THERAPEUTIC CLASS LABELING OF FDA-APPROVED EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) COMPANION DIAGNOSTICS

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INTRODUCTION

In cancer treatment, precision medicine involves using biomarker information to identify patients indicated for oncology products. In vitro companion diagnostics (CDxs) are used to identify such markers and consequently, a population of patients who are most likely to respond to a therapeutic product.1,2 This research evaluates the first companion diagnostics to incorporate therapeutic class labeling as supported by the 2020 Guidance for Industry released by the US Food and Drug Administration (FDA).3 Criteria for evaluating the potential for CDx therapeutic class labeling is provided to inform pharmaceutical industry professionals co-developing CDxs and oncology products.

OBJECTIVES

- Review CDx labeling for number of associated products, indication, and therapeutic group language.
- Examine the regulatory pathways of CDx products whose labels contain therapeutic class labeling.
- Describe criteria for CDx therapeutic group labeling for utilization by pharmaceutical industry professionals developing CDxs for oncology therapeutic products.

METHODS

The Intended Use language within CDx labels on the FDA's "List of Cleared or Approved Companion Diagnostic Devices (*In Vitro* and Imaging Tools)" website[4] and oncology product labeling from Drugs@FDA[5] were reviewed on November 1, 2021 for therapeutics class language. For CDx products with therapeutic class label language, the regulatory history was evaluated to determine the development approach taken to achieve the language.

RESULTS

A total of 47 *in vitro* companion diagnostics were identified, of which 26 (55%) were approved for use with 1 product, 18 (38%) for use with 2-5 products, 2 (4%) for use with
6-10 products, and 1 (2%) for use with >10 products, as shown in Figure 1. Therapeutic class labeling is not included in the number of named therapeutic products. Figure 2 shows the percentage of CDxs associated with each indication.

Figure 1. Number of Products Associated Per Companion Diagnostic

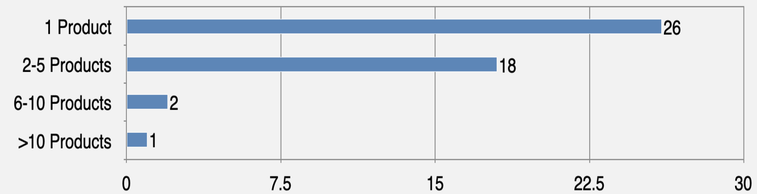
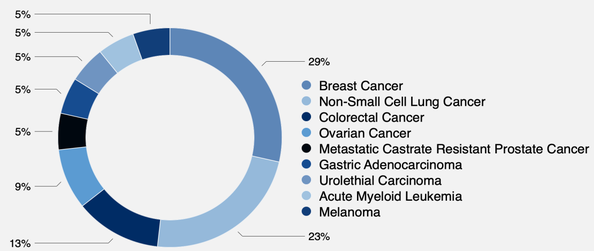


Figure 2. Indication and % Associated Companion Diagnostics



Two CDxs contained therapeutic class labeling as shown in Figure 3. The Intended Use of both CDxs were for the identification of epidermal growth factor receptor (EGFR) mutations for the treatment of non-small cell lung cancer (NSCLC). Three additional EGFR CDxs were approved; however, they did not contain therapeutic class labeling for this indication. The first CDx approved with therapeutic class labeling was the Cobas EGFR Mutation Test V2 manufactured by Roche Molecular Diagnostics, which received the language as a label supplement on October 27, 2020; however, prior to the therapeutic class labeling, three oncology products were named in the Intended Use: Tarceva (erlotinib), Tagrisso (osimertinib), and Iressa (gefitinib). The second CDx to incorporate therapeutic class labeling was the ONCO/Reveal Diagnostic Lung and Colon Cancer Assay, manufactured by Pillar Biosciences, on initial approval on July 30, 2021.

RESULTS CONT.

Figure 3. EGFR CDxs of Therapeutic Group Labeling

	Cobas EGFR Mutation Test v2	ONCO/Reveal Dx Lung & Colon Cancer Assay (O/RDx-LCCA)
CDx Therapeutic Group Label Language	EGFR Tyrosine Kinase Inhibitor (TK1)	EGFR Tyrosine Kinase Inhibitors approved by FDA
Initial Approval	05/14/2013	07/30/2021
Specified Product(s)	• Tagrisso® (osimertinib)	• Erbitux® (cetuximab) • Vectibix® (panitumumab)
Therapeutic Group Label Approval	10/27/2020	Initial approval
Targeted Genes	EGFR	EGFR, KRAS

CONCLUSION

EGFR CDxs are the first to shift towards therapeutic class labeling. Indication, molecular alterations, and mechanism of action of the approved therapeutic class products, number of products approved, as well as CDx analytical and clinical validation influence class label relevance. Discussions with the FDA are encouraged early in development.

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ACKNOWLEDGMENTS

New Jersey Alliance for Clinical and Translational Science Grant UL1TR003017 https://njacts.rbhs.rutgers.edu/