VALUE IN HEALTH 16 (2013) 1150–1155

Available online at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/jval

Patient-Reported Outcomes

Assessment of PRO Label Claims Granted by the FDA as Compared to the EMA (2006–2010)

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ABSTRACT

Background: The US Food and Drug Administration (FDA) provides formal guidance for the use of patient-reported outcomes (PROs) in support of labeling claims, whereas the European Medicines Agency (EMA) offers insight in a reflection paper relating to health-related quality of life in lieu of formal guidance. **Objectives:** PRO label claims granted for new molecular entities and biologic license applications from 2006 through 2010 were reviewed to evaluate consistencies and discrepancies in PRO label claims granted by the FDA and the EMA and to highlight trends in the acceptance of PRO claims across agencies. **Methods:** Products approved by both the FDA and the EMA were identified. By using US Drug Approval Packages and European Public Assessment Reports packages, any PRO label claims made for the same product by the same company were compared. **Results:** Both agencies approved a total of 75 products. Of these, 35 (47%) had at least one EMA-granted PRO label claim compared with 14 (19%) by the FDA. Most FDA-grated claims focused on symptoms; however, EMA-granted claims were more likely to include higher order concepts. Few (~12%) were granted the same label claims. Despite this discordance between the two agencies, where PRO label claims were granted by both the FDA and the EMA, there was similarity in the type of label claim. **Conclusions:** The EMA is more likely than the FDA to grant PRO claims and for higher order constructs. On a macro level, there appears to be poor concordance between claims granted by both agencies. On close examination, however, there appears to be greater concordance than previously recognized, which may be instructive in formulating future PRO strategies. Further research to create strategic alignment across agencies may be beneficial.

Keywords: EMA, FDA, labeling, patient-reported outcome.

Introduction

In late 2009, the US Food and Drug Administration (FDA) issued formal guidance, *Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims* [1], that set standards for the use of patient-reported outcome measures (PROMs) in support of product labeling claims. This guidance was intended to "increase efficiency of discussions with the FDA during the medical product development process, streamline the FDA's review of PRO instrument adequacy and resultant PRO data collected during a clinical trial, and provide optimal information about the patient perspective for use in making conclusions about treatment effect at the time of medical product approval" [1]. Related to this effort, a second initiative for drug development tools (DDTs) including patient-reported outcomes (PROs) was created by the Center for Drug Evaluation and Research as part of the FDA's Critical Path Initiative [2]. The purpose of this initiative was to provide a framework to facilitate the development and regulatory acceptance of scientific tools used in drug development programs. The guidance for this initiative is currently at draft stage but is intended to encompass multiple levels of instrumentation including PROs, biomarkers, animal models, and other clinical outcome assessments.

The European Medicines Agency (EMA), unlike the FDA, has not issued formal guidelines specific to PROs but instead offered a reflection paper [3] to provide broad recommendations on health-related quality-of-life (HRQOL) evaluation in the context of clinical trials. In addition, the EMA has developed the Biomarker's Qualification program (2008) that is somewhat similar to the DDT guidance in the United States. This qualification program provides a formal mechanism for ratifying clinical trial endpoints, including new or existing PROs [4].

Despite input into PROM standards from both the FDA and the EMA, there still appears to be disparity in the use and acceptance of PROMs in product labeling between the two agencies. It appears from early analyses that the EMA is more likely to grant

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1098-3015/$36.00 – see front matter

http://dx.doi.org/10.1016/j.jval.2013.08.2293

claims in the area of HRQOL or functioning, whereas claims in the United States are largely limited to claims of improvement in symptoms [5–7].

A review of PRO label claims from the United States showed that approximately 25% of product labels between 2006 and 2010 included PRO endpoints [6]. Coombs et al. [8] compared PRO claims by the FDA and the EMA for oncology products. To our knowledge, however, a formal comparison of all PRO label claims for products approved by both the FDA and the EMA is yet to be conducted. Therefore, the purpose of this article was to compare and contrast product labeling claims for new drug entities or biologic license agents approved by the FDA and the EMA in the years 2006 through 2010.

Methods

The FDA Drug Approval Reports Web site was used to identify first approvals of new drugs that were approved in the United States from January 2006 through December 2010, including only those products classified by the Center for Drug Evaluation and Research as new molecular entities or biologic licensed agents. Any product containing substances previously marketed with a different brand name or set of indications, as a different dosage form or strength, or as a combination product of previously marketed entities was excluded. This product list was then compared with the EMA Web site listing of authorized products. In the United States, Drug Approval Packages (DAPs) and approved product labels were reviewed. Information was retrieved from the medical review, summary review, cross-discipline team leader review, and other review sections from the DAP and from the Indication and Clinical Studies section of the approved product label. The DAPs were located on the FDA Web site Drugs@FDA (www.accessdata.fda.gov). In the European Union (EU), European Public Assessment Reports (EPAR) packages, the summary of product characteristics, and scientific discussion documents found on EMA Web site (www.ema.europa.eu) were reviewed.

For analysis purposes, PRO label claims were classified as one of the following five types: symptoms, functioning, HRQOL, patient global rating (PGR), or "other." As previously described [6], symptoms measures are defined as measures of "impairments," that is, any loss or abnormality of psychological, physiological, or anatomical structure or function [9]. Measures of functioning included activity limitation PROs that address physical, social, or psychological functioning, that is, any restriction or lack of ability to perform an activity in the manner or within the range considered normal for a human [9]. HRQOL has been defined as "the capacity to perform the usual daily activities for a person's age and major social role" [9]. Its emphasis is on the measurement of a combination of symptoms and functioning and, as such, HRQOL relates to health status. Consequently, measures of HRQOL are multidimensional, yielding a profile of scores. A product label may contain more than one PRO claim.

Statistical analysis consisted of frequencies and cross-tabulations of measured characteristics. Calculations were performed by using Microsoft Excel 2007. For analysis purposes, if a PRO appeared in the DAP or the EPAR, it was considered to be an attempt to seek a PRO label claim, despite sponsor intent, unless specifically noted otherwise.

Results

A total of 156 new drugs were approved between January 2006 and December 2010 [6]. Of these, 37 were excluded from analysis (33 generic products and 4 new products that were approved but had no data available on the FDA Web site at the time of review). Of the remaining 116 products, a total of 75 had been approved by both the FDA and the EMA. Table 1 shows that of these, 35 (47%) were granted at least one PRO claim by the EMA as compared to 14 (19%) by the FDA, representing a more than twofold increase in at least one PRO label claim granted by the EMA. Table 1 also shows that of the 70 PRO claims granted for the 35 products approved by both agencies, 48 (69%) were granted by the EMA. Products approved with at least one PRO label by either of the two agencies are listed in Table 2. The table shows that for all products for which the FDA granted a PRO label claim, the EMA did as well. Also, 14 products with PRO label claims were approved by both agencies and 10 of these products were approved by the EMA first and then by the FDA.

Table 1 – Number of products with PRO label claims approved by both the FDA and the EMA (2006–2010).

	FDA	EMA
Number of products with PRO label claims	14 (19%)	35 (47%)
Number of PRO label claims granted	22	48
Total number of products approved by both agencies (2006–2010)	75	75

EMA, European Medicines Agency; FDA, Food and Drug Administration; PRO, patient-reported outcome.

Table 3 summarizes the type of PRO claim granted by the FDA or the EMA. The table shows that the EMA granted PRO label claims to more products than did the FDA between 2006 and 2010. The majority of the claims in the United States focused on symptoms; however, claims granted by the EMA included higher order concepts such as HRQOL and functioning (EMA = 22; FDA = 7).

A total of 52 PRO label claims were granted by both agencies (FDA = 22; EMA = 30) for 14 products. Despite this discordance between the number of PRO label claims granted by the two agencies, concordance is found when label types (e.g., symptoms and functioning) are analyzed for products with PRO label claims granted by both the FDA and the EMA. Table 4 shows that for the 14 products with PRO label claims granted by both agencies, the type of PRO claims granted was similar: 12 of the 14 products had symptom claims granted by both agencies as were 5 functioning claims and 3 PGR claims. HRQOL-related claims were granted for Soliris and Letairis by both the FDA and the EMA. Drugs such as Arcalyst and Toviaz demonstrate the concordance in symptom labeling, with both the EU and FDA claims describing changes in symptoms scores.

Table 4 provides a listing of the type of PRO claim granted by each agency as well as the instruments used to secure the claim for the 14 products with at least one PRO label claim from the FDA and the EMA.

In addition, 21 products were granted PRO label claims by the EMA but not the FDA. Within these products bearing no FDA claims, 13 were granted HRQOL/QOL or functioning claims, 3 were granted treatment satisfaction, 5 were granted symptom claims, and the remainder of the claims were based on PGR questions. The Appendix in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2013.08.2293 provides a listing of measures that were used in support of these claims.

Discussion

This review provides the first attempt to compare all FDA-granted PRO label claims in approved products with all EMA-granted PRO label claims since the release of the FDA's final guidance in the recent past. At first glance, the two agencies appear to agree on

Table 2 – PRO claims—FDA as compared to EMA by product (2006–2010).

Product	FDA	US approval date	EMA	EU approval date
Azilect	Yes	5/16/2006	Yes	2/21/2005
Chantix	Yes	5/10/2006	Yes	9/26/2006
Lucentis	No	6/30/2006	Yes	1/22/2007
Omnaris	Yes	10/20/2006	Yes	3/19/2008
Invega	No	12/19/2006	Yes	3/4/2011
Soliris	Yes	3/16/2007	Yes	6/20/2007
Neupro	No	5/9/2007	Yes	2/15/2006
Torisel	No	5/30/2007	Yes	11/19/2007
Letairis	Yes	6/15/2007	Yes	4/21/2008
Micera	No	11/14/2007	Yes	7/20/2007
Arcalyst	Yes	2/27/2008	Yes	10/23/2009
Cimzia	Yes	4/22/2008	Yes	10/1/2009
Lexiscan	No	4/10/2008	Yes	9/6/2010
Toviaz	Yes	10/8/2006	Yes	4/20/2007
Rapaflo	Yes	10/8/2008	Yes	1/29/2010
Vimpat	Yes	10/8/2008	Yes	8/29/2008
Banzel	Yes	11/14/2008	Yes	1/16/2007
Afinitor	No	3/30/2009	Yes	8/3/2009
Simponi	Yes	4/24/2009	Yes	10/1/2009
Samsca	No	5/19/2009	Yes	8/3/2009
Ilaris	No	6/17/2009	Yes	10/23/2009
Extavia	No	8/14/2009	Yes	5/20/2008
Saphris	No	8/13/2009	Yes	9/1/2010
Stelara	No	9/25/2009	Yes	1/16/2009
Arzerra	No	10/26/2009	Yes	4/19/2010
Votrient	No	10/19/2009	Yes	6/14/2010
Ampyra	Yes	1/22/2010	Yes	7/20/2011
Acterma	Yes	1/8/2010	Yes	1/16/2009
Xiaflex	No	2/2/2010	Yes	2/28/2011
Treanda	No	3/20/2008	Yes	3/19/2010
Vpriv	No	2/26/2010	Yes	8/26/2010
Carbaglu	No	3/18/2010	Yes	1/24/2003
Zortress	No	4/20/2010	Yes	3/08/2009
Lumizyme	No	5/24/2010	Yes	3/29/2006
Jevtana	No	6/17/2010	Yes	3/17/2011

EMA, European Medicines Agency; EU, European Union; FDA, Food and Drug Administration; PRO, patient-reported outcome.

the exact type of labeling less than 12% of the time across approved products. On close inspection within the 14 products that had claims from both agencies, however, similarities in labeling exist. The majority of these 14 (91%), while not having the exact wording included in the claim, offered the same type of claim. For example, symptom or functioning claims may have been granted by both agencies but with slight differences in wording. In 12 of the 14 products, symptom claims were granted by both agencies with the exception of Letairis, which received a claim for dyspnea by the EMA, and Ampyra, which received a functioning claim by both agencies.

Table 3 – Summary of PRO label claim types granted by the FDA or the EMA (2006–2010).

Type of claim	n (%)	
	FDA-granted claims (N = 14 products)	EMA-granted claims (N = 35 products)
Symptoms	12 (54)	19 (40)
Functioning	5 (23)	9 (19)
HRQOL	2 (9)	13 (27)
Patient global rating	3 (14)	5 (10)
Other	0 (0)	2 (4)
Total claims	22 (100)	48 (100)

EMA, European Medicines Agency; FDA, Food and Drug Administration; HRQOL, health-related quality of life; PRO, patient-reported outcome.

Concordance between the two agencies can be understood in part by examination of the available guidance documents. The EMA broadly accepts patient assessed measurement of core symptoms of disease with no specific regulatory requirement for these endpoints [10]. This position aligns closely with the FDA position described in the PRO guidance that notes that the "question of what to measure may be obvious given the condition being treated." The guidance further elucidates this comment by using the effect on the treatment of pain as an example in which a symptom is readily recognized and accepted to support labeling claims. Given how close the agencies align in this acceptance, it is not unexpected to see concordance for symptom claims. In addition, differences in the symptoms claims may be fairly readily explained. The FDA has publicly taken a position that the concept of fatigue is multidimensional and therefore is not endorsed, whereas the EMA has accepted fatigue as a measurable concept. This is demonstrated by the fatigue claim granted to

Table 4 – Types of PRO label claims approved by the FDA and the EMA for the 14 products with claims granted by both agencies (2006–2010).

	EMA						Total
	PRO type	Symptom	Function	HRQOL	PGR	Other	None	
FDA	Symptom	Azilect Chantix Omnaris Soliris Arcalist Cimzia Toviaz Rapaflo Vimpart Banzil Simponi Acterma						12
	Function		Azilect Cimzia Simponi Ampyra Acterma					5
	HRQOL			Soliris Letairis				2
	PGR				Banzil Simponi Acterma			3
	Other							0
	None	Letaris	Arcalist	Azilect Cimzia Simponi Acterma	Toviaz	Cimzia		0
Total		13	6	6	4	1	0	EMA = 30 FDA = 22

EMA, European Medicines Agency; FDA, Food and Drug Administration; HRQOL, heath-related quality of life; PGR, patient global rating; PRO, patient-reported outcome.

Simponi by the EMA and not by the FDA. Finally, as noted by Girman et al. [5], it is important to recognize that regulatory requirements for registration often differ by regions, causing sponsors to launch multiple trials with differing endpoints to meet health authority requirements outside of both the FDA and the EMA. In some instances, these decisions may be more closely aligned with EMA guidance than with the FDA.

As anticipated by previous research [7], the EMA granted a greater number of higher order claims including HRQOL and functioning (Table 5). This difference is often widely discussed among peers and can be a point of contention for clinical teams planning a single PRO strategy for both the United States and the EU. It is helpful to recognize that this difference in acceptance rates may be in part due to the request in some EMA guidance documents to include HRQOL measures as key secondary endpoints. Within these guidance documents, the EMA will recommend specific, validated instruments for use within the therapeutic area, and so in a sense lend endorsement to these measures. The FDA, however, instead typically recommends the identification of concepts and does not endorse specific measures. Given the FDA position on the complex and multidimensional definition of HRQOL, the measurement of these concepts may not be recommended by the FDA and hence not endorsed as a claim. In addition, the EMA is open to claims of improved physical functioning based on the subset of domains within HRQOL measures [10], whereas the FDA would not likely accept such a basis for a functioning claim.

Azilect, Lucentis, Stelara, and Samsca provide instructive examples where the EMA granted HRQOL or functioning claims on the basis of measures that were rejected by the FDA. The FDA denied a HRQOL claim based on the PD-Qualif scale for Azilect noting that "the sponsor did not make statistically appropriate adjustments for these multiple comparisons" [11]; however, the EMA granted a claim of "significant and beneficial effect in quality of life" on the basis of the same scale. The VFQ-25 supported a claim of "patient reported benefits" for Lucentis by the EMA, whereas the FDA questioned whether the tool was fit for purpose. Stelara received no PRO claims in the United States but did receive endorsement for all claims sought by the EMA including HRQOL and symptoms (Dermatology Life Quality Index , short-form 36 health survey, Itch visual analogue scale). Finally, the EMA granted a HRQOL claim for Samsca on the basis of results from the short-form 12 health survey, noting that "mental scores showed statistically significant and clinically relevant improvements for tolvaptan treatment compared to placebo." A Study Endpoints and Label Development group review for Samsca, however, indicates that "The primary endpoint 'the SF-12' was developed as a generic health status instrument for the general population and not as a symptom assessment tool or HRQoL tool in patients with hyponatremia."

Ampyra received FDA marketing approval in January 2010 followed by conditional approval (marketed as Fampyra) by the EMA in July 2011. The EMA provided conditional approval because of concerns about the clinical relevance of the MS

Table 5 – Higher order claims granted by the EMA (2006–2010).

Product	PRO measure	Claim type
Azilect	Parkinson's Disease Quality of Life Scale	HRQOL
Soliris	EORTC-QLQ-C30	HRQOL
Letaris	SF-36 and Borg	HRQOL, symptoms
Lucentis	VFQ-25	HRQOL (patient-reported benefits)
Torisel	EQ-5D questionnaire	QALY
Treanda	EORTC-C30 and EORTC-QLQ-CLL25	HRQOL
Cimzia	HAQ-DI, Fatigue Assessment Scale, SF-36, Work Productivity Survey	HRQOL, functioning, work productivity
Afinitor	EORTC-QLQ-C30	QOL
Simponi	HAQ, SF-36, FACIT-Fatigue Scale	Functioning, HRQOL
Samsca	SF-12	HRQOL (mental component)
Stelara	DLQI, Itch VAS, SF-36, HADS, Work Limitations Questionnaire	HRQOL, Work productivity
Extavia	FAMS	No benefit but assessed and included in the SPC
Votrient	EORTC-QLQ-C30 and EQ-5D questionnaire	HRQOL (no difference between groups)

DI, Disability Index; DLQI, Dermatology Life Quality Index; EMA, European Medicines Agency; EORTC-C30, European Organization for Research & Treatment of Cancer Quality of Life Questionnaire Core 30; EORTC-QLQ-C30, European Organization for Research & Treatment of Cancer Quality of Life Questionnaire Core 30; EORTC-QLQ-CLL25, European Organization for Research & Treatment of Cancer Quality of Life Questionnaire chronic lymphocytic leukemia; EQ-5D, EuroQol five-dimensional; FACIT, Functional Assessment of Chronic Illness Therapy; FAMS, Functional Assessment MS Treatment; HADS, Hospital Anxiety and Depression Scale; HAQ, Health Assessment Questionnaire; HRQOL, heath-related quality of life; PRO, patient-reported outcome; QALY, quality-adjusted life-year; QOL, quality of life; SF-12, short-form 12 health survey; SF-36, short-form 36 health survey; SPC, summary of product characteristics; VAS, visual analogue scale; VFQ-25, Visual Function Questionnaire 25.

Walking Scale, noting a requirement "To conduct a double-blinded, placebo-controlled, long-term efficacy and safety study to investigate a broader primary endpoint clinically meaningful in terms of walking ability …" A Study Endpoints and Label Development review noted a similar concern with the clinical relevance and effect on the responder rate of the MS Walking Scale based on lack of significant difference on a patient global "how do you feel about the effects of the study medication over the past 7 days?" (scale 0–7, where 0 was "terrible" and 7 "delighted"); however, a "walking speed" label claim was granted.

Such examples appear to indicate that differing levels of evidence are needed to facilitate positive reviews by agencies. Importantly, in all instances in which higher order claims (HRQOL, functioning) were granted by the FDA, they were also granted by the EMA, suggesting that if the evidence to support a claim is deemed sufficient in the United States, it is likely to be sufficient for the EMA as well. Given the small number of these claims, however, this should be interpreted with caution and as always, clinical teams should carefully assess the specific measure and its context of use.

Similar findings are noted for treatment satisfaction tools. The EMA granted two treatment satisfaction claims to products that did not receive PRO labeling by the FDA (Xiaflex and Zortress).

Finally, it is important to note the limitations of this research. For analysis purposes, if a sponsor included a PRO in a DAP or an EPAR, it was assumed that a claim was sought. PROs are often included in clinical trials for reasons beyond labeling [5,9], and so this assumption may have skewed results somewhat. However, given the proprietary nature of labeling discussions, the true intent of a sponsor is often unknown to outside observers. In addition, the guidance documents (including the EMA reflection paper, FDA PRO guidance, and Biomarker and DDT Qualification programs) are all fairly recent regulatory developments. The effect of these guidance documents on trials planned before their release is unknown and perhaps is yet to materialize.

Conclusions

The EMA is more likely than the FDA to grant PRO claims and is more likely to grant claims for higher order constructs such as HRQOL and functioning. On a macro level, there appears to be poor concordance between claims granted by both agencies. This discrepancy in granting claims may necessitate that sponsors develop agency-specific PRO strategies, adding strain to limited resources and time required for drug development programs. On close examination, however, there appears to be areas of greater concordance than previously recognized for symptoms claims and functioning, which may be instructive in formulating future PRO strategies. Further research to understand where there is strategic alignment across agencies may be beneficial or help identify when multiple PRO strategies are needed or if a single approach may be found acceptable by both agencies.

Source of financial Support: This study was supported by Novartis Pharmaceuticals.

Supplemental Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at http://dx.doi.org/10.1016/j.jval.2013.08.2293 or, if a hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

REFERENCES

[1] US Department of Health and Human Services. Guidance for industry. Patient-reported outcome measures: use in medical product development to support labeling claims. 2009. Available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf. [Accessed January 14, 2011].

[2] US Department of Health and Human Services, Food and Drug Administration. Guidance for industry: qualification process for drug development tools. 2010. Available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM230597.pdf. [Accessed January 20, 2012].

[3] European Medicines Agency, Committee for Medicinal Products for Human Use. Reflection paper on the regulatory guidance for the use of health related quality of life (HRQL) measures in the evaluation of medicinal products. 2005. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003637.pdf. Accessed August 30, 2013.

[4] European Medicines Agency, Committee for Medicinal Products for Human Use. Biomarkers. Available at: http://www.ema.europa.eu/ema/

index.jsp?curl=pages/special_topics/general/general_content_000349.jsp&mid=WC0b01ac05800baedb. [Accessed October 19, 2012].
[5] Girman C, Ibia E, Menjoge S, et al. Regulatory requirements for trial endpoints in multiregional clinical trials. Drug Info J 2011;45:587–94.
[6] Gnanasakthy A, Mordin M, Clark M, et al. A review of patient-reported outcome labels in the United States: 2006 to 2010. Value Health 2012;15:437–42. Available at: http://www.sciencedirect.com/science/article/pii/S1098301511036011. [Accessed February 2, 2012].
[7] Marquis P, Caron M, Emery MP, et al. The role of health-related quality of life data in the drug approval processes in the US and Europe: a review of guidance documents and authorizations of medicinal products from 2006 to 2010. Pharm Pharm Med 2011;25:147–60.
[8] Coombs J, McBurney C, Gondek K, Copley-Merriman K. Evidence of patient reported outcomes in labeling for oncology products: evaluation of United States and European labels. MAPI Qual Life Newslett 2002;29:1–3.
[9] Doward LC, Gnanasakthy A, Baker MG. Patient reported outcomes: looking beyond the label claim. Health Qual Life Outcomes 2010;8:89.
[10] Isaac M, Vamvakas S, Pavlovic M. EMA perspective on PRO instrument qualification and harmonization. Presented at: First Annual Patient Reported Outcomes Consortium Workshop, March 23, 2010, Bethesda, MD.
[11] DeMuro C, Mordin M, Clark M, et al. Reasons for rejection of PRO label claims: an analysis based on a review of PROs among new molecular entities and biologic license applications 2006-2010. Poster presented at: International Society for Pharmacoeconomics and Outcomes Research 16th Annual International Meeting, May 22, 2011, Baltimore, MD.