THE COST-EFFECTIVENESS OF ELTROMBOPAG FOR THE TREATMENT OF CHRONIC ADULT IMMUNE THROMBOCYTOPENIC PURPURA (ITP) IN IRELAND

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OBJECTIVES: Immune thrombocytopenia (ITP) is a rare autoimmune disorder characterised by low platelet counts resulting in symptoms that are usually minor, e.g., petechiae. However, patients with very low platelet counts face the risk of serious but rare, bleeds, e.g., intracranial hemorrhage. The study objective was to estimate the cost-effectiveness of treating two groups of chronic adult ITP patients (refractory to splenectomy and where splenectomy is contraindicated) with oral eltrombopag versus romiplostim or rituximab from an Irish health care payer perspective.

METHODS: A Markov model with a four week model cycle, two year time horizon and seven health states was used. In one arm, patients were treated with eltrombopag and in the other romiplostim or rituximab. Patients began in either the 'controlled platelet' or 'uncontrolled platelet' health states. Response rates from clinical trials (eltrombopag and romiplostim) and a published literature review (rituximab) determined whether patients were controlled or not. Controlled patients experienced a higher level of utility and lower risk of transitioning to bleed health states. Utilities (using the SF-36v2) for bleeds and costs were taken from the literature. Costs and benefits were discounted by 4%. RESULTS: The model estimated that eltrombopag dominates romiplostim, i.e., cost savings of €13,000 and €18,000 with an incremental QALY of 0.1 and 0.03 for patients who are refractory to splenectomy and where splenectomy is contraindicated respectively. This result was driven by the fact that eltrombopag is less expensive, does not incur wastage or administration costs and has slightly better durable response rates compared to romiplostim. Eltrombopag is not cost-effective compared to rituximab for both groups of patients but rituximab is cost-effective compared to eltrombopag. CONCLUSIONS: The economic model showed that eltrombopag dominates romiplostim but is not cost-effective versus rituximab.

EARLY STAGE ECONOMIC EVALUATION OF PHARMACOGENOMIC-BASED DIAGNOSTICS IN CHRONIC MYELOID LEUKAEMIA

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OBJECTIVES: Uncertainty regarding the effectiveness of tyrosine kinase inhibitors (TKIs) for treatment of chronic myeloid leukemia (CML) has resulted in difficult decisions for some appraisal committees to recommend second-line TKIs. Implementation of pharmacogenomic-based diagnostics may facilitate individualized treatment with TKIs and improve overall treatment effectiveness. The objective of this economic evaluation was to estimate the potential cost-effectiveness of a companion diagnostic that predicts treatment response in CML patients eligible for dasatinib and nilotinib.

METHODS: A decision analytic model was created to assess the cost-effectiveness of individualized treatment with dasatinib and nilotinib using a companion diagnostic test relative to current care (i.e., treat all patients with dasatinib until progression or no response, then switch to nilotinib). Transition probabilities and utility values were taken from published RCTs. The cost analysis included costs of treatment, response monitoring and the companion diagnostic. Scenario analyses were conducted to assess the impact of unavailable or highly uncertain values. RESULTS: Total costs and effects for the base-case analysis were €99,011 and 1.84 quality-adjusted life-years (QALYs). A companion diagnostic strategy after a 2-year time horizon. In the current care situation, total costs and effects were €100,904 and 1.74 QALYs and 1.61 QALYs. The companion diagnostic was the dominant strategy with a savings of approximately €6,000/PF-LY or €2,000/QALY. Scenario analyses revealed that the cost-effectiveness of the companion diagnostic is sensitive to time to response, time to progression and comparative effectiveness between dasatinib and nilotinib. CONCLUSIONS: Treatment of CML patients eligible for second-line TKIs using a companion diagnostic may be cost-effective. More precise estimates for uncertain or unavailable parameters should be incorporated when available. This case demonstrates the use of economic evaluation methods at early stages of technology development for internal decision-making and communicating the potential value of pharmacogenomic-based diagnostics to stakeholders.

ASSESSING THE COST-EFFECTIVENESS OF PRIMARY PROPHYLAXIS FOR THE TREATMENT OF SEVERE HEMOPHILIA A

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OBJECTIVES: The objective of this analysis was to understand the economic consequences of different products in primary prophylaxis in severe hemophilia A patients. Miners’ (2002, 2009) hemophilia economic Markov model was revised to compare two different factor VIII products—a full-length recombinant FVIII (Advate) and a B-domain deleted recombinant FVIII (FVIII-BD) (Reflacto) in terms of their costs, effectiveness and safety in half life in a pharmacokinetic cross-over license study [1] with results submitted to EMA[2], this research evaluated the amount of clotting factor required to maintain the patient factor VIII trough levels above 1. If a product has a shorter half-life, more clotting factor is required to prevent factor VIII levels falling below the minimum trough level. METHODS: The same basic model structure of Miners’ hemophilia economic Markov model was used to analyze the effects of differences in half-life in an Italian economic setting, full-length recombinant FVIII (Advate) half-life 13.3 hours at a list price of $0.75 per IU versus BDDrFVIII (Reflacto AF) half-life 11.2 hours at a list price of $0.69 per IU. The model considers the amount of factor required to prevent trough clotting factor levels from falling below 1%. RESULTS: The analysis estimated that the mean expected, discounted lifetime (70 years) cost of treatment of primary prophylaxis in severe hemophilia A patients was less using full length recombinant FVIII (Advate) when compared to a BDDrFVIII (Reflacto AF), assuming a 2.1 hour shorter half-life; i.e. equal to or under $12,500 in cost savings per patient per year. CONCLUSIONS: This analysis shows that prophylaxis therapy using full-length recombinant FVIII (Advate) may be cost saving compared to or comparators or withdrew, switching to alternative 2nd line opioid (oxycodone, morphine or transdermal fentanyl) was considered. After initiating 3rd line therapy, patients could stay on this therapy or die according to morbidity rate. Data regarding efficacy, tolerability and utility values (EQ-SD) were derived from clinical trials and published literature. Switch rates to subsequent opioid therapies and resource consumption were estimated by clinical experts. Costs were calculated from the societal perspective. Direct costs were calculated based on official Swedish prices/tariffs, indirect costs were calculated based on figures obtained from the literature and current wages. Costs and benefits were not discounted. Impact of selected parameters on the results was evaluated in one-way sensitivity analyses (OWSA). RESULTS: Mean annual total costs per patient amount to 242,538 SEK (Swedish krona) for tapentadol vs. 247,813 SEK for oxycodone and 246,093 SEK for morphine. Tapentadol generates 0.4712 QALYs compared to 0.4518 QALYs for oxycodone or 0.4535 QALYs for morphine. More QALYs generated in the model reflect tapentadol's better tolerability profile than comparators. Cost parameter comprising visistatus, co-medications and non-drug therapy costs revealed highest impact in OWSA. CONCLUSIONS: Tapentadol, once approved, will generate more QALYs at lower costs than oxycodone and morphine. Tapentadol appears to be the favourable treatment option in the 1st line therapy of CNCP patients in Sweden from a societal perspective.

THE COST-EFFECTIVENESS OF DULOXETINE IN THE TREATMENT OF FIBROMYALGIA IN THE UNITED STATES

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OBJECTIVES: To evaluate the cost-effectiveness of duloxetine for the management of fibromyalgia assessed from the perspective of a health care payer in the United States. METHODS: A Markov model was used to evaluate the economic and clinical advantages in controlling fibromyalgia pain symptoms, considering duloxetine as an additional treatment option. The standard treatment sequence was defined based on clinical guidelines including tricyclic antidepressants (TCAs), second-generation anti-depressants (based on SNRIs), anticonvulsants, and opioid therapies. The model included 2 levels of pain response (a ≥30% and ≥50% change from baseline, using a standard 11 point severity scale). Clinical efficacy and discontinuation data were taken from a systematic literature review and mixed treatment comparison, including both placebo and active controlled trials. Utility data were linked to pain severity using trial-based EQOD data. Discounting was applied at 3% per year. RESULTS: The introduction of duloxetine resulted in additional symptom-controlled months (SCMs), defined as the amount of time at a ≥30% response level, and quality-adjusted life-years (QALYs), over a 2-year time horizon. First-line treatment resulted in an additional 665 SCMs and 12.3 QALYs, with a cost of $582,911 ($877 per SCM and $547,560 per QALY). Second-line treatment resulted in an additional 460 SCMs and 8.7 QALYs, with a cost of $143,752 ($312 per SCM and $16,565 per QALY). A cost-effectiveness frontier analysis suggested that second-line duloxetine is likely to be the most cost-effective option, however, in sensitivity analyses, the cost-effectiveness of first-line duloxetine improved when assumptions around continued treatment switching for long-term drop-outs were relaxed. CONCLUSIONS: There is currently a significant unmet need for patients with poorly controlled fibromyalgia where pain is the predominant symptom. These results show that the introduction of duloxetine increases QALYs and that the standard treatment sequence for fibromyalgia can provide additional patient benefits, which are cost-effective when compared to commonly adopted thresholds.

COST-EFFECTIVENESS AND BUDGET IMPACT ANALYSIS OF OROS HYDROMORPHONE IN PATIENTS WITH CHRONIC CANCER PAIN FROM THE PUBLIC PAYER PERSPECTIVE IN BRAZIL

OBJECTIVES: To conduct cost-effectiveness and budget impact analysis (BIA) of OROS hydromorphone versus CR morphine and CR oxycodone respectively. The incremental cost-effectiveness ratio (ICER) for golimumab was £15,353 per QALY.

RESULTS: Ankylosing Spondylitis Disease Activity Index (BASDAI) at 12 weeks. Direct costs including medication costs and AS management costs were included. Golimumab was active AS patients for 20 years. The primary outcome measure was quality-adjusted life-years (QALY) gain. Perspectives of the National Health Service (NHS) and society severe cancer pain from the public payer perspective in Brazil. METHODS: A decision tree followed by a Markov Model with a 12 month time horizon was developed with data from the Phase III trial Hanna 2008. The achievement of mild pain (worst pain scores < 4) was considered as outcome. Only direct medical costs were considered and unit costs were obtained from Brazilian official lists. For the BIA, 10% of currently used CR morphine daily doses was substituted for equivalent OROS hydromorphone doses. The same rationale was adopted for CR oxycodone comparison. Univariate deterministic sensitivity analyses showed that the results remained consistent through model parameters variation. RESULTS: OROS hydromorphone showed 1.66 additional months in mild pain per patient year when compared to both CR morphine and CR oxycodone. Annual treatment costs were 2,401 BRL and 5,114 BRL for CR oxycodone and CR morphine, respectively. The incremental cost-effectiveness ratio was 869 BRL per additional month in mild pain per patient year, when OROS hydromorphone was compared to CR morphine. Versus CR oxycodone, OROS hydromorphone was more effective with fewer costs, being cost saving (ICER: £1,834 BRL). BIA results showed that the substitution of 10% of current utilization of CR morphine for OROS hydromorphone and CR oxycodone would result in a budgetary impact of 118,722 BRL and 347,295 BRL, respectively.

CONCLUSIONS: OROS hydromorphone is cost saving when compared to CR oxycodone and is more cost-effective than CR oxycodone when both are compared to the current standard of chronic cancer pain treatment with CR morphine, with a lower budgetary impact.

OBJECTIVES: Golimumab is a novel TNF-α inhibitor for treatment of patients with severe active ankylosing spondylitis (AS). This study evaluated the cost-effectiveness of golimumab and its appropriate comparators in the treatment of AS from UK National Health Service (NHS) perspective. METHODS: A Markov model with an initial decision tree was developed to simulate the progression of a hypothetical cohort of active AS patients for 20 years. The primary outcome measure was quality-adjusted life-years (QALYs) estimated using Bath Ankylosing Spondylitis Functional Index (BASFI) whereas the primary response measure was ≥50% improvement in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) at 12 weeks. Direct costs including medication costs and AS management costs were included. Golimumab was compared with conventional treatment and other TNF-α inhibitors. Costs and outcomes were discounted at 3.5%. RESULTS: All TNF-α inhibitors were superior to conventional treatment and comparable to each other on BANDAI response. The incremental cost-effectiveness ratio (ICER) for golimumab was £15,353 per QALY compared to conventional treatment. The probability of golimumab being cost-effective at a threshold of £30,000/QALY was 92%. Compared to etanercept and adalimumab, golimumab generated marginally more QALYs at marginally more costs.

CONCLUSIONS: Golimumab may be considered as a cost-effectiveness alternative for patients with AS. With comparable costs and efficacy to other TNF-α inhibitors, golimumab’s position in the treatment pathway is likely to be driven by patient and physician choice.

REAL-WORLD COST-EFFECTIVENESS OF BORTEZOMIB IN RELAPSED OR REFRACTORY MULTIPLE MYELOMA IN THE NETHERLANDS

OBJECTIVES: The Dutch reimbursement policy for expensive inpatient medicines requires outcomes research after four years of temporary reimbursement. Based on a retrospective study, we explored the cost-effectiveness of bortezomib for relapsed/ refractory multiple myeloma in Dutch daily practice. METHODS: Detailed clinical data from a real-world cohort of 72 patients treated with bortezomib and 67 patients never treated with bortezomib were collected from medical records. Validity of the incremental cost-effectiveness was assessed by comparing baseline prognosis between bortezomib and non-bortezomib patients. Clinical effectiveness was evaluated by comparing Kaplan-Meier survival estimates. Costs of resource use from a hospital perspective were based on patient-level data. RESULTS: Prognostic factors for bortezomib patients were significantly different compared to non-bortezomib patients. Incremental analyses for bortezomib versus non-bortezomib patients were therefore not performed. Total mean costs and median survival from start of relapse/ refractory treatment for bortezomib patients were £84,042 and 33.2 months. Bortezomib accounted for 21% of total costs among these patients. For non-bortezomib patients, total mean costs and median survival from start of relapsed/refractory treatment were £54,042 and 21.6 months. The proportion of patients still in follow-up at the end of data collection was slightly higher in bortezomib versus non-bortezomib patients (51% vs. 46%). Total mean costs for bortezomib patients did not differ significantly when excluding patients still in follow-up. For non-bortezomib patients, total mean costs bortezomib preferred significantly when calculating patients still in follow-up, mainly due to high costs of lenalidomide treatment, stem cell transplants and inpatient hospital stays.

CONCLUSIONS: Our real-world data challenged the assessment of the incremental cost-effectiveness of bortezomib versus other treatments in the indication of relapsed/ refractory multiple myeloma. It was possible to estimate the cost and effects for bortezomib patients in daily practice to determine the real-world value. Data synthesis incorporating effectiveness for the relevant comparator might facilitate estimation of a valid ICER.

COST-EFFECTIVENESS OF PREGABALIN VERSUS USUAL CARE IN REFRACTORY OUT-PATIENTS WITH NEUROPATHIC PAIN FOLLOWED IN PRIMARY CARE SETTINGS

OBJECTIVES: Estimate the cost-effectiveness of Pregabalin (PGB) versus Usual Care (UC) in refractory out-patients being followed in primary care settings in Spain. METHODS: Data extracted from a 12-week non-interventional prospective study conducted to ascertain the cost of NeP were used. PGB naive patients treated with UC or PGB, matched by age (±5 years), sex and pain intensity (±5 pts), refractory (≥80/100 on VAS) to previous treatment during the prior 6 months, were selected in a 1:1 ratio. Patients could switch to PGB (monotherapy/add-on) or to UC (non-narcotics, opiates, antidepressants and/or anticonvulsants). Time horizon was 12 weeks. Effectiveness was quality-adjusted life-years (QALY) gain. Perspectives of the National Health Service (NHS) and society (2006) were included, and expressed as an incremental cost-effectiveness ratio (ICER). Bootstrapping techniques (10,000 re-samples) were used to obtain the probabilistic ICER, its 95% percentile confidence interval (CI) and the cost-effectiveness acceptability curve. RESULTS: A total of 169 patient-pairs were extracted. Compared with UC, PGB was associated with significantly higher QALY gain; 0.0374 ± 0.0367 vs. 0.0224 ± 0.0313 (p < 0.001). Notably, although drug costs were higher for PGB ($251 ± 123 vs. $104 ± 121, p = 0.001), its QALY gain did not incur a higher overall total cost ($1,335 ± 1,302 vs. $1,387 ± 1,489, P = 0.587), nor higher health care costs ($529 ± 438 vs. $560 ± 672; p = 0.682). In fact, the ICER was dominant for total and health care costs, with ICs respectively, dominant-£268, and dominant-£568, ICER for blood cost was £10,672/QALY (dominant-£19,858). The 99% of the re-samples were lower QALY gain than in PGB/UC. CONCLUSIONS: Versus CR oxycodone, OROS hydromorphone was more effective with fewer costs, being cost saving (ICER: £1,634 BRL). BIA results showed that the substitution of 10% of current utilization of CR morphine for OROS hydromorphone and CR oxycodone would result in a budgetary impact of 118,722 BRL and 347,295 BRL, respectively.

COST-EFFECTIVENESS OF BILOGICS IN PSORIASIS IN TWO LA COUNTRIES—COMPARISON WITH THE EUROPEAN EXPERIENCE

OBJECTIVES: To evaluate cost-effectiveness of biologics used in patients with psoriasis in Colombia and Peru. METHODS: We estimated direct costs of etanercept, adalimumab, ustekinumab and infliximab based on their labels for first/induction year and second/maintenance year (EUR1=COL=USD). We considered two induction schemes: 50 mg weekly 52 days-W1 and 100 mg 12 weeks-W2. Effectiveness was evaluated as 75% reduction in Psoriasis Area and Severity Index-PASI 75- from meta-analysis presented by Hawkins et al. in the 14th International ISPOR; infliximab: 80%; ustekinumab: 69%; adalimumab: 59%; etanercept2D: 52%; etanerceptD1: 39%. Infliximab and ustekinumab effectiveness were not significantly different. However, both were significantly superior to etanercept (D1 and D2). RESULTS: In Colombia, Ustekinumab was dominant ($29,012 in 2 years generating cost savings of €492; $1,714 vs. $1,520, respectively). In Peru, small differences were found with etanerceptD1 being more cost effective than etanerceptD1 and $25,340 vs. infliximab, with higher or same effectiveness than the other biologics used in that country. In Peru, all the options were more effective and more costly than the standard of care (etanerceptD1). The ICER per patient with PASI 75 of etanerceptD2, adalimumab, ustekinumab and infliximab, compared to etanerceptD1 were $21,654, $19,860, $13,036 and $29,008, respectively. Then, the efficiency frontier was formed by etanerceptD1, ustekinumab and infliximab. Given evidence shows the last two products do not have effectiveness significant differences, ustekinumab became the dominant