Comparison of the US Package Insert and the EU Summary of Product Characteristics

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Background

Health authorities (HA) utilize different label formats to convey product information. In the United States, the Food and Drug Administration (FDA) uses the United States Package Insert (USPI), while in the European Union, the European Medicines Agency (EMA) uses the Summary of Product Characteristics (SmPC) for product labels. Product labels describe a medicinal product based on its chemical, pharmaceutical, and pharmacologic properties. Each HA determines the type, format, and extent of efficacy and safety data to incorporate into the product label to best convey this information to healthcare professionals (HCPs).

Objective

To evaluate the qualitative differences between the USPI and SmPC to identify insights into how and what type of product information the FDA and EMA communicate to HCPs.

Methods

A standardized data collection tool was used to evaluate a select number of US and EU product information for nine drugs in three therapeutic classes. The drugs were selected due to the availability of Physician's Labeling Rule (PLR) Format USPIs, SmPCs, and the Summary Basis of Approval (SBA) from the FDA and the European Public Assessment Reports (EPAR) from the EMA. The most recent versions of the USPIs and SmPCs posted on the FDA and EMA website were used for the product label comparison, while the SBAs and EPARs were used to provide insight about the health authority reviews for the products.

Drugs selected:

Anti-Platelets: ticagrelor, clopidogrel, prasugrel
Anti-Psychotics: asenapine, paliperidone, aripiprazole
Anti-Depressants: olanzapine, fluoxetine, duloxetine

Data collection focused on seven sections and each section had pre-specified minimum criteria to determine whether a notable difference existed. The authors utilized the criteria listed below to uniformly evaluate each section for all products. If at least one of the two listed criteria differed, then the respective section was considered notably different. For the clinical trials section, two out of the three listed criteria needed to be different for there to be a notable difference for the section.

1. Indication (population, disease state)
2. Dose (dose, dosing regimen)
3. Clinical trials (# of pivotal trials, study design, overall trial data)
4. Primary endpoint (choice of endpoint(s), presentation of pivotal data)
5. Adverse events (severe ADE presentation, frequency of ADE presentation)
6. Black box warning (presentation and criteria for severe warnings)
7. Order of information (length of label, order of sections)

Results

Overall, notable differences 73% (46/63) were identified between the two product label formats. The overall difference was driven primarily by variations in adverse events, black box warning, and order of information. For indication, the most notable difference was in the number of approved indications with a notable difference identified in six of nine drugs (67%). For dose, the most notable difference was in the dosing regimen with a notable difference identified in three of nine (33%) drugs. For clinical trials, the most notable difference was in the number of trials described and the different presentation of overall trial data, with a notable difference identified in five out of nine (56%) drugs.

Figure 1. Health Authority Insights Obtained from SBA and EPAR Analysis

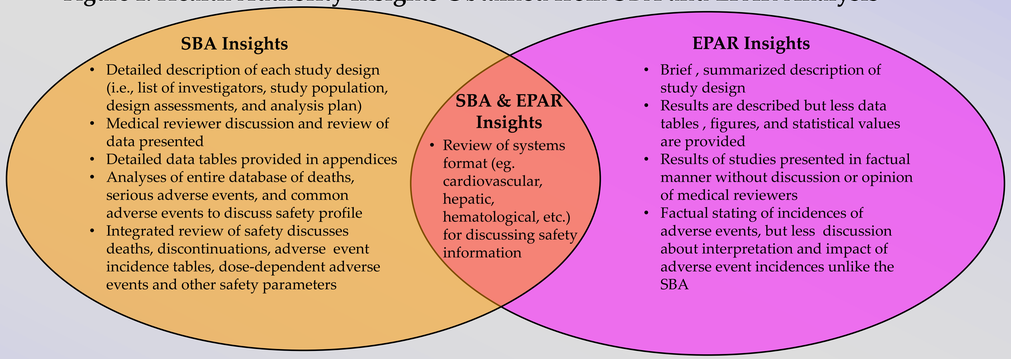
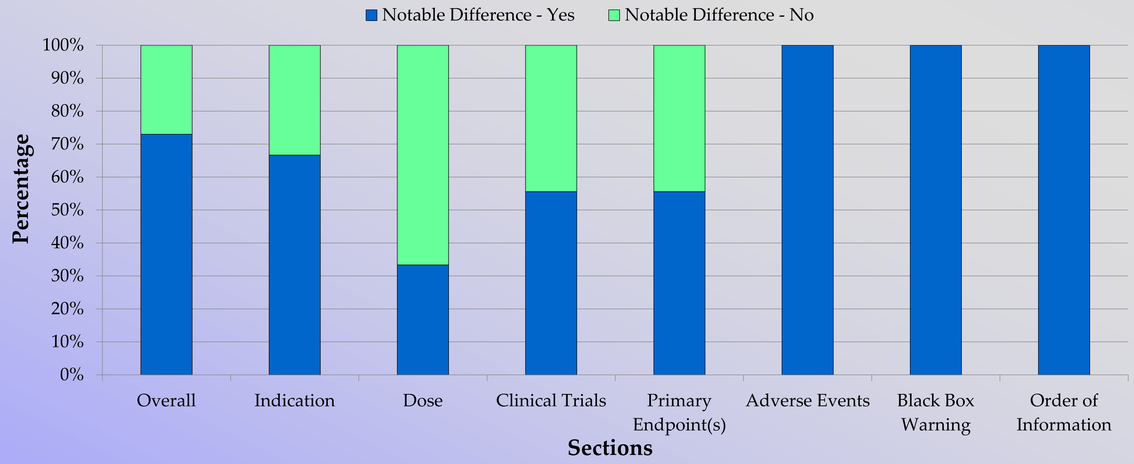


Figure 2. Percentage of Notable Differences Between Selected USPI and SmPC Sections



Results (continued)

The primary endpoints were consistent for pivotal trials; however, the level of detail provided about the pivotal endpoint(s) was notably different for five of nine (56%) drugs. For adverse events, all drugs (100%) were different for this section because the USPI described safety data as incidence (percentage) of patients reporting reaction in trials for approved indications; whereas the SmPC described safety data in order of frequency from very common to very rare. For black box warnings, all drugs (100%) were different because of the different presentation for severe warning(s). While the SmPC contained the same severe warning(s), it did not highlight the information as prominently as the boxed warning in the USPI. For order of information, all drugs (100%) were notably different.

Limitations

Limitations of this study include the small sample size and the use of a standardized, but not validated data collection tool. Therefore, further study with a larger sample size could provide more information about how FDA and EMA choose to present product information labeling to healthcare providers. Another limitation is the challenge to compare the product labels at initial approval for both regions because only the FDA provides a launch label. Thus, we compared the most up to date versions of the USPI and SmPC available.

Conclusions

The clearest areas (100%) where notable differences were identified between the USPI and SmPC were in adverse events, black box warning, and order of information. The USPI placed importance in identifying the incidence of patients experiencing adverse events in trials numerically by percentage, whereas the SmPC presented the information more generally by frequency (very common to very rare).

The PLR format in the USPI also presented order of information differently by providing highlights of prescribing information, unlike the SmPC. The USPI prominently displayed severe warnings as black box warnings, whereas the SmPC made no distinction between severe warnings and other warnings. The notable differences identified in the product labels between the US and EU may influence how HCPs interpret product information in different regions.

Disclosure

Jay Bordoloi – Genentech, Inc.
Roshni Shah – Genentech, Inc.
Sonali Patel – Genentech, Inc.
Julie Kim – Hoffmann-La Roche
Evelyn Hermes-DeSantis – Nothing to disclose

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