HEMATOLOGICAL DISORDERS—Cost Studies

**PHM1**

**COSTEFFECTIVENESS OF ONCE-DAILY ORAL CHELATION THERAPY WITH DEFERASIROX VERSUS INFUSIONAL DEFEROXAMINE IN TRANSFUSION-DEPENDENT THALASSEMA PATIENTS**

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**OBJECTIVES:** Deferasirox is a recently approved once-daily oral chelator that has been shown to produce reductions in liver iron concentrations and serum ferritin similar to those with infusional deferoxamine. The cost-effectiveness of deferasirox vs deferoxamine in β-thalassemia major patients has not been examined. METHODS: A Markov model was used to estimate the total additional lifetime costs and quality-adjusted life years (QALYs) gained with deferasirox versus deferoxamine in patients with β-thalassemia major and chronic iron overload from blood transfusions. Patients were assumed to receive prescribed dosages of deferasirox and deferoxamine that have been shown to be similarly effective in such patients. Compliance with deferoxamine as well as costs of deferoxamine administration and complications of iron overload were based on analyses of health insurance claims data of transfusion-dependent thalassemia patients. Probabilities of complications of iron overload and death by level compliance with chelation were estimated using data from published studies. Because data on compliance with deferasirox in typical clinical practice are unavailable, we used published data on compliance with the oral chelator deferiprone vs deferoxamine. Utilities (weights representing patient quality of life) were based on a study of patient preferences for oral vs infusional chelation therapy, as well as published literature and assumption. A US healthcare system perspective was employed. RESULTS: Deferasirox results in a gain of 3.9 QALYs per patient at an additional expected lifetime cost of $133,321 per patient. Cost-effectiveness is $33,792 per QALY gained. Cost-effectiveness is sensitive to the estimated costs of deferoxamine administration and the quality of life benefit associated with oral vs infusional therapy and is more favorable in younger patients. CONCLUSIONS: The cost-effectiveness of deferasirox vs deferoxamine in patients with transfusion-dependent β-thalassemia is within the range considered generally-accepted in the United States.

**PHM2**

**ECONOMIC AND QUALITY OF LIFE BURDEN OF HIGH-RISK ACUTE LYMPHOBlastic LEUKEMIA**

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**OBJECTIVES:** Patients with high-risk acute lymphoblastic leukemia (ALL), including Philadelphia chromosome positive (Ph+) ALL, typically have extremely poor prognosis, experience poor quality of life (QoL) and incur high economic cost. This study examined the economic and humanistic outcomes for high-risk ALL. METHODS: A systematic search of the English-language literature published between 1990 and 2005 was conducted. Additional searches were conducted from the retrieved article bibliographies and appropriate conference proceedings (2000–2005). Articles selected for inclusion were prospective or retrospective studies specifically designed to examine burden of illness, direct medical costs, cost drivers, or QoL outcomes of ALL and treatments. RESULTS: Of 798 abstracts screened, 106 met selection criteria and were reviewed in detail. Forty-nine and 47 studies focused on the economics and QoL aspects of ALL, respectively. The average annual direct medical cost per high-risk ALL patient ranged from $100,000 to $136,000. Hospitalization was the major cost component comprising 50%–80% of total direct costs. Major hospital cost drivers included infections, chemotherapy, growth factors, transfusions, and transplantation. These drivers resulted in more frequent hospitalizations and longer ICU lengths of stay for high risk patients. High-risk ALL patients typically had psychological problems and physical complaints, especially in domains of emotion, cognition, and pain. Furthermore, high-risk patients were more likely to have poorer QoL than standard-risk patients due to higher relapse rates and increased need for transplantation. CONCLUSIONS: ALL exacts a substantial economic and humanistic burden on patients, their loved ones and society in general. This burden appears particularly heavy for high-risk patients, such as Ph+ ALL. Imatinib, a molecularly targeted therapy, has been reported to prolong disease-free-survival in Ph+ ALL with good tolerability in clinical studies. Research is warranted to evaluate the economic and humanistic benefits of imatinib as compared to the current therapies in the treatment of Ph+ ALL.

**PHM3**

**ECONOMIC ANALYSIS OF RECOMBINANT ACTIVATED FACTOR VII IN THE HOME TREATMENT OF MINOR-TO-MODERATE BLEEDS IN HEMOPHILIA PATIENTS WITH INHIBITORS: A U.S. COST-OF-BLEED MODEL**

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**OBJECTIVES:** To compare the cost of treatment for three “on-demand” treatment regimens using recombinant activated Factor VII (rFVIIa [NovoSeven®]) and activated prothrombin-complex concentrate (APCC [FEIBA® VH]) for home treatment of minor-to-moderate bleeds in hemophilia with inhibitors. METHODS: A decision analytic model was developed from the payer’s perspective to calculate the projected cost per bleeding episode and the 1-year cost of treatment for three “on-demand” treatment strategies consisting of first, second, and third-line treatments: rFVIIa/rFVIIa/rFVIIa, APCC/rFVIIa/rFVIIa, and APCC/APCC/rFVIIa. Published literature was used to define treatment algorithms, number of bleeds, dosing, costs, efficacy, and re-bleeds. Evaluable bleeds controlled with rFVIIa and APCC ranged from 88–93% and 78–81%, respectively. Number of bleeds was assumed to be 15 per year (range 10–20). Drug costs were based on 2005 U.S. average wholesale prices; other direct medical costs reflected 2005 values. Univariate and probabilistic sensitivity analyses (PSA) were conducted on key variables to ascertain model robustness. RESULTS: The cost per bleed (and 1-year cost of treatment) per patient was $28,076 ($421,137), $30,883 ($463,251), and $32,150 ($482,253) using rFVIIa/rFVIIa/rFVIIa, APCC/rFVIIa/rFVIIa, and APCC/ APCC/rFVIIa, respectively. Annual cost offsets ranging from $42,115–$61,116 per patient occurred for the rFVIIa-only regimen through avoidance of second and third lines of treatment. Univariate sensitivity analyses showed consistent results with the base case. In PSA, the rFVIIa-only strategy was less expensive than either alternative in 68% of 10,000 model simulations. CONCLUSIONS: The management of minor-to-moderate bleeds extends beyond the initial line of treatment, and should include the economic impact of rebleeding over multiple lines of therapy. The annual cost of treatment for minor-
to-moderate bleeds in a hemophilia patient with inhibitors is very high. When considering the impact of rebleeding over multiple lines of treatment, the rFVIII-only regimen, versus APCI-containing strategies, may provide cost savings of up to $60,000 annually per patient.

HEMATOLOGICAL DISORDERS—Patient Reported Outcomes

COSTS AND CONSEQUENCES OF INADEQUATE COMPLIANCE WITH DEFEROXAMINE THERAPY IN PATIENTS WITH TRANSFUSION-DEPENDENT THALASSEMIA

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OBJECTIVES: Patients with transfusion-dependent thalassemia require chelation to prevent complications from transfusional iron overload. Deferoxamine (DFO) is an effective iron chelator, but must be administered as a subcutaneous or intravenous infusion over 8–12 hours 5–7 times per week leading to poor compliance and/or quality of life in many patients. METHODS: We developed a Markov model using data from published studies and other sources to estimate the lifetime incidence and medical care costs of complications of iron overload that are attributable to inadequate compliance with DFO therapy in patients with transfusion-dependent thalassemia. Complications considered included cardiac disease, diabetes, hypogonadism, hypoparathyroidism, hypothyroidism, and death due to cardiac disease. Current compliance with DFO therapy as well as costs of complications were obtained from an analysis of health insurance claims data. Adequate compliance was defined as 260 infusions per year (i.e., five per week). Costs were discounted at 3% annually. RESULTS: Current mean DFO use was estimated to be 169 infusions annually. At this level of compliance, 95% of patients are projected to experience cardiac disease during their lifetime, diabetes 46%, hypogonadism 77%, hypoparathyroidism 32%, and hypothyroidism 26%. Cardiac-disease-free life expectancy is projected to be 23 years; overall life expectancy, 28 years. The expected lifetime cost of complications of iron overload is $54,151 per patient. If mean compliance were to increase to 260 infusions per year (i.e., five per week), Costs were discounted at 3% annually. RESULTS: Current mean DFO use was estimated to be 169 infusions annually. At this level of compliance, 95% of patients are projected to experience cardiac disease during their lifetime, diabetes 46%, hypogonadism 77%, hypoparathyroidism 32%, and hypothyroidism 26%. Cardiac-disease-free life expectancy is projected to be 23 years; overall life expectancy, 28 years. The expected lifetime cost of complications of iron overload is $54,151 per patient. If mean compliance were to increase to 260 infusions per year, the lifetime risk of cardiac disease would decline to 60%, diabetes to 9%, hypogonadism to 47%, and hypothyroidism to 14%. Cardiac-disease-free and overall life expectancy would increase by 22 and 19 years respectively. The discounted expected lifetime costs of complications of iron overload would decline by $30,222. CONCLUSIONS: Inadequate compliance with DFO therapy in patients with transfusion-dependent thalassemia results in substantial morbidity and mortality, as well as increased medical care costs associated with complications of iron overload.

PILOT STUDY TO ESTABLISH PREFERENCES TOWARDS COAGULATION FACTOR CONCENTRATES USED TO TREAT HAEMOPHILIC PATIENTS WITH INHIBITORS

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OBJECTIVES: Haemophilia is a very expensive disease. This situation becomes extreme when patients develop inhibitors that compromise the effectiveness of treatment, with potential increase of morbidity and mortality. Treatment of haemophilia is the result of interactions between patients, physicians, pharmacists and budget holders, each carrying their own set of preferences. A pilot study was conducted to identify which characteristics of coagulation products are considered more important to treat patients with inhibitors: these characteristics will be included with a price proxy characteristic in a Discrete Choice Experiment, with the objective to elicit preferences and willingness to pay towards treatments of patients with inhibitors.

METHODS: Eight characteristics were identified during focus groups with patients and clinicians and rated from 0 (not important) to 10 (very important) by 35 people (adult patients, caregivers, physicians, pharmacists). RESULTS: The following median (mean) scores were found: “viral safety”: 10 (8.9); “time to stop bleeding”: 9.5 (9.0); “risk of anamnestic response”: 9.0 (8.5); “possibility of undergoing major surgery”: 9.0 (8.8); “regular use in prophylaxis”: 9.0 (8.4); “time to pain recovery”: 9.0 (8.3); “number of injections to stop bleeding”: 8.0 (7.9); “time to prepare and give/have the injection”: 7.0 (6.6). All groups of respondents considered as more important “viral safety”, “possibility of undergoing major surgery”, “risk of anamnestic response”, “time to stop bleeding”, while “time to prepare and give/have the injection” was considered the least important. Different preferences were attributed to “time to pain recovery”, considered more important by patients; “regular use in prophylaxis”, considered more important by caregivers.

CONCLUSIONS: Viral safety and effectiveness are considered as the most important characteristics in the treatment of haemophilic patients with inhibitors. Different levels of preferences are present between patients, or their caregivers, and physicians. Understanding these differences is important to guide optimal therapeutic strategies in patients with inhibitors.

HEALTH CARE USE & POLICY

A COMPARISON OF CLINICAL TRIAL PARTICIPANTS TO THE GENERAL PATIENT POPULATION

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OBJECTIVE: To determine and quantify the unique characteristics of clinical trial participants in comparison to the general patient population. METHODS: Data were obtained from the U.S. National Health and Wellness Survey, an annual, nationally representative, Internet-based study of the health care attitudes and behaviors of non-institutionalized adults age 18+. The sample for analysis included 18,419 respondents who reported a diagnosis of hypertension, high cholesterol, or diabetes. Respondents reported ever participating in a clinical drug trial. They also provided information on demographics, healthcare attitudes, health habits, quality of life measured by the SF-8, and healthcare resource use in the past six months. RESULTS: Among respondents diagnosed with hypertension, high cholesterol, or diabetes, 7% (n = 1,333) have participated in a clinical drug trial. Clinical trial participants significantly differ from the general patient population in many key characteristics. Clinical trial participants are significantly older (mean age 60.5 versus 55.1, p < 0.001) and more educated (college graduates 43% versus 36%, p < 0.001). They experience worse physical well-being (sf-8 physical component summary score 43.1 versus 45.3, p < 0.001), though are more likely to maintain a healthy diet (50% versus 46%, p = 0.002) and less likely to smoke (18% versus 23%, p < 0.001). Clinical trial participants are more