Rejection was more common for manufacturer’s comments on outcomes (6/8, 75%) and companion diagnostics (8/13, 61.5%). Rate of final recommendation by NICE was higher for those MS where all (29/40, 74%) or certain changes (14/20, 70%) were requested by the manufacturer were implemented in the final scope than for those where NICE rejected all manufacturer requests (7/11; 64%), and similar to overall recommendation and corresponding ECHOES: The data indicates that the NICE process, although frequent does not meet manufacturer’s expectations. However, manufacturer’s suggestions are often incorporated in the final scope. NICE not implementing manufacturer’s suggestions to the final scope does not decrease the likelihood of being funded.

PHP159
AN EXAMINATION OF THE REGULATORY AND REIMBURSEMENT PROCESSES FOR BIOBETTERS AND COMPARISON WITH BIOSIMILARS
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OBJECTIVES: Biosimilars and biobetters are subsequent versions of licensed innova-
tor biotechnologies. Whereas biosimilars are comparable to the originator product in terms of quality, safety and efficacy, biobetters incorporate intentional modifi-
cations to the original molecule profile with the aim of producing a superior product. This distinction between biosimilars and biobetters has important impli-
cations from a regulatory perspective, with biosimilars following class-specific guidance whereas biobetters are considered innovator drugs. This study sought to examine and compare the regulatory and reimbursement approaches to the appraisal of biobetters and biosimilars. METHODS: Biobetters and biosimilars of the same product class were identified, and qualitative analyses of the recommen-
dation and reimbursement decision processes were conducted. Decision drivers, and the criteria taken using available regulatory and HTA reimbursement decision documentation from six European countries. RESULTS: Findings for filgrastim are presented as an example; 7 biobetters, and the pegylated filgrastims (pegfilgrastim and lipi-
glifilgrastim) considered biobetters, were identified. Biosimilar filgrastims were granted European marketing authorisation based on demonstration of clinical comparability to filgrastim in one indication and extrapolation of their use to scope to all 5 approved indications. Pegfilgrastim demonstrated clinical non-inferiority to filgrastim in one indication and was approved solely for this indication; the subsequently developed lipiglifilgrastim was approved for the same indication but used pegylated filgrastim as a reference product. Pegfilgrastim, against similar to biosimilar filgrastims, economic evidence in the form of cost-minimisation analyses was considered in HTA recom-
medations of both pegylated filgrastims. This differs from the approach for certain other biobetters that have demonstrated clinical superiority and cost-effectiveness versus their originator. CONCLUSIONS: Biosimilars and biobetters are subject to distinct regulatory processes and the decision driving factors for reimbursement also differ among currently licensed biosimilars. With the development of these products, regulatory approval will happen more swiftly. Further research is needed to identify the appraisal processes evolve to address the scope and variety of emerging biobetters.

PHP160
TIME LIMITS RESTRICTION IN GERMANY
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OBJECTIVES: In Germany, with the introduction of the Pharmaceutical Market Restructuring Act (AMNOG) in January 1st 2011, pricing and reimbursement deci-
sions for biologics have been driven by the only benefit assessment (EBA). G-BA
can decide to set or not a time limitation to the decision. The objectives of this study were, first, to review the number of time-limited decisions over time and second, to identify drivers of these decisions. Short-term limitations (≤2 years) were in the use of published literature, health technology assessment reports, clinical trials data, and third-party websites to identify the critical path and data most valuable to the reimbursement decision. To evaluate the impact of time-limited decisions, we compared the outcomes of the first reimbursement decision to those where NICE rejected all manufacturer requests (7/11; 64%), and similar to overall recommenda-
tions by indication, evidence considered, and key decision drivers were under-
stood. Conclusions: Biosimilar filgrastims were granted

PHP161
REIMBURSEMENT TRENDS AND EVIDENCE REQUIREMENTS FOR ULTRA-ORPHAN PRODUCTS ACROSS EUROPE: OPTIMISING MARKET ACCESS IN INCREASINGLY CHALLENGING MARKETS
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OBJECTIVES: Ultra-orphan diseases are extremely rare conditions many of which are severe, chronic, and progressive with high mortality rates. There is a growing number of therapies for ultra-rare diseases currently on the market. Reimbursement decisions for these therapies have been characterized by reduced evidence require-
ments with unmet need weighing heavily into health technology assessment (HTA) and access decisions as well as a general paucity of evidence. To gain insight into evolving market access requirements, we conducted a review of pan-European ultra-orphan therapy HTA requirements and reimbursement deci-
sions. METHODS: Applying the National Institute for Health and Care Excellence (NICE) criteria for ultra-orphan medicines, we identified all HTA reports on ultra-orphan therapies published through May 2014 were identified and reviewed to compare evidence requirements and reimbursement decisions across countries for health-economic, clinical, and value based criteria. RESULTS: Over sixty published ultra-orphan HTAs were identified across nine markets. A small portion of these submissions were rejected for reimbursement largely due to lack of evidence on clinical benefit. For therapies recommended with access restrictions, payers often requested additional follow-on studies or ongoing moni-
toring of outcomes, whereas biobetters generally required evidence in the form of cost-minimisation analyses was considered in HTA recom-
medations of both pegylated filgrastims. This differs from the approach for certain other biobetters that have demonstrated clinical superiority and cost-effectiveness versus their originator. CONCLUSIONS: Biosimilars and biobetters are subject to distinct regulatory processes and the decision driving factors for reimbursement also differ among currently licensed biosimilars. With the development of these products, regulatory approval will happen more swiftly. Further research is needed to identify the appraisal processes evolve to address the scope and variety of emerging biobetters. Review of published literature, health technology assessment reports, clinical trials data, and third-party websites to identify the critical path and data most valuable to the reimbursement decision. To evaluate the impact of time-limited decisions, we compared the outcomes of the first reimbursement decision to those where NICE rejected all manufacturer requests (7/11; 64%), and similar to overall recommenda-
tions by indication, evidence considered, and key decision drivers were under-
stood. Conclusions: Biosimilar filgrastims were granted

PHP162
GLOBAL HTA ASSESSMENTS OF ULTRA-ORPHAN PRODUCTS: A CASE STUDY OF ECULIZUMAB (SOLIRIS) AND IDURONATE-2-SULFATASE (ELAPRASE)
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OBJECTIVES: To describe a very small patient population, defined by the National Institute for Health and Care Excellence (NICE) as those diseases with a prevalence of ≤ 50,000. Medicines for these indications are difficult to develop in part due to challenges associated with recruiting for clinical trials from the very small patient population. Within this context, we have assessed these therapies with modified evidence requirements and opportunity for very high prices. We performed a health technology assessment (HTA) review of two ultra-orphan products – eculizumab/Soliris and iduronate-2-sulfatase/Elaprase – to gain insight into the evolving HTA evidence requirements for ultra-
orphan medicines and comparatively evaluate key decision drivers across geogra-
phies. METHODS: We scanned global HTAs published before end of May 2014 to identify all HTAs of ultra-orphan therapies that have variable reimbursement decision outcomes (eculizumab/Soliris and IDS/Elaprase). To evaluate pivotal decision drivers, we analyzed HTAs across several criteria, including clinical efficacy, unmet need, strength of evidence, cost-effectiveness and burden of illness. RESULTS: We identified HTAs in seven countries. For both products, reimbursement decisions varied across agencies. Key decision drivers included cost-effectiveness, clinical efficacy, risk-sharing schemes, and lowered evidence requirements for ultra-orphan medicines. Assessments rejecting

PHP163
EVIDENCE-BASED MARKET ACCESS VALUE RESOURCE: NAVIGATING THE HURDLES FOR A BIOLOGIC OBTAINING A LICENSE IN A SECOND INDICATION IN KEY EUROPEAN COUNTRIES
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OBJECTIVE: Market access for an innovative technology, such as a biologic obtaining a license in a second indication, can be complex and time consuming. Reimbursement is critical to rapid adoption of and optimal patient access to a new technology. This study aimed to determine the best approach for communicating value and providing field-based staff with value resources to facilitate dialogue with stakeholders in various scenarios. METHODS: We conducted desktop research of published literature, health technology assessment reports, clinical trials data, and manufacturer websites and critical path analysis to develop a guide to reimbursement decision making in order to prepare a communication resource. We conducted a country-affiliate workshop and qualitative one-on-one interviews with external opinion leaders in key markets to understand access as well as the most appropriate means of communicating value to external decision mak-
ers. RESULTS: The process and restrictions for biologics may be stricter than for other medications because of perceived high cost. There are multiple appropriate access strategies for various patient care needs, all with similar access and value drivers. It is critical to understand the needs of external decision makers and provide field-based staff with a consistent yet customizable means of communicating the value of new technologies. All evidence and insights were synthe-
ized into an evidence-based market access value resource for key stakeholders.