OBJECTIVES: In Poland there is currently no specific pathway for orphan drugs assessment. Nevertheless the planned amendment of the Reimbursement Act is to include more flexible approach to orphan drugs with price justification instead of standard cost per QALY criterion for assessment. The aim of this research is to review current situation of orphan drugs in Poland and to assess if shift in health technology assessment (HTA) approach is desired. **METHODS:** Orphan drugs with EMA approval since beginning of 2012 were identified. HTA reports of Polish HTA Agency (AOTMiT) were searched for each case. Date, decision and decision drivers were extracted from reports. Final Minister of Health (MoH) decisions on reimbursement status were also collected. **RESULTS:** Fifty two orphan drugs were granted EMA approval since 2012. Sixteen of them were submitted for AOTMiT assessment, with 4 still under evaluation. Of the 12 assessed interventions only 2 (Adempas® and Signifor®) were granted positive and 1 (Adcetris®) positive with restrictions recommendations. Final MoH decision was positive for Adcetris®, Adempas® and in addition for Opsumit®, which was negatively assessed by AOTMiT (clinical benefit demonstrated; positive recommendation possible providing price reduction). All 3 drugs were reimbursed under time-limited drug programs (programs specific for expensive drugs). Weak clinical evidence and lack of cost-effectiveness were commonly cited reasons for negative AOTMiT recommendations. **CONCLUSIONS:** Patient access to orphan drugs in Poland is very limited. Only 6% of orphan drugs approved in EU in last 5 years were reimbursed in Poland. Given the high cost of orphan drugs and the difficulties encountered in providing sufficient effectiveness evidence, these products routinely exceed the limits of threshold for cost-effectiveness in Poland. Holding orphan drugs to the same standards for decision-making as "standard" therapeutics causes patient access to be jeopardized. There is a strong need for shift in approach for orphan drugs assessment in Poland.

PHP22

THE SHIFT FROM A COMPASSIONATE DRUG USE TO THE COMMON MARKET–ACCESS PROCESS: AN INFLATIONARY NO MAN'S LAND?

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OBJECTIVES: In cases of rare or severe diseases without alternative therapeutics, the French "Temporary Authorization for Use" (ATU) program allows the use and the reimbursement of drugs before their marketing authorization (MA). It creates a window of free prices in a highly regulated market. After the MA, the patient access is maintained during the market access process (HTA assessment and agreements on reimbursement and price). The objective of this work is to assess the economic impact of this post-ATU transition period (that has been reframed in 2014) and during which drugs begin to spread. **METHODS:** We included all drugs that experienced the post-ATU period from 2014 to April 2016 or that are still going through it thanks to the list established by the French authorities. We assessed the time spent during the post-ATU period and the financial impact for the 37 public hospitals of Paris (AP-HP). We collected explicative variables from different sources (orphan drug, target population, added medical benefit). **RESULTS:** 45 International Nonproprietary Name (INN) are on the post-ATU list. Within the 17 INN that were regularized since 2014, 6 of them were direct-acting HCV antivirals and 6 were orphan drugs. The average post-ATU period was 237 days. Only 6 (35%) remained less than 180 days. Within the 28 INN that still have post-ATU status, 17 (61%) are in market process since more than 180 days. 40/45 INN are referenced in AP-HP and have costed, during their post-ATU period, approximately €600 million since 2014 until today. In 2015, post-ATU drugs represented 12% (€181 million) of the drug budget. **CONCLUSIONS:** Post-ATU drugs represent an important financial impact whereas these drugs are still under a derogation procedure. It seems that the market access procedures last longer than usual, as patient access is maintained, but for a higher financial risk for hospitals.

PHP23

FUNDING EXPENSIVE DRUGS IN HOSPITALS: WHERE IS FRANCE GOING?

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OBJECTIVES: In 2004, a national list of expensive drugs was implemented in France to entirely cover their expenditures in an egalitarian manner all over the territory. Since then, a numerous of regulatory measures have tried to curb these expenditures (1.6 billion of euros in 2005, 2.9 billion in 2014) and to limit the deadweight effects for pharmaceutical companies and hospitals. In March 2016, following a decision of the Court of Justice of the European Union, the process of inscription and radiation of the list has been published by decree. This decree reinforces the possibility of a management by indication and not anymore by product. The objective of this work is to anticipate the economic consequences of these new measures. **METHODS:** We identified all the critical points that could be generated for the different stakeholders: patients, payers (hospitals and the national health insurance), producers. Then, we assessed the financial impact of the application of these new criteria to the current list, for the 37 public hospitals of Paris based on drug consumption in 2015. **RESULTS:** The access to the list is tightened. Expenditures of the potential delisted indications would be more or less covered by the DRG tariffs. Prices are then determined through public tenders and become confidential. They will no longer serve as a reference for external price referencing. Out of the 154 indications of the 46 cancer and immunosuppressive listed drugs (64% of the expenditures), 24 are likely to be delisted for an amount for hospitals of Paris of €25.2 million, essentially concentrated on ipilimumab, bevacizumab and pemetrexed. **CONCLUSIONS:** Controlling drug expenditures in order to maintain a sustainable system could entail the risk of a creation of inequalities within hospitals according to their case-mix. Moreover, it raises technical issues as it is currently impossible to track reimbursement by indication.

PHP24

ASSESING THE AVERAGE PRICE LEVEL OF GENERICS IN GREECE AND OTHER COMPARABLE EUROPEAN COUNTRIES RELATIVE TO THEIR VOLUME MARKET SHARE

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OBJECTIVES: Generic prices in Greece have been drastically reduced since 2009 as a means to generate savings. Scientific literature suggests that generics price levels are lower in countries with mature generic markets compared with countries with lower generic penetration.The purpose of this study was to assess the current price level of generics in Greece relative to their market share and compare it with European counties with a) approximately the same population size and b) similar fiscal ability, as measured by the per capita GDP. **METHODS:** Expenditure and consumption data for several European countries was collected regarding on-patent, off-patent, and generic medicines. The study focused on the retail outpatient market. The comparator countries were chosen based on the information from the EUROSTAT database. **RESULTS:** Among the European countries studied, Greece had the lowest generic penetration (31.1%). In contrast, Greece had the highest volume market share on on-patent medicines (10.6%) and the second highest on off-patent (34.3%). In terms of generic pricing, Greece had the highest average unit price among the comparator countries. **CONCLUSIONS:** There were clear evidence of a negative relationship between average unit price and volume market share, as literature suggests. The current generics price level in Greece was in line with the one expected relative to the volume market share. If rebates and clawback were taken into account, the current price level of generics in Greece would have been below the projected average. Generic penetration in Greece remains at a low level, despite the significant price reductions in the previous years. This suggests that, further price reductions for generics would, most probably, not lead to an increased volume market share. Future policies should focus on demand side measures to alleviate the existing disincentives for generic uptake as a means to allow for increased competition and, ultimately, further price reductions.

PHP25

IMPACT OF US HEALTH EXCHANGES (HIX) ON THE PHARMACEUTICAL INDUSTRY

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OBJECTIVES: This study intends to provide an overview of the new US insurance health exchanges and its impact on the pharmaceutical industry. **METHODS:** A literature review was conducted from the Centers of Medicare and Medicaid Services website, Managed Care Organisation websites, Pubmed, and available grey literature. **RESULTS:** In the US, health insurance marketplaces, also called health exchanges (HIX), are organizations set up to facilitate the provision and purchase of government-regulated and standardized health care plans in each state in accordance to the Patient Protection and Affordable Care Act (ACA). All HIX were certified and operational since January 1, 2014 and has ushered approximately 280 formularies by over 330 insurers, both public and private. Open enrolment for 2016 coverage period ended with about 12.7 million individuals and is projected to grow to 29 million by 2019. Enrolees are not as healthy as expected. Moroever, 91% of current enrolees chose lower cost options bronze and silver plans rather than platinum and gold which have higher cost-sharing for prescription drugs, and more than 8 in 10 individuals qualified for financial assistance. Data reflects a price-sensitive cohort and lower cost medication choices and utilisation. Insurers will continuously track enrolment and utilization patterns and modify breadth and depth of pharmaceutical coverage in their plans. **CONCLUSIONS:** Health exchanges are still in flux but will continue to grow and become a significant component of managed care, pharma's most influential sales channel. It will create opportunities for pharma as it will cover previously uninsured population. However, with the competition and transparency of the framework, and the cost-sensitivity of both the insured and payer, greater cost control, pricing negotiations, rebates, and cost-sharing requirements are expected. Pharma needs to monitor how the health plans evolve and what payers need as the enrolment numbers grow and new drug utilization patterns emerge.

PHP26

WHAT HAPPENS TO ORIGINATOR MEDICINES WHEN (GENERIC) FOLLOWERS ENTER THE PUBLIC MARKET

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OBJECTIVES: Many pharmaceutical companies claim that because of European national pricing regulations, namely the wide-spread policy of external reference pricing some off-patent originator products disappeared from the public market. We investigated likelihood and timelines for occurrence. **METHODS:** Panel data from Euripid database were extracted for seven major substances in national public markets. All strengths, presentations and packs were considered. We defined public market as fully or partly publicly funded reimbursable medicines. Euripid features information on reimbursable medicines (including prices) from 28 European countries. We checked if originators were marketed at different time periods between 2010 and May 2016 and if relevant – when they had been delisted. **RESULTS:** In 2016 the originator brand was not reimbursed Atorvastatin in Poland and Estonia, Clopidogrel in five countries Donezepil in eight countries, Omeprazole in 13 countries, Olanzapine in Estonia, Latvia, Poland and Slovakia, Paroxetine in six countries, Valproic acid in Bulgaria, Iceland and Estonia. Regarding timelines no 1:1 connection could be found between generic entry and the delisting of originator brands. We

found countries (e.g. Estonia or Czech Republic) where originators disappeared when generics entered the market, but there are examples like Clopidogrel in Hungary, where the originator stayed in the national formulary despite a number of generics was listed for further six years. **CONCLUSIONS:** The likelihood of delisting for an originator product after generic market entry is high, but the timelines vary considerably from immediately till never. Some manufacturers (e.g., Pfizer) adapted their dissemination strategy by marketing generic versions of their products in national formularies. Delisting might be stimulated by external pricing referencing but even more by internal referencing. In the case of olanzapine and also atorvastatin almost 2,500 different medicines where marketed in the 28 countries, many of them much cheaper than the originator. The highest likelihood of a not listed originator occurs in Estonia.

PHP27

MARKET EXCLUSIVITY PERIODS AND PATENT CHALLENGES IN PHARMACEUTICALS IN SOUTH KOREA

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OBJECTIVES: According to the Free Trade Agreement between South Korea and the US, patent linkage in pharmaceuticals came into force in March, 2012. The patent linkage is expected to influence the dynamics of pharmaceutical market. This study aims to analyze brand-name and generic drug competition in South Korea. **METHODS:** We gathered and analyzed the information on marketing approval of pharmaceutical products and patent rights of drugs on the Green List (drug-patent list). Among 1,088 drugs on the Green List, 130 brand-name drugs which have had their generic drugs approved and 160 patents which have been challenged by their generics were included in this study. Market exclusivity period was defined as the period between market approval of a brand-name drug and market approval of its first generic. The period between patent application of a brand-name drug and the first patent challenge was calculated. The factors that affect market exclusivity periods and the period up to the first patent challenge were also identified using multiple regression models. **RESULTS:** The average market exclusivity period was 7.2 years and showed a declining trend. The market exclusivity period tended to decrease if the brand-name drug of interest is for diabetes and when the number of its generic is large while it tended to increase if the drug of interest is a new one. Meanwhile, patent challenge has increased drastically in recent years. The average period up to the first patent challenge was 11.4 years. It tended to increase if the patent includes substance patent while it decreased in the case of biopharmaceutical products. **CONCLUSIONS:** As a result from brand-name and generic drug competition, market exclusivity periods were shortened and the patent challenge became more frequent in South Korea. Further studies are warranted to analyze the effect of implementing patent linkage in a full scale.

PHP28

IMPLICATION OF EXTERNAL PRICE REFERENCING ON PHARMACEUTICAL LIST PRICES IN EUROPE

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OBJECTIVES: Policy-makers introduce pharmaceutical cost-containment measures, such as external price referencing (EPR), due to limited healthcare budgets and high cost of innovative medicines. However, EPR may result in price convergence and delayed market access in lower income countries. The objective of this study was to determine the effect of EPR on ex-factory prices of selected pharmaceuticals. **METHODS:** We applied a survey to collect prices for 22 pharmaceuticals and 17 non-pharmaceutical services in 7 European countries. Averages of maximum and minimum prices for all pharmaceuticals and services were considered to calculate price corridors. The Hungarian Health Insurance Fund Administration provided pharmaceutical price-data on the statistical level for an additional 8 European countries based on the EURIPID database. Univariate and multivariate linear regression analyses were applied to evaluate the effect of variables potentially influencing pharmaceutical list prices (4 variables describing use of EPR, GDP-per capita and population size) in 15 countries. **RESULTS:** The price corridor was narrower for pharmaceuticals (79%-143%) compared to non-pharmaceutical services (28%-252%). According to the univariate analysis GDP-per capita, population size and number of other countries referencing an individual country significantly increase published ex-factory prices whilst mandating the lowest price among the basket of referenced countries reduces the price. Number of referenced countries and frequency of price-revision did not influence list prices significantly. In the multivariate analysis only 2 variables remained significant, resulting in 1,1% price increase per an additional €1000 GDP-per capita and 0,3% price increase per 1 million population. **CONCLUSIONS:** Although EPR does not significantly affect pharmaceutical list prices, price corridor for innovative pharmaceuticals is narrower in comparison to price corridor of non-pharmaceutical technologies. There is a modest list price variation according to GDP-per capita and population size, however, European drug prices still do not reflect the wealth of a country sufficiently.

PHP29

INNOVATION : A VALUE FOR HEALTH AND GROWTH, AN INTERNATIONAL STUDY ON MARKET ACCESS STAKES FOR THERAPEUTIC INNOVATION

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Access to therapeutic innovation is a major issue, in terms of delay, equality and financing, addressed differently by each country. A study has been performed in order to investigate how the French regulatory framework benefit from the processes in place in other developed countries.**OBJECTIVES:** Identify measures which can be organized at national level in France to favor the emergence and the access to therapeutic innovation. This study should highlight interesting mechanisms and evaluate their possible transposition in France. **METHODS:** 6 countries have been selected (Germany, Sweden, UK, Australia, the USA and Denmark), based on the following criteria: visibility in the field of pharmaceutical innovation, Healthcare system and culture close to France, originality of the health system mechanisms, attractiveness for companies. For each country, the analysis was based on available documents, reports and publications (2012-2015). **RESULTS:** Numerous countries recognize the strategic position of life sciences and the pharmaceutical sector, in particular with regard to capacities and potential of innovation, positive effects of which are medical as much as economic.Regarding accessibility: Access to the immediate market further to the MA approval (Germany, UK), For Orphan drug: flexibility of the assessment allowing an access more rapid (Sweden, Germany). Regarding financing: Specific financing (UK, Australia), follow real life evidence for a better use and set-up agreements (UK). Regarding attractiveness: politic consideration / dialogue possibility (UK), Collaborations between Researchers/pharmaceutical companies/university/public health authorities (Sweden, Denmark, UK) **CONCLUSIONS:** Among the concrete and potentially interesting initiatives to resume other countries for France: Reduce the deadlines of access and set up a fast-track: possibility of reducing significantly the deadlines after MA approval (Denmark), even of deleting them (Germany and UK) and develop follow-up of real life evidence (following the example of Denmark, Sweden and UK).

PHP30

BIOSIMILAR INFLIXIMAB: FEEDBACK AFTER A NINE MONTHS EXPERIENCE OF THEIR USE IN THE 37 PUBLIC HOSPITALS OF PARIS

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OBJECTIVES: In 2015, the Committee on Medicinal Products of the 37 Publics Hospitals of Paris (AP-HP) authorized the tender between two infliximab biosimilars (BIOSIM-INFLIX) and their originator (ORIGIN-INFLIX) only for naïve-patients, as the current French law does not allow the switch from originator biologics to biosimilars for pretreated-patients. A BIOSIM-INFLIX won the tender and two infliximab have been listed in the hospital drug formulary (HDF) of AP-HP since September 2015: BIOSIM-INFLIX for naive-patients and ORIGIN-INFLIX for pretreated-patients. This study analyzes the spread of BIOSIM-INFLIX and of ORIGIN-INFLIX in AP-HP. **METHODS:** Infliximab consumption and expenses data from AP-HP were analyzed over the January 2015 to May 2016 period to retrospectively assessed BIOSIM-INFLIX and ORIGIN-INFLIX market shares within all AP-HP hospitals. **RESULTS:** Infliximab expenses in AP-HP in the January-May 2016 period was down 7% compared to the January-May 2015 period (€15.2 vs. €16.3 million respectively), while infliximab consumption in volume globally increased by 12.3% between the two periods. The rise in infliximab consumption was offset by a negative price effect due to the competition of BIOSIM-INFLIX (-45% and -12.1% price discounts for BIOSIM-INFLIX and for ORIGIN-INFLIX respectively). In May 2016, infliximab products were used in 19 AP-HP hospitals and the BIOSIM-INFLIX uptakes in volume reached 29.9% (vs. 3.7% in France in 2015). However, BIOSIM-INFLIX uptakes are heterogeneous among AP-HP hospitals: >80% for 2 hospitals, between 60% and 30% for 5 hospitals, <20% for 12 hospitals. Two hospitals initially decide to only list the BIOSIM-INFLIX in their local HDF but recently returned back to meet patients' expectations. **CONCLUSIONS:** Pending the development of a new law governing the substitution for treatment-naïve or pretreated patients receiving biologics in France, today the BIOSIM-INFLIX uptakes are depending on hospital decision-makers. The therapeutic indications in which BIOSIM-INFLIX and ORIGIN-INFLIX are used and the naive/pretreated status of patients have now to be explored.

PHP31

PRICE AND UTILIZATION OF NEW DRUGS UNDER A SINGLE PUBLIC PAYER SYSTEM: EVIDENCE FROM TAIWAN

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OBJECTIVES: This study provides empirical evidence regarding the price dynamics and market penetration of new drugs in a single public payer health care system that regulates prices of prescription drugs. **METHODS:** The main data source was the 3 million sampling cohort claims data compiled by the National Health Insurance Research Database (NHIRD) from 1997-2012 in Taiwan. We defined new drugs as those added to the National Health Insurance formulary after 1996, and traced the price and utilization of drugs with new molecules, formulations, combinations, and indications launched in Taiwan's NHI drug formulary during 1997-2006 for up to 6 years. **RESULTS:** Our results indicate that therapeutic innovation is positively associated with the price ratios of current price (CPI-deflated) versus the launch prices. The increase in therapeutic competition at the 4th level ATC market slightly decreases the price ratio. With respect to market shares, because of the fairly low launch prices, there is no price effect. The market penetration of new drugs does not depend on whether the product contains a new molecule. Biologics have a disadvantageous position to compete with other new drugs. The therapeutic competition at the 4th level ATC market leads to substitution among drugs with similar therapeutic value. The elasticity of market share of large-scale providers with respect to market share of new drugs was around 3.00, and that for the market share of private providers was around 0.84. **CONCLUSIONS:** This study suggests that the penetration of new drugs largely depends on the concentration of large-scale providers in a single public payer system that regulates prescription drug prices. Whether new drugs are adopted by large-scale medical providers is critical in determining access to new drugs. The government agency may need to