PHP26

BREAKTHROUGH THERAPY STATUS & EXPEDITED FDA REGULATORY APPROVAL: BUT WHAT ABOUT THE PAYERS?

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OBJECTIVES: The breakthrough therapy pathway provides an expedited Food and Drug Administration (FDA) review where preliminary clinical evidence suggests potentially substantial clinical improvement for a serious, life-threatening condition. This has enabled regulatory approval on data packages as early as 182 days prior to clinical data. Our objective was to investigate the questions of whether such clinical data would be sufficient for US payer coverage. METHODS: On 5th December 2014, publicly available benefit documents were extracted from 3 national (AETNA, Anthem, and United Healthcare (UHC)) and 1 regional (Rocky Mountain) insurance companies for the 14 therapies approved by the FDA under this pathway. The coverage status, prior authorisation criteria, and price were recorded. RESULTS: Our review of the 14 FDA approved therapies revealed that Therapy designation were covered by these insurers (AETNA: 10/14, UHC: 10/14; Anthem: 9/14, Rocky Mountain: 7/14). Most instances of drugs not covered reflected those approved very recently. However, the majority were subject to prior authorisation (AETNA: 10/9, Anthem: 9/9, UHC: 5/10, Rocky Mountain: 7/7). These prior authorizations sometimes included clinical criteria more stringent than those in the FDA label (15/31 similar to FDA label, 9/31 slightly more restrictive, 7/31 much more restrictive). The drugs most frequently subject to much greater restrictions than the FDA label were Sovaldi and Harvoni. The level of restrictions were not seemingly related to the patient cost per treatment which ranged up to $307,000 (Kalydeco) but rather seemed correlated with budget impact (very large with Sovaldi and Harvoni, indeterminate with Hep-cure), hence the need for the HCV drug manufacturers to seek a deal with the payer. CONCLUSIONS: The sustainability of the largely free-pricing of pharmaceuticals has long been questioned against the background of increasing pharmaceutical spend. The recent US payer approval in addition to regulatory approval. Insurers may place additional restrictions through prior authorizations but this relates more to the budget impact of the drugs than the cost per patient or level of supportive clinical evidence.

PHP27

A NECESSARY CONVERGENCE? US PAYERS ADOPTING EU BEHAVIORS?

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OBJECTIVES: The US is the largest prescription drug market in the world, characterised by high drug prices and internationally few price controls. This sustainability of the largely free-pricing of pharmaceuticals has long been questioned against the background of increasing pharmaceutical spend. The recent market entrants of innovative Hepatitis C virus (HCV) therapies with potentially substantial budgetary implications have driven US public and private payers to implement a range of cost-containment mechanisms. This research aims to compare these new changes with European processes and predict how the future price payments (P&R) landscape will develop in the US. METHODS: A systematic analysis of P&R changes and activities in the US December 2013-January 2015 was undertaken, with the outcomes analysed in the context of European P&R processes. RESULTS: The range of novel cost-control mechanisms in the US includes major pharmacy benefits management organisations (CVS and Express Scripts) agreeing exclusivity deals with a particular HCV drug manufacturer, based on the most competitively priced. Further, the California Technology Assessment Forum, which had previously evaluated one drug in its 13 year history, has undertaken already one review of HCV therapies (with another one ongoing) recommending restricting SOVALDI and OLYSIO to the most severe patients based on a cost-utility analysis. Another review at the Department of Health, nearly rejected SOVALDI beyond the FDA-approved label. CONCLUSIONS: Cost-control mechanisms in the US have started to reshape the P&R landscape with European-style price competition, restricting drugs to subpopulations beyond the label, and cost-effectiveness analyses utilized. The key drivers of such changes are to grow such cost-management tools will become further embedded in a wider variety of US payers. With variable usage of distinct cost-containment tools by different payer bodies, the US payer landscape will likely increasingly resemble that of Europe.

PHP28

UNITED STATES DECISION MAKER PERCEPTIONS OF DATA FROM OBSERVATIONAL STUDIES AND OTHER HEALTH ECONOMICS AND OUTCOMES RESEARCH

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OBJECTIVES: To identify United States (US) decision makers perceptions of data from observational studies and other health economics and outcomes research and to evaluate the impact on the success of new health technologies. METHODS: We conducted qualitative one-on-one interviews with payers, clinicians, and, health administrators in the US to determine perceptions of data collected outside of randomized controlled trials in the evaluation of emerging health technologies. RESULTS: Clinical efficacy and safety postmarketing assessments have more of an impact on decision making than other types of data collected outside clinical trials. Compared with other stakeholders, clinicians placed a particularly high value on patient registries, whereas, hospital administrators placed a high value on budget-impact analysis. Annual/semiannual review of drug classes by health plans and hospital formularies are key processes. Available TDA documentation is not always an impetus to buy new technologies. Clinicians, and non-oncology stakeholders in particular, are afraid of running water, the feasibility of constructing a moat around the NICE headquarters should be explored. Alternatively, regulators and HTA bodies should continue to view efficacy claims on the basis of post-hoc sub-group analyses with great scepticism.

PHP30

CHARACTERISTICS OF NURSING ASSOCIATED WITH COMPLETION OF COMPLIANCE MONITORING PROGRAM FOR SUBSTANCE ABUSE

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OBJECTIVES: To identify the predictors of the nurses undergoing a Compliance Monitoring Program (CMP) for substance/drug abuse successfully and accessing the effect of these variables on the successful completion of program. METHODS: This was a retrospective cross-sectional cohort study using the de-identified data from the Florida Intervention Project for Nurses (FNIP). Status of CMP program categorized as ‘completed’ and ‘incomplete’ formed the dependent variable. The independent variables were characteristics of the nurses - demographic (education, marital status), type of treatment employed, years of nursing experience, healthcare institutional setting that employed the nurses, healthcare specialty of nurses, diagnostic and medical variables of mental disorders (DSM-axes), lab results for presence of drugs, presence of substance related disorders (dependency, abuse), family history of biological, non-biological and mental diseases, lab test results during relapse, if aftercare is required at end of program, status of treatment at end of program, type of comprehensive reason for discharge, and hospital management to take hold. As independent variables grow such management tools will become further embedded in a wider variety of US payers. With variable usage of distinct cost-containment tools by different payer bodies, the US payer landscape will likely increasingly resemble that of Europe.

PHP31

FDA BREAKTHROUGH THERAPY STATUS - A SYSTEMATIC ANALYSIS OF ALL THERAPIES APPROVED UNDER THIS NEW EXPEDITED APPROVAL PATHWAY

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OBJECTIVES: Since July 2012, a new therapy may be allocated Breakthrough Therapy Status if it a) treats a serious and life-threatening condition, and b) preliminary evidence suggests substantial clinical improvement over existing therapies based on an early-stage study of such aged evidence. For such therapies, the FDA can accelerate its development and review. This research aimed to systematically analyse all therapies have been approved under this new FDA expedited review pathway. METHODS: All therapeutic areas, non-oncology and oncology, approval dates, marketing status, and date and whether individual treatment conclusions. CONCLUSIONS: The FDA in the US are seeking more comparative effectiveness and economics information to better inform decision making. The impact of comparative effectiveness research and economics on formulary decision making will likely have more impact in the future. If study data are to be considered valuable in supporting health care decision-making, the rigor, transparency, and the customer perspective needs to drive the study methods and designs.

PHP29

EVIDENCE THAT WEREFOLDS AFFECTS THE NICE APPRAISAL PROCESS

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OBJECTIVES: Post-hoc subgroup analyses are still used in clinical trials of medical technologies. Health payer populations in whom greatest benefits can be achieved, despite this being derided as an analytical approach. Indeed, using post-hoc analyses, aspirin has been shown to be ineffective in acute myocardial infarction patients born after the signing of the Declaration of Helsinki (1964, Lancet) and endarterectomy is only efficacious in treating symptomatic stenosis patients born on a Monday, Wednesday, or Friday (ECST group, 1998, Lancet). This research aimed to determine whether National Institute of Health and Care Excellence (NICE) determinations were identified up to October 2014 from which the date and decision was extracted. Full moon dates for Manchester were extracted from www.timeanddate.com. Statistical comparisons were performed using a Chi-squared test. RESULTS: 532 appraisals were identified, 408 (77%) of which were approved (defined as ‘recommended’ or ‘optimised’). However, among the 38 recommenda-
tions issued 1 day of a full moon this recommendation rate significantly rose to 89% (34/38, p<0.05). Significantly fewer appraisals also occurred in the 14-day period bisected by full moons versus the 14-day period bisected by new moons (183 vs. 359, p<0.05). CONCLUSIONS: Based on our post-hoc analysis these results are unduly afraid of werewolves leading them being less productive around the period of the full moon. However, if they are pushed to issue a final recommendation close to a full moon they will more likely issue a positive recommendation. As werewolves are afraid of running water, the feasibility of constructing a moat around the NICE headquarters should be explored. Alternatively, regulators and HTA bodies should continue to view efficacy claims on the basis of post-hoc sub-group analyses with great scepticism.
the level of supportive clinical data (Phase 1: a mean of 158 days, Phase 2: 170 days, Phase 3: 196 days), whether the drug was a first approval line extension (175 vs. 192 days), or whether it was approved under an accelerated FDA pathway or not (172 vs. 184 days). **CONCLUSIONS:** The FDA breakthrough therapy designation is proving a popular means by which promising drugs can gain patient access on preliminary data, which has resulted in a broadening of indication and/or claims, superiority, broadening of indication and/or claims, and economic claims issued. Warning letters were primarily directed to manufacturers of oncology (17.5%), psychiatry (6%), cardiovascular (9.6%), and pain (8%) products. Approximately half (49.5%) of claims contained promotional materials directed to physicians. **CONCLUSIONS:** We found that misleading clinical outcome claims, specifically omission of risk information and inaccurate efficacy, formed the majority of the promotional violations. Compared to the preceding 6 years (2004-2009) substantially more warning letters were possibly indicating greater surveillance by the FDA of pharmaceutical promotional materials 2009-2013.

**PHP3**

**PROFILE OF DEMANDED MEDICINES AND INFLUENCE ON INTELLECTUAL PROPERTY RIGHTS PROTECTION IN MINAS GERAIS, BRAZIL**

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**OBJECTIVES:** This study analyzes the influence of intellectual property rights protection on the profile of drug request by litigation in the Health Department of Minas Gerais state (SES-MG), Brazil, the public spending and its interfaces with the rational use of drugs and the incorporation of new technologies in the Unified Health System (SUS).

**METHODS:** In 2010, SES-MG attended 28,104 prescriptions requirement of legalization, the average being 2.2 medications per patient. The prevalence of polypharmacy was 10.6%. In addition to individual lawsuits, the SES-MG attended 19 civil suits which included 135 medicines. The ten most demanded drugs were protected by patents. Of these, only three were included on the list of essential medicines. For all products there were prescriptions by brand name, an average of 50% of the requests had required supply trade marks, and the society increased a prevalence of jurisdictional injunction and the use of prescription drugs cited as evidence, without medical expertise. Ensuring the constitutional right to health was the speech used in more shares. It was observed that the government is connected with the name of medicines recommended by the World Health Organization (WHO).

**CONCLUSIONS:** The annual expense to ensure access to medicines for litigation is growing and represents a major challenge for the public manager. The high prevalence of new medicines prescribed by trademark and generation of biological drug prescriptions show the need to review and strengthen the policy of generic drugs in Brazil.

**PHP3**

**COMPETITION AND STRATEGIC REGULATION IN THE ARGENTINE PHARMACEUTICAL MARKET: A COMPARATIVE STUDY OF SIX THERAPEUTIC CLASSES**

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**OBJECTIVES:** To analyze how main determinants of competition in six therapeutic target groups - analgesics, tranquilizers, peptic ulcer treatment, cholesterol treatment, anti hypertensive and antidepressants - are affected by regulatory and trade policies implemented at national level during the last decade in the pharmaceutical market in Argentina. **METHODS:** The database corresponds to the annual information on retail sales in the Argentine pharmaceutical sector generated by IMS for the period 2005-2012. The estimation strategy takes the form of econometric models of ordinary least squares with year fixed effects and robust standard errors. We used multiple strategies to pre-identify products with price changes. In addition, purchase and sales data were obtained from a chain pharmacy in Alexandria for all transactions (January - April - June 2012 and 2013) to validate the price changes. Bivariate analysis and a logistic regression model were done to identify determinants of price changes. **RESULTS:** A total of 206 products were subject to price changes: 66% of the products had price increase, 70% were generics, 36% were essential drugs, 40% of the products had prices less than 1EGP/DDD, 30% were between 1 and 5EGP/DDD, 7% were higher than 5EGP/DDD. Half of the products were produced by domestic private companies, 27% by multinational firms, 21% by state-owned companies and 2% were imported. The products of state-owned firms had 23 times the odds of products of multinational firms to have a price increase. Similarly, the cheapest products had 9 times the odds of a price increase compared to high priced products. Compared to brand name drugs, generics had 6.8 times the likelihood of a price increase. **CONCLUSIONS:** Being the product of State-owned, and a product whose price was <= 3EGP/DDD for a generic were the main determinants of price increase. [1] 1 EGP=$0.14 USD

**PHP7**

**A FRAMEWORK FOR STRENGTHENING PHARMACEUTICAL MANUFACTURING IN SUB-SAHARAN AFRICA**

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**OBJECTIVES:** The pharmaceutical industry in Sub-Saharan Africa is changing due to economic growth, an increasing middle class, urbanization, and rising incidence of non-communicable diseases. These factors increase the demand for medicines. Pharmaceutical spending in the region is projected to reach $45 billion by 2016. Despite this rapid growth and gap between availability and demand, companies have yet to initiate local pharmaceutical manufacturing due to the challenges of doing business in the region. To address these challenges and feasibility of overcoming them. **METHODS:** We undertook a series of key stakeholder interviews in Namibia, including distribution, private sector, regulatory, and governmental representatives. Namibia has virtually no drug manufacturing at the time of assessment despite political will to undertake manufacturing. **RESULTS:** In-country pharmaceutical manufacturing is viewed as important for health and economic development and stability. Key areas identified for concern included product selection, education, training, quality control, perceptions of quality, supply chain, role of public and private sectors, and market demand. Creation of a facility at the local university was recommended to build public trust, enhance training, and facilitate distribution. Product areas for initial consideration may include sterile water/saline, alcohol hand rub, oral preparations, topical preparations, total parenteral nutrition, or cancer chemotherapy. **CONCLUSIONS:** In order to create a sustainable health care system, sub-Saharan African pharmaceutical manufacturing will be necessary to provide a consistent supply of medicine. Product selection is key to identify main local demand and be reasonably competitive economically. Viable choices could be niche products or large volume generics. Regulatory and quality concerns will have to be thoroughly addressed to establish a successful system. Technical expertise will have to be increased and maintained. Overall, if concerns are addressed early and thoroughly, local manufacturing can be a popular means by which promising drugs can gain patient access on preliminary data, which has resulted in a broadening of indication and/or claims, superiority, broadening of indication and/or claims, and economic claims issued. Warnings letters were primarily directed to physicians of oncology (17.5%), psychiatry (6%), cardiovascular (9.6%), and pain (8%) products. Approximately half (49.5%) of claims contained promotional materials directed to physicians. **CONCLUSIONS:** We found that misleading clinical outcome claims, specifically omission of risk information and inaccurate efficacy, formed the majority of the promotional violations. Compared to the preceding 6 years (2004-2009) substantially more warning letters were possibly indicating greater surveillance by the FDA of pharmaceutical promotional materials 2009-2013.

**PHP3**

**CHARACTERISTICS OF PRODUCTS WITH PRICE CHANGES AFTER A POLICY CHANGE IN EGYPT**

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**OBJECTIVES:** In Egypt, the Ministry of Health and Population (MOHP) sets pharmaceutical prices from ex-factory to retail. In July 2012, the pricing policy changed from a cost plus to an external reference pricing method which was effective in October 2012. Our goal was to identify the characteristics of products with price changes after the policy implementation. **METHODS:** We used MOHP lists and IMS data to identify products. **RESULTS:** 2015 A1–A307

**PHP3**

**AN ANALYSIS OF WARNING LETTERS ISSUED TO PHARMACEUTICAL COMPANIES REGARDING MISLEADING HEALTH OUTCOMES CLAIMS 2009-2013**

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**OBJECTIVES:** While analyses of FDA warning letters issued to pharmaceutical companies regarding promotional claims provide important insights, this study analyzed warning letters from 1997-2008 (Stewart 2002; Salas 2008; Covington, 2009; Yang 2010, Chatterjee, 2012; Neumann 2012), there are no published analyses to date that specifically identify the forms of promotional claim violations from 2009-2013. **METHODS:** Warning letters for promotional materials issued by the FDA to pharmaceutical manufacturers from 2009-2013 were downloaded and assessed by two investigators for misleading claims broadly classified as clinical, quality of life (QoL), and economic. Clinical claim violations were also classified according to underlying category: unapproved indications, efficacy and safety/tolerability, superiority, broadening of indication and/or omission of risk information. QoL claims categories included unsubstantiated and/or health related (HRQoL). Economic claim categories included competitiveness savings of one drug compared to another. **RESULTS:** In the 5-year study period, 178 letters containing 655 violations for 204 drugs across multiple therapeutic areas were identified by the FDA of all which were clinical. Most often multiple violations for >1 drug were contained in a single letter. On average, ~36 warning letters were issued per year. Omission of risk information was the most frequently violation claim (29.0%) followed by unsubstantiated/overstatement of efficacy claims (24.4% and 11.6%). There were no warning letters, or economic claims issued. Warning letters were primarily directed to manufacturers of oncology (17.5%), psychiatry (6%), cardiovascular (9.6%), and pain (8%) products. Approximately half (49.5%) of claims contained promotional materials directed to physicians. **CONCLUSIONS:** We found that misleading clinical outcome claims, specifically omission of risk information and inaccurate efficacy, formed the majority of the promotional violations. Compared to the preceding 6 years (2004-2009) substantially more warning letters were possibly indicating greater surveillance by the FDA of pharmaceutical promotional materials 2009-2013.