported in the July 17, 2003 New England Journal of Medicine publication.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling.

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement

NDA 20-180/S-029." Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for this application.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Jennifer Mercier, Regulatory Health Project Manager, at (301) 827-4244.

Sincerely,

{See appended electronic signature page}

Daniel Shames, M.D.
Director
Division of Reproductive and Urologic Drug Products (HFD-580)
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

Sherman, Aaron

From: Cox, Edward M
Sent: Tuesday, April 24, 2007 10:05 AM
To: Jenkins, John K; Kweder, Sandra L; Colangelo, Kim M; Burke, Laurie B
Cc: Roeder, David L
Subject: Re: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format

Yes, this is a case where we need to do further review of the data. The CBE provides the safety info in the label in the interim.
Thanks.
-Ed

----- Original Message -----
From: Jenkins, John K
To: Cox, Edward M; Kweder, Sandra L; Colangelo, Kim M; Burke, Laurie B
Cc: Roeder, David L
Sent: Tue Apr 24 08:23:55 2007
Subject: RE: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format

Ed

Is this a case where you expect to need to do further review of the data before you can affirmatively sign off on the new labeling? In other words, was the CBE labeling and interim step until you have time to review the data?

John

John K. Jenkins, M.D.
Director, Office of New Drugs
10903 New Hampshire Avenue
Bldg #22, Room 6304
Silver Spring, MD 20993
301-796-0700
301-796-9856 (fax)
NOTE, New E-mail Address: john.jenkins@fda.hhs.gov

From: Cox, Edward M
Sent: Tuesday, April 24, 2007 7:22 AM
To: Jenkins, John K; Kweder, Sandra L; Colangelo, Kim M; Burke, Laurie B
Cc: Cox, Edward M; Roeder, David L
Subject: RE: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format

John,
The CBE that comes to mind is a recent CBE that added a Warning re: mortality findings in studies of catheter-related bacteremia for Zyvox (linezolid). The change in the label (a CBE) was able to be made in about a week. If you need more details, just let me know. We are also checking with the divisions for other examples and will follow-up with others after we have collected more info.
Thanks.
-Ed

From: Jenkins, John K
Sent: Monday, April 23, 2007 4:53 PM
To: Temple, Robert; Meyer, Robert J; Beitz, Julie G; Cox, Edward M; Ganley, Charles J; Pazdur, Richard; Kweder, Sandra L; Colangelo, Kim M; Burke, Laurie B
Subject: FW: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format

Folks

See the e-mail string below. Bottom line is that we are tying to find a way to allow us to waive the pre-approval requirement in the PLR for changes to the Highlights section. I know that we sometimes allow a sponsor to make significant safety labeling changes using the CBE route with our informal agreement but not our formal approval since we have not yet fully reviewed the data. Please send me any examples you have of major safety labeling changes that have occurred via the CBE route as well as any examples you have seen in the PLR era (limited number of labels so far) where this issue may have come up.

John

From: Axelrad, Jane A
Sent: Monday, April 23, 2007 4:50 PM
To: Sadove, Elizabeth; Kweder, Sandra L; Colangelo, Kim M; Jenkins, John K
Cc: Bernstein, Michael; Norden, Janet M
Subject: RE: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format

I would like concrete examples of safety changes that we thought were important that have been implemented through CBEs.

From: Sadove, Elizabeth
Sent: Monday, April 23, 2007 4:22 PM
To: Kweder, Sandra L; Colangelo, Kim M; Jenkins, John K
Cc: Axelrad, Jane A; Bernstein, Michael; Norden, Janet M
Subject: FW: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format
Importance: High

Jane and Seth spoke about this and Seth agreed to discuss this again with Sheldon if we could come up with very specific and narrow criteria for when a waiver would be applied. However, Jane thought that the case would be strongest if we first identify several compelling examples of important changes to safety information in Highlights that sponsors could not immediately distribute because of the PAS requirement. In other words, we need to articulate why this is such a big problem. It would help to have an explanation of how long it takes to review these labeling supplements and why.

If possible, we could use this ASAP... If Jane gets this information by Wednesday, she can brief Dr. Galson.

Thanks,
Liz Sadove

From: Axelrad, Jane A
Sent: Thursday, March 29, 2007 6:06 PM
To: Jenkins, John K
Cc: Kweder, Sandra L; Colangelo, Kim M; Sadove, Elizabeth
Subject: RE: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format

Liz is out this week, but I will discuss it with her early next week and get back to you. I have to refresh my recollection of how this was supposed to work and talk to Seth, who is also out this week. Then I'll get back with you with suggestions.

From: Jenkins, John K
Sent: Thursday, March 29, 2007 4:04 PM
To: Axelrad, Jane A
Cc: Jenkins, John K; Kweder, Sandra L; Colangelo, Kim M; Sadove, Elizabeth
Subject: FW: Summary of issue regarding timely safety updates to

Sherman, Aaron

From: Norden, Janet M
Sent: Wednesday, July 16, 2008 1:15 PM
To: Sherman, Aaron
Subject: Print

-----Original Message-----
From: Jenkins, John K
Sent: Thursday, August 09, 2007 1:50 PM
To: Colangelo, Kim M
Cc: Burke, Laurie B; Kweder, Sandra L; Norden, Janet M
Subject: Re: Internal discussion on NDA 22-059, Tykerb (lapatinib)

Jane is hoping to get some relief on this issue in the next few months, but it is clear we are not going to get an immediate fix. Not sure of the value of meeting to develop a strategy until we better understand whether there might be a "fix" of the regulations (there is a techical fix of the CBE regs that OCC is pushing on a very fast track that we might be able to attach something to) or if we will need to work out some sort of waiver process with OCC.

For now we are just going to have to live within the PAS requirements and decide how to prioritize these for action.

John

----- Original Message -----
From: Colangelo, Kim M
To: Jenkins, John K
Cc: Burke, Laurie B; Kweder, Sandra L; Norden, Janet M
Sent: Thu Aug 09 09:27:50 2007
Subject: RE: Internal discussion on NDA 22-059, Tykerb (lapatinib)

John,

We had scheduled an internal meeting (you, Sandy, Laurie, Janet Norden and myself) to discuss this matter as well (August 21 at 2:00). Is there still value in holding this meeting, or are we in a holding pattern again?

Kim

-----Original Message-----
From: Jenkins, John K
Sent: Wednesday, August 08, 2007 9:06 PM
To: Jones, Glen D (CDER); Axelrad, Jane A; CDER SEALD Labeling; Burke, Laurie B; Bernstein, Michael; Rosario, Lilliam; Pierce, William (CDER); Colangelo, Kim M; Sadove, Elizabeth; Kweder, Sandra L; Ray, Seth; Loewke, Sally A; Norden, Janet M
Cc: Weiss, Karen; Pazdur, Richard; Justice, Robert; Honig, Susan L; Ibrahim, Amna; Jenkins, John K
Subject: RE: Internal discussion on NDA 22-059, Tykerb (lapatinib)

We had some discussions with OCC today about options regarding a waiver of the PLR requirement that all changes to the Highlights section be made via PAS. No decisions were made, but Jane and I made strong appeals that we find a way to address this issue as quickly as possible. In the interim OODP will need to decide how to allocate resources and how to prioritize this supplement in relation to your other pending work.

John

-----Original Message-----
From: Jones, Glen D (CDER)
Sent: Thursday, August 02, 2007 8:36 AM

To: Axelrad, Jane A; CDER SEALD Labeling; Burke, Laurie B; Bernstein, Michael; Rosario, Lilliam; Pierce, William (CDER); Colangelo, Kim M; Sadove, Elizabeth; Jenkins, John K; Kweder, Sandra L; Ray, Seth; Loewke, Sally A; Norden, Janet M
Cc: Weiss, Karen; Pazdur, Richard; Justice, Robert; Honig, Susan L; Ibrahim, Amna
Subject: RE: Internal discussion on NDA 22-059, Tykerb (lapatinib)

We can discuss that internally, but I think it will be difficult to justify putting this labeling supplement before other labeling supplements (also strengthening safety issues) that have been pending for months. The difference is the others are CBEs, but this one requires prior-approval.

Glen

-----Original Message-----
From: Axelrad, Jane A
Sent: Thursday, August 02, 2007 8:25 AM
To: Jones, Glen D (CDER); CDER SEALD Labeling; Burke, Laurie B; Bernstein, Michael; Rosario, Lilliam; Pierce, William (CDER); Colangelo, Kim M; Sadove, Elizabeth; Jenkins, John K; Kweder, Sandra L; Ray, Seth; Loewke, Sally A; Norden, Janet M
Cc: Weiss, Karen; Pazdur, Richard; Justice, Robert; Honig, Susan L; Ibrahim, Amna
Subject: Re: Internal discussion on NDA 22-059, Tykerb (lapatinib)

Up to you to decide whether to expedite review based on normal criteria for expediting.

Sent from my BlackBerry Wireless Handheld

----- Original Message -----
From: Jones, Glen D (CDER)
To: CDER SEALD Labeling; Burke, Laurie B; Axelrad, Jane A; Bernstein, Michael; Rosario, Lilliam; Pierce, William (CDER); Colangelo, Kim M; Sadove, Elizabeth; Jenkins, John K; Kweder, Sandra L; Ray, Seth; Loewke, Sally A; Norden, Janet M
Cc: Weiss, Karen; Pazdur, Richard; Justice, Robert; Honig, Susan L; Ibrahim, Amna
Sent: Thu Aug 02 08:09:31 2007
Subject: RE: Internal discussion on NDA 22-059, Tykerb (lapatinib)

We have a supplement in house to add a new warning, submitted 7/25 as a prior-approval supplement with a request for an expedited (3 days) review. Please advise.

-----Original Appointment-----
From: CDER SEALD Labeling
Sent: Wednesday, August 01, 2007 5:08 PM
To: Burke, Laurie B; Axelrad, Jane A; Bernstein, Michael; Rosario, Lilliam; Pierce, William (CDER); Colangelo, Kim M; Sadove, Elizabeth; Jenkins, John K; Kweder, Sandra L; Jones, Glen D (CDER); Ibrahim, Amna; Ray, Seth; Loewke, Sally A; Norden, Janet M
Cc: Weiss, Karen; Pazdur, Richard; Justice, Robert; Honig, Susan L
Subject: Canceled: Internal discussion on NDA 22-059, Tykerb (lapatinib)
When: Thursday, August 02, 2007 12:00 PM-1:00 PM (GMT-05:00) Eastern Time (US & Canada).
Where: CDER ONDIO Instant Meeting; CDER WO 6305 conf rm Bldg22
Importance: High

This meeting is cancelled. More information to follow. So very sorry for the short notice.

LT Peat

This is an internal meeting to discuss GSK's proposal to submit revisions to approved Tykerb (lapatinib) labeling to include an additional adverse reactions (interstitial lung disease and pneumonitis). This change would be inserted into the 'Warnings and Precautions' section of labeling. Before PLR, this form of revision to the labeling would

be submitted as a Change Being Effected (CBE) to the NDA because the change would strengthen the 'Warnings and Precautions' and lead to increased safe use of the drug. Based on the Rule, this form of change impacts the "Highlights" section hence we can no longer submit such a change as a CBE but rather as a PAS. This meeting is to discuss this policy.

For those that can not attend in person, the call in # is 888-560-9406, pass code 141762.

Background email:
<< Message: FW: Summary of issue regarding timely safety updates to prescription drug labeling in PLR format >>
An agenda will be sent as we approach the meeting.
POC: LT Peat, 301-796-0700

Locicero, Colleen L

From: Francis, Meredith
Sent: Wednesday, December 19, 2007 4:02 PM
To: Burke, Laurie B; Roeder, David L; Thompson, Elizabeth; Locicero, Colleen L
Cc: Francis, Meredith; Sadove, Elizabeth
Subject: RE: Internal discussion on NDA 22-059, Tykerb (lapatinib)

Hi Laurie,

I have had no involvement with the waiver issue you've raised so I just consulted with Liz Sadove to look into it. Liz indicated that the waiver issue is being handled by Jane Axelrad and John Jenkins directly in consultation with OCC and she does not believe that any decision has been made as of yet. Therefore, it seems to me that what you are telling the review divisions (i.e., "that a wavier is not an option . . .") is appropriate for the time being. However, I would recommend that you touch base with John Jenkins for additional information about the status.

--Meredith

Meredith S. Francis
Regulatory Counsel
CDER, Office of Regulatory Policy
301.443.5520

-----Original Message-----
From: Burke, Laurie B
Sent: Monday, December 17, 2007 3:18 PM
To: Francis, Meredith; Roeder, David L; Thompson, Elizabeth; Locicero, Colleen L
Subject: FW: Internal discussion on NDA 22-059, Tykerb (lapatinib)

Hi Meredith,

Attached is an example of the PAS waiver issue that we were referring to in the SPLAT meeting today. Looks like Seth Ray was involved at OCC and Liz Sadove and Michael Bernstein from your office. Several months ago, I heard that there were other CBE-related regs under development that trumped attention to this matter. We are still telling review divisions that a waiver is not an option and it's their job to decide how to allocate their resources and prioritize these PASs (that have always been CBEs in the past) in relation to all other pending work. As PLR labels become more prevalent and these types of PASs become more common, it would be good to have to have a final decision on the waiver option.

Laurie

-----Original Message-----
From: Jenkins, John K
Sent: Wednesday, August 08, 2007 9:06 PM
To: Jones, Glen D (CDER); Axelrad, Jane A; CDER SEALD Labeling; Burke, Laurie B; Bernstein, Michael; Rosario, Lilliam; Pierce, William (CDER); Colangelo, Kim M; Sadove, Elizabeth; Kweder, Sandra L; Ray, Seth; Loewke, Sally A; Norden, Janet M
Cc: Weiss, Karen; Pazdur, Richard; Justice, Robert; Honig, Susan L; Ibrahim, Amna; Jenkins, John K
Subject: RE: Internal discussion on NDA 22-059, Tykerb (lapatinib)

We had some discussions with OCC today about options regarding a waiver of the PLR requirement that all changes to the Highlights section be made via PAS. No decisions were made, but Jane and I made strong appeals that we find a way to address this issue as quickly as possible. In the interim OODP will need to decide how to allocate resources and how to prioritize this supplement in relation to your other pending work.

John