their relative importance weights (%) were: robustness of clinical evidence (31%), robustness of CEA analysis (25%), availability of alternative treatments (8%), incremental efficacy (8%), relative safety (7%), ease of adoption (7%), incremental impact on QOL (5%), budget impact (4%), unmet need (3%), size of population (1%). The attribute levels and relative value for a positive reimbursement recommendation (0-1) for the most important attribute, robustness of clinical evidence, were: ‘endpoint very relevant’ (60%), ‘endpoint relevant’ (30%), ‘not relevant’ (10%). For later clinical endpoints, indirect comparisons needed’ (0.25); ‘all clinical endpoints and comparators relevant for NHS’ (1). The estimates of the probability of a favorable reimbursement recommendation for the hypothetical products included in the post-workshop questionnaire were developed in countries with established reimbursement processes using health technology assessment (HTA). The objective of this study is to determine the criteria used in decision-making to determine value in OECD countries’ decision-making processes using health economic analysis (HEA). METHODS: A review of reimbursement criteria and qualitative criteria, relevant literature and contact with individual agencies identified the criteria used to determine value for medicines in processes using HEA. Countries are categorised by how HEA is used in decision-making processes, nature of the cost-effectiveness threshold range (explicit, implicit, no threshold), threshold range where identified and the use of such evidence alongside other decision-making criteria (burden of disease, severity, innovation, and others). Details of the judgments reported with respect to the criteria in documents justifying the decision are examined. RESULTS: Twenty-four OECD countries’ formal HTA of which 17 require HEA in submissions for certain medicines. Cost-effectiveness thresholds are identified in nine countries, explicitly stated in three. Implicit threshold ranges are identified in four (based on past decisions), whilst in two implicit willingness-to-pay thresholds are used for decision-making. Use of clinical evidence is more noticeably compared by other criteria (severity, need, burden of disease, end of life, innovation, amongst others). Some countries use cost-effectiveness thresholds central to their decision-making, some report them equally amongst other criteria, whilst in others it is unclear how such criteria is judged. CONCLUSIONS: Multiple criteria are common in countries using HEA, although some are country specific. Reporting of these criteria and their respective use and interpretation alongside the cost-effectiveness threshold range suggests variation in the meaning of value. Multi-criteria decision analysis could provide clarity in the justification of the reimbursement decision and the meaning of value.

PHP120
NEW PRICING DYNAMICS IN BIG FIVE EU: CASE STUDY OF BIOSIMILAR GM-CSF PRODUCTS
Appraisal 8
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OBJECTIVES: During 2011-2012 significant price cuts were implemented in various markets in the European Union. These price cuts have introduced new pricing dynamics affecting reference pricing and intra-EU parallel export of expensive drugs. METHODS: To understand new pricing dynamics in the big five EU (UK, France, Germany, Italy and Spain) we analyzed the trend in pricing for branded and biosimilar GM-CSF products. Price cuts were analyzed for percentage discount compared to branded GM-CSF product and relative price levels in five selected markets. Recent reimbursement policy changes, and price cuts were also analyzed. RESULTS: The 2012 prices for GM-CSF products show significant variation across UK, France, Germany, Italy and Spain. The prices for GM-CSF products were dramatically lower in Spain and UK compared to France, Germany and Italy. For example, the branded GM-CSF product prices in Spain were 80% lower than prices in the UK. Similarly, the prices for biosimilar GM-CSF products were 72% lower in Spain than in the UK. The percentage price discount for biosimilar products versus branded product also shows large variation in big five EU markets. For example, Spain and UK prices were almost at parity while the prices in France, Germany and Italy were 12%, 31% and 46% discount, respectively. CONCLUSIONS: Recent pricing reforms have significantly changed the pricing dynamics across big five EU markets. Case study of GM-CSF products illustrates wide variation in pricing for branded and biosimilar products.

PHP121
DRUGS REIMBURSEMENT MAINTENANCE: A FRENCH CHALLENGE IN 2011
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OBJECTIVES: In France, reimbursement of drugs is based on the therapeutic value of drugs (SMR level for each indication) as assessed by HAS, going from the “insufficient” to “weak” (15% reimbursement), “moderate” (30%) and “important” (65%). HAS and manufacturer have the right to ask for re-assessment anytime after the initial reimbursement listing; in all cases, a relisting process is compulsory every 5 years. We analyzed HAS reimbursement and relisting activities over the year 2011, going from the hypothesis that the Mentor safety “affair” would have impacted the process. METHODS: We considered all complete procedures for relisting, re-assessments and class reviews and focused on drugs for which a HAS advice was published between Jan and Dec 2011. We compared previous outcomes of the relisting process, corresponding to 33 different indications, out of which 31 cases were analyzed. HAS modified 14 SMRs while 17 SMRs remained unchanged. Almost 50% (6/13) of SMR initially rated as “important” were changed to “moderate” or “insufficient” (2). All initially insufficient SMR (8) were confirmed. 19 drugs have gone through re-assessment process, corresponding to 24 SMRs’ indication, out of which only 21 were analyzable: 10 SMRs have been modified (only 2 increased and the rest lowered) and 11 unchanged. In 8 of these cases, the manufacturer was asked for the re-assessment. 6 full therapeutic classes have been reviewed in 2011, including Alzheimer’s and antipsychotics, resulting in a harmonization and a decrease of the SMR levels.

PHP122
THE USE OF QUANTITATIVE AND QUALITATIVE CRITERIA FOR MAKING DRUG FUNDING DECISIONS
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OBJECTIVES: Every day health care decision makers on the national, regional and local level face the challenge of making complex funding decisions. The complexity in drug funding decisions comes from balancing quantitative criteria such as clinical effectiveness thresholds central to their decision-making, some report them amongst other criteria, whilst in others it is unclear how such criteria is judged. CONCLUSIONS: Some countries use cost-effectiveness thresholds central to their decision-making, some report them equally amongst other criteria, whilst in others it is unclear how such criteria is judged. Further research work is necessary to extend knowledge about the impact of qualitative criteria in drug funding decision-making.

PHP123
IMPORTANCE OF HEALTH-RELATED QUALITY OF LIFE AS AN ENDPOINT IN BENEFIT ASSESSMENT ACCORDING TO THE GERMAN AMNOG
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OBJECTIVES: Health-related quality of life (HRQol) might be one important patient reported endpoint (PRO) in determining the additional benefit of pharmaceuticals recently evaluated according to the newly established German law for reforming the market for pharmaceuticals (AMNOG). A comparative analysis is performed to gain insight how HRQol was implemented in the benefit dossier by the pharmaceutical manufacturer on the one hand and how it was assessed in the benefit assessment by the Institute for Quality and Efficiency in Health Care (IQWiG) on the other hand. METHODS: We reviewed 23 published benefit dossiers and the corresponding benefit assessments, which the IQWiG performed since the implementation of the AMNOG in 2011. Corresponding statements concerning HRQol in benefit dossiers and benefit assessment were faced narrative. RESULTS: Eighteen benefit dossiers included HRQol and a number of validated instruments were used, which were generally accepted by the IQWiG if not for major mistakes in the benefit dossier (for example the use of another appropriate comparator). Overall, the pharmaceutical manufacturers have difficulties to clearly prove an additional benefit due to HRQol because the used studies do not contain data on this endpoint or the results are statistical non-significant. The IQWiG draws a similar conclusion as the pharmaceutical manufacturers and attests none of the benefit dossiers an additional benefit due to HRQol. A common methodological problem reported in the benefit assessments is for example a low response rate so that the data has high bias potential. CONCLUSIONS: None of the published benefit assessments state an additional benefit in HRQol although this is an important PRO and the pharmaceutical manufacturers presented a range of accepted validated instruments to assess it. Further research work is necessary to extend knowledge about the impact of qualitative criteria in drug funding decision-making.

PHP124
COMPARISON OF HTA DOSSIER REQUIREMENTS ACROSS EUROPE
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OBJECTIVES: Submitting an HRA dossier a cardinal step in gaining market access for new drugs. While the decision-making process is often regarded as relatively transparent, the dossier characteristics, the decision-making process, and the outcome of decisions vary across countries, and there are opportunities for improving the process.

METHODS: In this study market access trajectories of the three main TNF α-blockers, and several smaller trajectories of pharmaceutical and medical devices companies have been analysed. Governmental and company documents and value dossier were studied and used in the analysis. Companies were included with decisions held by the Dutch Health Insurance Board, physicians, patient organizations, and responsible persons from the companies. Because the financial reimbursement scheme in the Netherlands has been changed by January 1st2012, the results are reanalysed and latest results are added. RESULTS: Within the Dutch health care system, based on a neo-corporatist structure, many parties are involved in decision making processes. Pharmaceutical, scientific associations of physicians, and well-developed patient organizations are being invited to consultations with policy makers and the Ministry. Our analysis shows that in depth knowledge of Dutch financing scheme needs to be accompanied with mutual trust and converging goals of the several parties. Those goals can easiest be converged on patients’ level.

CONCLUSIONS: Although Dutch policy makers are emphasising HE&OR for accessing the insurance package, our study shows that important arguments for successful market access are institutional trust and converging goals of the several parties and, from January 1, 2012, in-depth knowledge of the Dutch dedicated DRG-system.

PHP127 REIMBURSEMENT OF ORPHAN DRUGS: WHAT IS THE DIFFERENCE?

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OBJECTIVES: Orphan drugs are subject to regulatory and reimbursement regulations that differ with respect to application process and necessary documentation. An orphan drug status granted by the European Commission gives marketing extension of up to 10 years in the EU for 10 years after approval. Reimbursement hurdles are also supposedly lower for orphan drugs in Europe than usually.

METHODS: Definition and assessment process of orphan drugs for reimbursement were reviewed and analyzed. Differences to other drugs are outlined and reimbursement decisions are reported. Results are compared with the orphan drug dossier submitted in 2011 requiring that with market access newly approved products demonstrate their innovation through a reimbursement dossier to avoid reference group pricing. For orphan drugs, manufacturers must also submit a dossier but the additional medical benefit needs to be demonstrated by the market authorization itself. Thus proof of additional benefit does not need to be demonstrated but information on relevant patient groups and on the extent of this additional benefit. However, if annual sales of an orphan drug within the statutory health insurance exceed 50 million EUR, a full assessment is made. For pirfenidone, the first approved orphan drug assessed under the new orphan drug regulation (Institutional and Efficiency in Health Care) declined an additional therapeutic benefit due to the orphan drug status. In Italy pirfenidone was grouped into the lowest reimbursement class.

CONCLUSIONS: Although orphan drugs are often regarded as unquestioned reimbursable, differences in respective processes and assessments exist. Manufacturers are requested to build Market Access strategies carefully and expect challenges in orphan drug indications as well.

PHP128 AMNOG IN YEAR 2: INSIGHTS FROM EARLY BENEFIT ASSESSMENT IN GERMANY

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OBJECTIVES: In 2011, Germany’s new health care reform (AMNOG) came into effect requiring that with market access newly approved products demonstrate their innovation to avoid reference group pricing. The manufacturer has to submit a dossier proving additional benefit versus the appropriate comparator recommended by the G-BA (Joint Federal Committee). On request of the G-BA, IQWiG (Institute for Quality and Efficiency in Health Care) reviews the dossier and performs the benefit assessment. Manufacturers, associations and experts can submit comments and attend a hearing; thereafter the G-BA publishes its final resolution.

METHODS: Assessments and G-BA decisions to date were reviewed and analyzed by case. Differences between IQWiG and G-BA evaluations are outlined and consequences depicted. RESULTS: Up to now 32 dossiers have been submitted, 19 completed the whole process and further 8 will be finally assessed shortly. About half of the products additional therapeutic benefit was granted allowing price negotiations with the statutory health insurance. Not in all cases did the dossier prove for IQWiG’s conclusion and, for Erlotinib and Pirfenidone (an Orphan drug) the selection of the appropriate comparator treatment was the most controversial issue between G-BA and pharmaceutical companies, followed by questions about evidence for and interpretation of benefit. Thus for Linagliptin no additional benefit against the appropriate comparator was proven and the manufacturer challenges the process. Other critical methodology issues included the definition of patient-relevant endpoints, use of surrogate endpoints, determination of target patient populations and use of subpopulations.

CONCLUSIONS: Although in its second year, AMNOG is still a learning process for all parties involved. Before initiating a dossier it is crucial to investigate possible pitfalls around dossier development. New questions will emerge when it comes to the assessment of drugs already on the market as it is now planned for DPP-4 inhibitors.

PHP130 ECONOMICS WITHOUT GUIDANCE: THE CASE OF EPIDEMIOLOGICAL DATA BEYOND CLINICAL TRIALS

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OBJECTIVES: Exploring the use of population-level epidemiological data (i) within the reimbursement decision making process, (ii) identifying recommendations and requirements on that data, and (iii) investigating the role of that data for reimbursement decisions as stated in pharmacoeconomic guidelines.

METHODS: We piloted a comparative review of all national pharmacoeconomic guidelines published in English (N=26 out of 33) available through the ISPOR Website (http://www.ispor.org/EFGuidelines/index.asp). RESULTS: The use of population-level epidemiological data was addressed by 20 guidelines.16 mentioned the use for economic evaluations, 4 (additionally) for budget impact analyses, and 4 (also) for broader technology assessments. 14 guidelines provided explicit recommenda-