# Patient-Reported Outcomes (PROs) claims in products indicated for treatment of non-small-cell lung carcinoma (NSCLC) and approved in Europe and in the USA

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## OBJECTIVES

The objectives were twofold:

- (1) To identify products indicated for treatment of non-small-cell lung carcinoma (NSCLC) approved with a PRO labeling claim in Europe and the USA; and
- (2) To list the differences found in Europe vs. the USA in terms of products and labeling.

## METHODS

- The PROLabels database was searched for NSCLC products.
- The analysis was performed on medicinal product labels approved by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) as well as on FDA medical reviews and EMA scientific discussions.

## RESULTS

- A total of 15 products (generics excluded) were identified (see Table 1):
  - six at the EMA, and
  - nine at the FDA.
- The six products approved by the EMA were also approved by the FDA (i.e., bevacizumab, docetaxel, erlotinib, gefitinib, paclitaxel, and permetrexed disodium).
- Four products with a PRO claim were identified in Europe (i.e., docetaxel, erlotinib, gefitinib and paclitaxel), and two in the USA (i.e., paclitaxel and gemcitabine).
  - Most of the PROs identified in the claims were “quality of life” and “symptoms.”
  - For four products (i.e., docetaxel, erlotinib, gefitinib and paclitaxel), the EMA and FDA showed disagreement in terms of their PRO labeling.
    - ✓ The EMA gave a PRO claim (“quality of life” and “symptoms”) to three products, but not the FDA;
    - ✓ For paclitaxel, the FDA did not include a “quality of life” claim in the label.
- Except for gefitinib, the reviews of both agencies were conducted on the same clinical studies. The analysis of the medical reviews and scientific discussions showed that the FDA did not include the PROs in the label because of concerns about the quality of the study design, of the analyses, or the questionnaires’ content validity.

## CONCLUSION

- Our review showed that the patients’ perspective in the treatment of non-small-cell lung carcinoma is important for the EMA and FDA. However, differences exist in the evaluation of PRO data for inclusion in the label.
- Our analysis suggests a higher receptivity of the EMA to quality of life as a global concept.

### Table 1. Products approved for the treatment of NSCLC (EMA and FDA)

| Reference Number(s) | Regulatory Agency | INN | Brand Name | MAH | Date of Approval | PRO Claim | |
|---|---|---|---|---|---|---|---|
| EMEA/H/C/000582 | EMA | bevacizumab | Avastin | Roche Registration | 12/01/2005 | No | |
| BLA 125085 | FDA | | | Genentech | 26/02/2004 | No | |
| EMEA/H/C/000564 | EMA | pemetrexed disodium | Alimta | Eli Lilly | 20/09/2004 | No | |
| NDA 021462 | FDA | | | | 04/02/2004 | No | |
| EMEA/H/C/000216 | EMA | paclitaxel | Paxene | Norton Healthcare | 19/07/1999 | Yes | The higher response rates (37 % vs. 26 %), lesser overall side effects and improved short term QoL with cisplatin/paclitaxel vs cisplatin/tenoposide were considered important results in a palliative population. In the second study, a greater proportion of paclitaxel-treated patients had improvements in short-term QoL. |
| NDA 020262 | FDA | | Taxol | Mead Johnson | 29/12/1992 | Yes | In the ECOG study, the Functional Assessment of Cancer Therapy-Lung (FACT-L) questionnaire had 7 subscales which measured subjective assessment of treatment. Of the seven, the Lung Cancer Specific Symptoms subscale showed a lesser rate of deterioration for the treatment arm of Taxol 135 mg/m2/24 hours plus cisplatin arm compared to the cisplatin/etoposide arm. |
| EMEA/H/C/000073 | EMA | docetaxel | Taxotere | Aventis Pharma | 27/11/1995 | Yes | Secondary end-points included change of pain, global rating of quality of life by EuroQoL-5D, Lung Cancer Symptom Scale, and changes in Karnosfky performance status. Results on these end-points were supportive of the primary end-points results. |
| NDA 020449 | FDA | | | Sanofi Aventis | 14/05/1996 | No | |
| EMEA/H/C/000618 | EMA | erlotinib | Tarceva | Roche Registration | 19/09/2005 | Yes | *- ITT population results:* Quality of life data did not suggest a detrimental effect from erlotinib compared with placebo.<br>*- NSCLC treatment after failure of at least one prior chemotherapy regimen (Tarceva administered as monotherapy):* Tarceva resulted in symptom benefits by significantly prolonging time to deterioration in cough, dyspnoea and pain, versus placebo. |
| NDA 021743 | FDA | | | Osi Pharms | 18/11/2004 | No | |
| EMEA/H/C/001016 | EMA | gefitinib | Iressa | Astra Zeneca | 24/06/2009 | Yes | Quality of life outcomes differed according to EGFR mutation status. In EGFR mutation-positive patients, significantly more IRESSA-treated patients experienced an improvement in quality of life and lung cancer symptoms vs carboplatin/paclitaxel.<br>In the IPASS trial, IRESSA demonstrated superior PFS, ORR, QoL and symptom relief with no significant difference in overall survival compared to carboplatin/paclitaxel in previously untreated patients, with locally advanced or metastatic NSCLC, whose tumours harboured activating mutations of the EGFR tyrosine kinase. |
| NDA 021399 | FDA | | | | 05/05/2003 | No | |
| NDA 202570 | FDA | crizotinib | Xalkori | Pfizer | 26/08/2011 | No | |
| NDA 020509 | FDA | gemcitabine hydrochloride | Gemzar | Eli Lilly | 15/05/1996 | Yes | QOL was a secondary endpoint in both randomized studies. In the Gemzar plus cisplatin versus cisplatin study, QOL was measured using the FACT-L, which assessed physical, social, emotional and functional well-being, and lung cancer symptoms. In the study of Gemzar plus cisplatin versus etoposide plus cisplatin, QOL was measured using the EORTC QLQ-C30 and LC13, which assessed physical and psychological functioning and symptoms related to both lung cancer and its treatment. In both studies no significant differences were observed in QOL between the Gemzar plus cisplatin arm and the comparator arm. |
| NDA 020451 | FDA | porfimer sodium | Photofrin | Axcan Scandipharm | 27/12/1995 | No | |

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