OBJECTIVES: To examine the frequency and nature of FDA regulatory actions against pharmaceutical companies for unsubstantiated or misleading economic and quality-of-life (QOL) claims.

METHODS: Review of publicly-available FDA warning letters and notices of violation (n = 566) sent to pharmaceutical companies between January 1997 and November 2001 for inappropriate promotional claims. A standard data collection form was developed to capture the frequency and type of violation and the medium in which violations were found. We classified economic violations into several categories (e.g., “unsupported comparative claim of effectiveness, safety or interchangeability,” “claims of cost-savings when there are obvious additional costs that may affect cost savings,” “implied claims of cost-savings to a broader audience than applicable”). QOL violations for false or misleading claims using the words improved ‘quality of life’ or ‘patient well-being’ were classified into the following categories: “lack of substantial evidence for QOL claims,” “promoting QOL claims in investigational or unapproved drug,” and “selective presentation of QOL information”.

RESULTS: 28 (4.9%) letters cited false and/or misleading economic claims. The most common economic violation was an economic claim containing an “unsupported comparative claim of effectiveness, safety or interchangeability” (n = 14). 28 (4.9%) letters cited QOL violations (4 letters contained both economic and QOL violations). The most common QOL violation was “lack of substantial evidence for QOL claims” (n = 15). Violations were found most frequently in brochures and on websites.

CONCLUSIONS: A body of evidence is emerging that illustrates how the FDA is regulating promotional material containing misleading or unsubstantiated economic and QOL claims. Knowing what constitutes an economic or QOL violation remains unclear, because there are no formal guidelines about what constitutes a violation, nor what level of substantiating evidence is required. More guidance may be needed to ensure appropriate use in drug promotions.

Asthma & Respiratory Disorders/Infections

Relationship Between Different Measures of Asthma Severity: Patient-Perceived, Symptom Derived, and FEV1-Determined Severity Measures

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Objective: In health services research, obtaining objective measures of pulmonary function to classify asthma severity is often not possible. Researchers must rely on methods such as frequency of self-reported symptoms and patient perceived severity. This study examined the relationship between FEV1 determined severity and severity determined by patient-reported information.

Methods: Data from adult patients with asthma were obtained from a pulmonary clinic via chart review and patient self-report during a scheduled physician visit. Patients in acute exacerbation were excluded. Patient-Perceived Severity (PPS) was determined by asking “How severe do you think your asthma is?” with a five-point Likert scale from Very Mild to Very Severe. Overall Symptom-derived Severity (OSS) and Nocturnal Symptom-derived Severity (NSS) were determined from two separate questions regarding symptom frequency during the preceding four weeks. Responses were based on the NHLBI 1997 Asthma Guidelines. Pulmonary function tests were obtained the same day as part of standard care. FEV1-Determined Severity (FEV1-DS) was derived by comparing the FEV1 with the Guideline classification of severity based on spirometry. Three severity categories were derived for each severity method. Percent agreement between FEV1-DS and each patient-reported severity was determined by constructing 3 x 3 tables. Correlations (Spearman’s rho) were conducted between FEV1-DS and the patient-reported severity measures.

Results: 57 patients with a mean FEV1 percent predicted of 80.2% (27.5) were studied. The percent agreement between FEV1-DS and PPS was 59.7% (33.3% over-estimate, 7.0% under-estimate); 56.4% between FEV1-DS and OSS (14.5% over-estimate, 29.1% under-estimate); and 40.7% between FEV1-DS and NSS (25.9% over-estimate, 33.3% under-estimate). The correlations between FEV1-DS and PPS were 0.58 (p < 0.01); 0.53 with OSS (p < 0.01); and 0.13 with NSS (p = 0.13).

Conclusions: PPS and OSS demonstrated reasonable agreement and correlation to FEV1-DS, albeit opposite trends in over- and under-estimates. These two measures of asthma severity appear useful for population based studies when FEV1 is unavailable.

Directly Elicited Preferences Compared to Preferences Derived from the SF-36 in Adult Asthmatics

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OBJECTIVES: Several empiric algorithms have been developed to derive preference estimates from the SF-36. The objective of this study was to compare the validity and responsiveness of SF-36 derived preference estimates to directly elicited preferences in persons with persistent asthma.

METHODS: We used data from a one-year clinical trial of adult asthmatics to derive preferences from the SF-36. Preferences were estimated using five published algorithms for converting SF-36 scores to non-choice based preference estimates. Derived preferences were compared to directly elicited visual analog scale (VAS) values.
RESULTS: The average VAS value at baseline was 0.65 (SD = 0.19), 0.83 (SD = 0.14) at the end of the study and the average change score from baseline to end of study for the VAS was 0.17 (SD = 0.20). The differences between the VAS value and the derived preferences ranged from −0.07 to 0.02 at baseline. Three of the five 95% confidence intervals (CIs) for the difference between derived preferences and VAS values at baseline included zero. At the end of the study the mean of the VAS was higher than the means for all of the derived preference methods. The difference between the averages for the VAS and the derived preferences ranged from 0.01 to 0.11 and only one of the 95% CIs for the difference included zero. The change scores for the VAS preferences were greater than the derived preferences (Differences from 0.07 to 0.13). None of the 95% CIs for the difference in change scores between VAS preferences and derived preferences crosses zero.

CONCLUSIONS: The derivation methods produce valid and responsive measures of patient preference. However, the derived preference values differ from each other and directly elicited preference values. Differences in the distributions of the directly elicited and derived preferences will affect inferences and can lead to differing conclusions in a cost-utility analysis.

MOXIFL oxacin IV/PO MONOTHERAPY IS COST-EFFECTIVE TO THE GERMAN AND FRENCH HEALTHCARE SYSTEMS WHEN COMPARED TO IV/PO AMOXICILLIN/ CLAVULANATE ± CLARITHROMYCIN IN THE TREATMENT OF COMMUNITY-ACQUIRED PNEUMONIA

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OBJECTIVE: To evaluate the cost-effectiveness analysis, from the perspectives of the German and French healthcare systems, of sequential IV/PO moxifloxacin (MXF) monotherapy versus standard comparators in hospitalized patients with community-acquired pneumonia (CAP) requiring parenteral treatment.

METHODS: Costs and consequences over 21 days were evaluated based on clinical cure rates 5–7 days post-treatment and resource use reported for the intention-to-treat population of the TARGET multinational, prospective, randomized, open-label trial. This trial compared sequential IV/PO MXF (400mg OD) to IV/PO amoxicillin/clavulanate (AMC) (1.2g IV/625mg PO TID) ± clarithromycin (CLA) (500mg BID) for 7–14 days in CAP patients. Since the treatment effect on resource use (hospital length of stay [LOS]) was similar across countries, resource data from all 10 countries were pooled and valued using German and French unit prices to estimate the CAP-related cost to the German Sickness Funds and French public healthcare sector.

RESULTS: Compared to AMC ± CLA, treatment with MXF resulted in 5.3% more patients having clinical cure 5–7 days post-therapy (95% CI −0.1%, 12.3%), a statistically significant faster response (return to apyrexia 1 day sooner), and reduction in LOS by 0.81 days within the 21-day period. Treatment with MXF resulted in per patient savings of €266 (Germany) and €381 (France) compared to AMC ± CLA, primarily due to a shorter LOS. Sensitivity analyses found these results to be robust to several costing scenarios. Using bootstrap analysis of the trial data, the probability of MXF being cost saving in both countries was estimated to be 95% or greater, while the probability of MXF being cost-effective was commensurately higher for acceptability thresholds up to €2,000 per additional patient cured.

CONCLUSION: MXF shows clinical benefits and is less costly versus AMC ± CLA in the treatment of CAP. Treatment with MXF is likely to result in cost savings to the German and French public healthcare systems.

PSYCHOMETRIC PROPERTIES OF THE ACUTE BRONCHITIS SYMPTOM SEVERITY SCALE IN AN INTERNATIONAL SAMPLE

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OBJECTIVES: To evaluate the psychometric characteristics of the Acute Bronchitis Symptom Severity (ABSS) Scale, a new 7-item bronchitis-specific instrument designed to measure outcomes in chronic bronchitis (CB) patients.

METHODS: Data were obtained from the screening phase of an international clinical trial comparing the effectiveness of moxifloxacin to a standard oral antibiotic treatment in treating an acute exacerbation of CB. Subjects had a primary diagnosis of CB (having presented with ≥2 episodes of exacerbation in the preceding year, FEV1 < 85% of predicted value, and history of smoking), but were not currently experiencing an acute exacerbation. Patients from 19 countries completed the ABSS (14 languages) for 8 consecutive evenings. Psychometric characteristics evaluated were item performance, internal consistency reliability (Cronbach’s alpha), day-to-day reproducibility (intraclass correlation coefficient (ICC)), construct validity (based on correlation with the St. George’s Respiratory Questionnaire (SGRQ)), and discriminant validity (based on stratification by pulmonary function (FEV1 % predicted)).

RESULTS: 1935 patients were enrolled. Mean age was 63.4 years (± 9.7) and 68% were male. Mean CB duration was 11.7 (± 9.6) years, with a mean of 2.9 (± 1.3)