Evolving Indications – An Analysis of Indication Fields over time based on German Prescribing Information

Objectives
Approved indication fields for new drugs form the basis of numerous drug pricing processes in Europe, also in Germany. Differences between drugs in overlapping indications over time can cause problems of comparability. The aim of this analysis is the systematic collection of indication fields in German prescribing information over time and the linkage with existing evidence for approval. Questions to be answered include how indication fields develop over time, whether there are specifications or generalizations and if these are adequately covered by approval evidence, i.e. submitted trials?

Methods
The German “Rote Liste” and “Fachinfot” was searched from 19-FEB- to 9-MAR-2018 for current prescribing information. The search was limited to the following diseases: Acute coronary syndrome, chronic obstructive pulmonary disease (COPD), diabetes, epilepsy, multiple sclerosis (MS), hepatitis, human immunodeficiency virus (HIV), melanoma, lung/prostate/breast cancer [1-2]. Indication fields and years of approval were extracted. Indication fields were compared for drugs within one indication. If changes in indication fields were detected, it was checked whether approval evidence supported these developments (taken from European Public Assessment Reports) [3].

Results 1 – Systematic collection of indication fields and common differences
A total of 356 prescribing informations were evaluated. Comparable generalizations of indication fields were present for various diseases. For example generalizations like synonyms and focus in degree of severity. These generalizations were not further analyzed as relevant differences. However, a large number of indication fields showed differences, mainly triggered by varying severity of disease or formulations. In the indication field breast cancer different degrees in severity of disease caused differences, exemplary. The most frequent disease severity was metastatic breast cancer (49,3%), followed by locally advanced breast cancer (18,3%) (Fig. 1).

Results 2 – Linkage with existing evidence for approval
As to approval evidence, especially diabetes mellitus type-2 drugs were approved for indications not completely supported by submitted clinical trials. Since 2007 a stronger focus has been placed on drugs without insulin, mainly dipeptidyl peptidase-4 inhibitor (DPP4) and glucagon-like peptide-1 agonists (GLP1) (Fig. 2). Moreover patient-oriented therapies were aimed at, e.g. for patients with contraindications or intolerances to other antidiabetics (Fig. 3).

Conclusions
Indication fields develop over time and are partially not completely supported by underlying approval evidence. Between-drug-comparability within one indication could also be enhanced. Missing evidence and between-drug-differences pose a challenge for drug pricing processes, not only in Germany.

References

Abbreviations
COPD: Chronic Obstructive Pulmonary Disease; MS: Multiple Sclerosis; HIV: Human Immunodeficiency Virus; DPP4: Dipeptidyl Peptidase-4; GLP1: Glucagon-Like Peptide-1; EMA: European Public Assessment Report

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