Limitations of Use: Intermezzo is not indicated for the treatment of middle-of-the-night insomnia when the patient has fewer than 4 hours of bedtime remaining before the planned time of waking."

DPP recommends that you revise this page of the journal advertisement to present the full indication for Intermezzo, including the limitations of use. In addition, we recommend that you also present the proprietary and established names along with the dosage form and strength for Intermezzo on this page of the proposed journal advertisement.

Communication Suggestion

The proposed journal advertisement presents the claim, "[i]n a sleep laboratory study, Intermezzo . . .*" (reference omitted) along with efficacy results from this study. The sleep laboratory study is a highly artificial model of middle-of-the-night insomnia. However, the important qualifying contextual information regarding the sleep laboratory study is presented in the footnote at the bottom of the page in smaller type size. We recommend that you revise this presentation, and any future presentations of the sleep laboratory study, to present the important contextual information in the footnote, with equal prominence, and in direct conjunction, with efficacy claims related to this study.

Brief Summary

Omission of Risk Information

The proposed brief summary minimizes the risk of overdose associated with Intermezzo by omitting important information regarding signs, symptoms, and recommended treatment for overdose with zolpidem. DPP recommends that you revise the proposed brief summary to include this important risk information.

In addition, the proposed brief summary omits important risk information in the SPECIAL SAFETY STUDIES section (14.2) of the PI. DPP recommends that you revised the proposed brief summary to include these important risks.

If you have any questions or comments, please direct your response to the undersigned by facsimile at (301) 847-8444, or at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, Division of Professional Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266.** Please note that the Division of Drug Marketing, Advertising, and Communications (DDMAC) has been reorganized and elevated to the Office of Prescription Drug Promotion (OPDP). OPDP consists of the Immediate Office, the Division of Professional Promotion (DPP) and the Division of Direct-to-Consumer Promotion (DDTCP). To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP.

In addition, OPDP recently migrated to a different tracking system. Therefore, OPDP letters will now refer to MA numbers instead of MACMIS numbers. Please refer to the MA#2 in addition to the NDA number in all future correspondence relating to this particular matter. OPDP reminds you that only written communications are considered official.

Sincerely,

{See appended electronic signature page}

[redacted], PharmD, BCPP
Regulatory Review Officer
Division of Professional Promotion
Office of Prescription Drug Promotion

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

/s/

[redacted]

02/06/2012

Reference ID: 3083430

To: Gasdia, Russell[redacted]@pharma.com]
From: Fisher, Windell
Sent: Sun 2/12/2012 1:15:58 PM
Subject: RE: 10 Year Plan - A Dose of How at Least One Board Member is Feeling - FYI ONLY

Got it.

From: Gasdia, Russell
Sent: Sunday, February 12, 2012 1:06 PM
To: Fisher, Windell
Subject: Re: 10 Year Plan - A Dose of How at Least One Board Member is Feeling - FYI ONLY

Windell

We have budget for 525. We should have 525. If we don't fill them, it sends the wrong message to the board. I want to start messaging that we need more reps, not less. We are not able to get to thousands of high prescribers with 525 reps. Endo has 600, JandJ 1000, how many would Pfizer put behind Remoxy? 1000?

Have them get us to 525 soon. We have places to put the. If a DM pushes back. They aren't "on the bus".

Russ

From: Fisher, Windell
Sent: Sunday, February 12, 2012 11:06 AM
To: Gasdia, Russell
Subject: RE: 10 Year Plan - A Dose of How at Least One Board Member is Feeling - FYI ONLY

Russ,

We are down two territories (523), and[redacted] has a proposal to close another vacant one (Phoenix area). I have given direction to Phil & Jane to add back the headcount to get us where we are budgeted. Do we need to discuss this? Do we need to think about holding on adding back the territories? I am concerned that there may be a BOD push for some headcount reduction cost savings and if so, it's easier to deal with vacant positions than staffed ones.

WF

From: Gasdia, Russell
Sent: Tuesday, February 07, 2012 9:15 AM
To: Fisher, Windell; Innaurato, Mike
Subject: FW: 10 Year Plan - A Dose of How at Least One Board Member is Feeling - FYI ONLY

Guys

FYI for your eyes only

Things are not good at BOD level. I met with Dr Raymond for one hour yesterday.

Russ

From: Mahony, Edward
Sent: Tuesday, February 07, 2012 8:04 AM
To: Sackler, Mortimer D.A.
Cc: Sackler, Dr Raymond R; Sackler, Beverly; Sackler, Dr Richard; Sackler, Jonathan; Sackler, Theresa; Sackler, Dr Kathe; Boer, Peter; Boer, Peter; Pickett, Cecil; Lewent, Judy; Stewart, John H. (US); Baker, Stuart D.; [redacted] Gasdia, Russell; Strassburger, Philip; [redacted]
Subject: Re: 10 Year Plan

Thank you - all good questions. I have added a few answers or comments in all caps below. We will try to be sure all are also answered either in the formal deck / presentation or in supplementary exhibits.

Best Regards,

Ed

On Feb 6, 2012, at 7:53 PM, "Sackler, Mortimer D.A." [redacted]@pharma.com> wrote:

> A couple of comments:
>
> 1. I think it is important to also risk adjust things such as IP extensions such as our ability to extend Butrans patent life through the introduction of the second generation patch. That to me is far lower likelihood than what was in the risk adjustment for it in the last plan. One must assume that the generics are able to develop a version that will have a much lower load than our current generation (as Mylan did with their fentanyl patch) and possibly even lower than our second generation patch and hence how will we keep that off the market? PHIL's PRESENTATION DOES COVER THE RANGE OF PATENTS ISSUED, PATENT APPLICATIONS, REGULATORY ETC. PHIL WILL HAVE TO ADD / INCLUDE ANALYSIS OF THE LOAD ISSUE YOU DESCRIBE.

2. Will the new 10 year plan give risk adjusted product P&Ls and NPVs so we can see product by product how they look and if they are still have positive NPVs given the risk adjusted 10 year plan? YES THE PLAN DOCUMENTS WILL INCLUDE SCENARIOS FOR EACH PIPELINE PROJECT.
3. How will you risk adjust Intermezzo? We know it will come to market but the big unknown is how it will do once launched??? WE HAVE NOT UPDATED OUR INTERMEZZO SCENARIOS -WE ESSENTIALLY HAVE ONE INTERMEZZO FORECAST. I UNDERSTAND YOUR POINT. WE WILL DEVELOP THOUGHTS ON THIS.
4. Given the already heated press on the development of a CR Hydrocodone, can we REALLY say that the likelihood of approval is 80%? I would have thought more like 50% given the politics that are already happening and the difficulty getting ANYTHING approved by the FDA these days, especially on time unless it is truly a life saving/extending medicine.MORE ON THIS IN THE PRESENTATION.
5. Have you budgeted further savings and cost reductions given the current further set backs to the business including the higher Medicaid rebates and continued slower growth of Butrans? I am hoping you will be coming back to the Board with further reductions for this year (and future years) to offset those further setbacks as well as as we discussed to have all departments share in the cost reductions not just R&D.UNDERSTOOD. JOHN AND I WILL TALK TO THIS BUT FIRST LETS HEAR RUSS' SALES

ACTION PLAN.

6. How have you handled "spare" R&D capacity as trials finish? In the past you have kept that capacity on board assuming it will get filled by new products. Is that the same here or have you changed it to reduce headcount and cost when those product developments come to an end? THE SPARE R&D IS IN THE PLs

I have limited the distribution of these comments given the sensitive nature of some of the comments. I leave it to you to decide who to share them with.

Regards,

Mortimer

From: Edward Mahony [redacted]@pharma.com>
Date: Mon, 6 Feb 2012 14:46:12 -0500
To: "Sackler, Dr Raymond R" [redacted]@pharma.com>, "Sackler, Beverly" [redacted]@pharma.com>, "Sackler, Dr Richard" [redacted]@pharma.com>, "Sackler, Jonathan" [redacted]@pharma.com>, Theresa Sackler [redacted]@mdsackler.co.uk>, "Sackler, Dr Kathe" [redacted]@pharma.com>, Mortimer Sackler [redacted]@pharma.com>, "F. Peter Boer" [redacted]@boer.org>, "F. Peter Boer" [redacted]@pharma.com>, Cecil Pickett [redacted]@pharma.com>, "Lewent, Judy" [redacted]@pharma.com>
Cc: JOHN STEWART [redacted]@pharma.com>, "Abrams, Robin" [redacted]@pharma.com>, James Dolan [redacted]@pharma.com>, "Gasdia, Russell" [redacted]@pharma.com>, Craig Landau [redacted]@pharma.com>, "Lundie, David" [redacted]@pharma.com>, "Mallin, William" [redacted]@pharma.com>, "Silbert, Richard W" [redacted]@pharma.com> [redacted]@pharma.com>, "Strassburger, Philip" [redacted]@pharma.com>, Stuart Baker [redacted]@chadbourne.com>, [redacted]@pharma.com>, "Lowne, Jon" [redacted]@pharma.com>, [redacted]@pharma.com> [redacted]@pharma.com>
Subject: 10 Year Plan

Colleagues,

We are finalizing the 10 Year Plan and want to share with you some additional thoughts. As always, your comments on how to make the format and content of the 10 Year Plan more meaningful are welcome.

1. We plan to incorporate an estimated cost to settle the OxyContin patent litigation. That cost will be about $275 mm in lost sales for each of 2014 to 2017. For a projected total lost net sales of $1.1 billion over 9 settlements, this compares to total lost sales of $0.9 billion for the 5 settlements we made during 2008 through 2010. While the timing and ultimate total of the settlements is unknown, we believe that this is a reasonable estimate.

2. As these settlements are developed, we are mindful that settlement amounts will have to consider the risk that the OxyContin market could be smaller in 2014 to 2017 than it is today.

3. We plan to incorporate the cost of the potential for higher Medicaid Rebates on OxyContin as a result of the "line extension" proposed regulation, described in our email last week.

4. The previous 5 year plan had the cost and risk adjusted revenue expected from the second generation Butrans patch and the higher strength Butrans patches. Following the 2012 budget decision, we plan to remove the cost of the higher strength efficacy studies and the related sales from the 10 year plan. We will leave the second generation patch in the plan, but for now, limited to the lower strengths. Consistent with the 2012 budget, the plan does contain funding for the higher strength QTc studies. If these studies are positive, and if the sales of Butrans meet expectations and the second generation patch looks positive - we will likely seek approval to invest in the higher strength studies via the 2013 budget.

5. We will add Intermezzo to the plan, not in the previous plan.

6. We have updated each products IP, commercial and R&D plan - and they will be presented.

7. We plan to include the estimated cost of a new manufacturing facility which, of course, will require Board approval.

Your thoughts in advance on these or other matters will be appreciated.

Ed

From: Mahony, Edward
Sent: Tuesday, January 17, 2012 8:51 PM
To: P. Boer, J. Lewent, C. Pickett, Dr. Raymond Sackler, Beverly Sackler, Dr. Richard Sackler, Jonathan Sackler, Dr. Kathe Sackler, Mortimer D. A. Sackler, Theresa Sackler
Cc: Dolan, James; Gasdia, Russell; Landau, Dr. Craig; Long, David; Lundie, David; Mallin, William; sdb; Stewart, John H. (US); [redacted] Weinstein, Bert; Lowne, Jon; [redacted]
Subject: 10 Year Plan --- seeking your input

Colleagues,

The Purdue team is updating the 10 Year Plan and plans to present that update at the February Board Meeting.

As we prepare for that presentation, there are several financial modeling and presentation assumptions that we would like your feedback on. We hope that your advance input will make the presentation more useful to you and will ensure that it contains / covers those items of greatest interest.

To start, the following is a list of financial modeling and presentation assumptions that we used last year – and which we believe should continue:

1. Pipeline project prelaunch development cost projections are not risk adjusted. Instead, 100% of the expected prelaunch development cost is included in the ten year plan. While industry experience would suggest

that some projects might terminate early, we prefer this approach because it earmarks funds for programs.

2. Pipeline project forecasted sales, launch spending and profit are developed with high, medium and low potential commercial / sales outcomes. From this range of outcomes, we include the middle case in the 10 year plan. That middle case outcome is multiplied that by the probability of FDA approval of the product's NDA. So, if a product's middle range forecast is $500 million in revenue, $100 million pretax earnings and the product has a 50% chance of approval --- we would include 50% of those amounts in the plan.
3. Where we use probabilities in the 10 Year Plan we apply industry average success rates --- adjusted slightly for the nature of our projects. For example, TR Hydrocodone is in Phase 3 and we have assigned it an 80% probability of receiving FDA approval.
4. Potential IN OR OUT-licensed products, company acquisitions or like transactions are not included in the plan, since the number of transactions, the amounts and the timing of such transactions are very uncertain. In past years we included a "war chest" in the plan to fund such potential opportunities - but discontinued that approach due to the uncertainties described above . We plan to not include such a war chest in this update to the 10 Year Plan.
5. The 10 Year Plan financials are summarized in two ways - (a) a simple sum of all the projects not risk adjusted and (b) a sum of all the projects risk adjusted as described above.
6. The 10 Year Plan summaries include standard financial statements and a multi- page summary of each pipeline project including the target product profile.
7. The 10 Year Plan projects on a product-by-product basis the marketing period without generic completion, based on our Legal group's evaluation of the IP, Regulatory and Commercial landscape. This period is typically shorter than the full patent life. This same approach will be used in the 10 Year Plan Update.

After we presented the 10 Year Plan last year the Board members asked for some additional information. The management team also sought detailed input from a few Board members, including Peter, Judy and Dr Richard. Some of their

comments and our thoughts are included below for comment. We will use your comments, especially on these items, as we complete development of this update to the plan.

1. The past 10 Year Plans did not include upside potential to the OxyContin brand due to positive findings in the epidemiology studies now underway with the new formulation. As the amount and timing of this upside is uncertain we suggest no change to this approach. However, we are considering market research later this year to evaluate the potential magnitude of positive findings in these studies.
1. The past 10 Year Plan did not include the cost of potential IP challenge settlements as the cost, timing and upside potential of such settlements is uncertain. In this year's 10 Year Plan, we propose including the cost but not the upside of expected settlements. The approach we would take is as follows --- essentially there are now 9 companies challenging some or all of the OxyContin patents. We propose to include in the 10 Year Plan settlements with each of these 9 companies. While the settlements and their terms and conditions are uncertain, we propose assuming settlement with each of the companies at roughly the average terms and conditions of our recent settlements with KV, Rambaxy, Apotex and Actavis with those settlements impacting Purdue over the years 2014 to 2018. (NOTE: please direct questions on this point to Phil Strasburger under privilege.)
2. Peter Boer suggested that the 10 Year Plan include more detail on the planned build out of R&D capabilities, a SWOT analysis on the Purdue organization and succession planning. We suggest addressing these topic separately.
3. Peter Boer suggested that the 10 Year Plan include an assessment of Purdue's bulk API strategy and how it might add value --- like low-ABUK did for OxyContin. We suggest that this topic be handled by the Strategic Manufacturing Group, which includes representation from BOTH Purdue and Rhodes.
4. A number of Board members asked for further information on THE Burtans life cycle plan --- especially how the new formula will HELP avert the threat of generics to the current formula. This will be covered.
5. A number of Board members asked how managed care was considered in developing the commercial opportunity for the OAD TR Hydrocodone formulation. This will be covered.

6. The Board asked that the world wide pipeline be ranked, more projects have global potential and for more diversification beyond opioids. This was presented by John and [redacted] at the November budget meetings and is being further pursued.
7. Certain Board members asked for a further description of how the development of the U.S. economy is expected to impact the 10 Year Plan, how the U.S. pharmaceutical market is expected to develop, and how Purdue will succeed in that market. We were asked to and plan to include:
    i. Payer consolidation
    ii. Payer influence over medicine choices
    iii. Resistance to increased prices
    iv. Slower launch uptake due to payer medical and formulary review.

    These factors are taken into consideration on a product-by-product basis, in the process of developing sales projections – so are to a certain extent already included. However, we will address the ways in which we are planning to generate / bring additional supportive data to payers.
8. Board member asked that we consider the possibility of commercial failure for each project after launch and regulatory approval. The 10 year plan project evaluations generally include 4 cases: no approval after full R&D investment, low case (usually a loss), base case and high case. We think that these reasonably bookend the potential outcomes. NOTE: In the case of a commercial failure, Purdue is generally able to downward adjust its investment in S&P. Generally, licensing terms give Purdue that flexibility. We suggest not adding additional cases to the 10 Year Planning Process.
9. Board members asked that the 10 year plan discuss competing pipelines more deeply especially their expected product attributes compared to Purdue's expected offerings. This will be covered.

Best Regards,

Ed Mahony