Impact Of The FDA Draft Guidance On Patient Reported Outcomes (PRO) Label Claims For Approved Drug Products In The US: Has It Made A Difference?

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Abstract

The purpose of this study was to examine the impact of the US Food and Drug Administration (FDA) Guidance for Industry on Patient Reported Outcomes (PRO) in the labeling of approved drug products.

Background

In February of 2006, the FDA Study Endpoints and Label Development (SEALD) group issued a Draft Guidance on Patient Reported Outcomes (PRO) label claims, describing how the FDA will evaluate PRO data in drug product labeling. This was followed by a 2007 SEALD written feedback on the Guidance. This study aimed to analyze the labeling claims for drug products approved from February 2006 to August 2008.

Objectives

To evaluate the influence of the FDA Draft PRO Guidance on obtaining PRO label claims for drug products in the US, since its release in February 2006. Specifically, the three following questions were addressed:

1. Has the FDA PRO draft guidance affected the release of the draft guidance?
2. Has the draft PRO label claims been granted since the release of the draft guidance?
3. Has the FDA PRO label guidance made a significant impact on the ability of new drug products in the US to obtain PRO label claims?

Methods

All US drug products with a PRO label claim approved by FDA between Feb 2006 and Aug 2008 were identified from the MEDLINE®/PubMed® database (Medical Package Insert (indication, clinical trials sections) and medical review sections in the draft guideline summary tables of approvals (SBA)) for these products were reviewed. As available, the following information was collected for each US product identified:

- Brand name
- Generic name
- Date of approval
- Label indication
- PRO claim language
- PRO instruments evaluated in label
- Type of claim
- Signs and symptoms
- Functioning
- Treatment
- Patient global assessment (not further specified)
- Patient-rated global impression of change
- Patient global impression of cure
- PRO instruments available in SBA
- PRO review by the SEALD
- PRO review comments on content validity and/or PRO label claims

Due to the level of rigor required by the guidance, concerns have been raised that the draft PRO guidance would not suffice the number of PRO label claims.

The ISPOR Task Force that reviewed the guidance called upon “… the FDA to recognize that an acceptable level of evidence may include less than the full set of criteria as outlined in the Guidance.”

In addition, PHARM outlined that “… it is important that there be a balance between what may be considered ideal evidence and practical limitations of what can be accomplished in the context of the clinical trial setting.”

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The FDA requires a case-by-case basis whether existing documentation of content validity and other measurement properties is sufficient.

Results

- 33 drug products were identified as having 46 total PRO label claims
- 24 of the 33 drug products had SBA Medical Reviews available for review
- SEALD was involved in the review of 4 of 24 drug products with an available Medical Review (based only on the evidence submitted within each drug product’s summary basis of approval)
- Has the FDA PRO draft guidance made a significant impact on the ability of new drug products in the US to obtain PRO label claims?

Conclusions

- Since the release of the Draft PRO Guidance, many PRO claims continue to be approved for FDA review divisions.
- PRO label claims are most likely to be granted for data based on signs and symptoms.
- Based on information available from the FDA website, SEALD was involved in the review of very few drug products that achieved PRO label claims.
- Certain FDA review divisions (e.g. DARMS, DMMP) appear to be more comfortable adding claims using specific PRO measures (usually as secondary endpoints).
- Reviewing divisions may or may not be adhering to the Draft PRO Guidance criteria when assessing PRO data for a claim.

Limitations

- We limited information was included in the SBA about development and validation of the PRO measures upon which the 46 claims were based for the 33 drug products.
- It was not possible to make conclusions about the content validity of the reviews or whether they were fit for purpose.
- Based on limited SEALD involvement, evaluating PRO claims for the 33 drug products are limited by the information that is publicly available on the FDA website.

References

- The use of patient-reported outcome measures in the evaluation of medical products for regulatory approvals. Clinical Pharmacology & Therapeutics. 84 (2), p281-283.
- Renaissance Orlando Resort at SeaWorld.
- Life Questionnaire (EORTC QLQ-C30).
- FDA website; undocumented informal consultations or conversations between SEALD and FDA Reviewing Divisions cannot be ruled out.
- Information in SBA.
- "A Standard questionnaire (not specified). . ."
- Very limited information was included in the SBAs about development and validation of the PRO measures upon which the 46 claims were based for the 33 drug products.