SAFETY AND IMMUNOGENICITY OF RBIF® NEW FORMULATION (RNF) A NEW SUBCUTANEOUS FORMULATION OF INTERFERON BETAL-1A 44 MCW THREE TIMES WEEKLY: 1-YEAR RESULTS OF A PHASE IIII STUDY IN PATIENTS WITH RELAPSING MULTIPLE SCLEROSIS

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OBJECTIVES: To compare the safety and immunogenicity of a new human serum albumin (HSA)-free formulation of interferon (IFN) betal-1a (Rebi® New Formulation; RNF) with historical Rebi® data. RNF was developed through an extensive research program to maximize treatment benefit and patient outcomes by improving injection tolerability and reducing neutralizing antibodies (NABs). METHODS: This 48-week analysis of a 96-week phase IIIb multicenter single-arm open-label study (25,632) compared RNF (44 mcg/0.5 mL, self-injected subcutaneously three-times weekly [tiw]) with historical Rebi® 44 mcg tiw data (EVIDENCE study) in patients with relapsing multiple sclerosis (18–60 years; EDSS < 6.0). Safety analyses included eight pre-specified adverse event (AE) groups of interest, including injection-site reactions (ISR) and flu-like symptoms (FLS; includes “influenza-like illness” or ≥2 other FLS terms within 48-hours). NAb titers ≥20NU/mL at last assessment up to week 48 were considered NAb+; “persistent NAb’s” was defined as NAb+ at 24 and 48 weeks. RESULTS: At week 48, 227/260 patients (87.3%) remained on treatment. Compared with historical data, incidence of pre-specified AEs in the RNF study was markedly lower for ISR (29.6% versus 83.8%; a three-fold reduction), and similar or lower for cytopenia (9.6% versus 11.8%), depression and suicidal ideation (5.8% versus 19.8%), hepatic disorders (13.1% versus 16.8%), skin rashes (5.4% versus 12.1%), thyroid disorders (2.3% versus 5.0%) and hypersensitivity reactions (5.4% versus 3.2%). As expected with an HSA-free formulation, incidence of FLS was higher with RNF (70.8% versus 48.1%) and most events were mild/moderate in severity. Compared with historical data, a markedly smaller proportion of RNF patients had persistent NABs (2.5% [95% CI: 1.0–5.4%] versus 14.3% [95% CI: 10.7–18.6%]) or NABs at week 48 (13.9% [95% CI: 9.9–18.7%] versus 24.4% [95% CI: 19.9–29.4%]). 50% of NAB+ titers were low (below 200 NU/mL). CONCLUSION: These data suggest that RNF has better overall safety and lower immunogenic potential than Rebi®.

NEUROLOGICAL DISORDERS—Cost Studies

THE BUDGETARY IMPACT OF THE UTILIZATION OF NATALIZUMAB FOR THE TREATMENT OF RELAPSING MULTIPLE SCLEROSIS

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OBJECTIVES: Natalizumab was recently introduced to the U.S. market for the treatment of relapsing multiple sclerosis (MS). A model was designed to determine the budgetary impact of utilization of natalizumab from a managed care perspective.

METHODS: The model inputs were drug acquisition costs, costs of drug administration and monitoring, costs of treating relapses, anticipated reduction in relapse rates after 2 years of therapy, and estimated market utilization of natalizumab. Outcomes included per member per month (PMPM) and 2-year overall costs, including costs of relapses, in a hypothetical health plan of 1 million members. These were calculated using total pharmacy and medical costs of each therapy. The budgetary impact of an estimated 10% shift in utilization of current disease-modifying therapies (DMTs) to natalizumab was determined by calculating the difference between baseline and adjusted market values. Utilization of DMTs was based upon market share distribution prior to the launch of natalizumab and adjusted by 10%; from 40% to 36% for intramuscular interferon (IFN)β-1a, from 14% to 12.6% for IFNβ-1b, from 30% to 27% for glatiramer acetate, and from 16% to 14.4% for subcutaneous IFNβ-1a. RESULTS: If natalizumab captured 10% of the DMT market for relapsing MS, there would be a $1,369,194 increase in annual costs to the hypothetical health plan (baseline annual cost = $25,960,384 versus adjusted annual cost = $27,329,578). This equates to an increase in PMPM costs of $0.11 (baseline cost = $2.16 versus adjusted cost = $2.28). Pharmacy costs contributed most to the total cost of therapy in both the current and adjusted market scenarios. Addition of natalizumab as a treatment option resulted in a savings for total annual cost of relapses to the plan of $162,347 or $0.01 on a PMPM basis. CONCLUSION: Natalizumab will likely result in a minimal increase in health plan PMPM costs.

RESOURCE UTILIZATION PATTERNS WITH TOPIRAMATE FOR MIGRAINE PREVENTION IN THE MANAGED CARE SETTING

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OBJECTIVES: To determine the pattern of headache-related resource utilization in a sample of managed care plan members before and after initiation of topiramate (TPM). METHODS: The HealthCore Database provided pharmacy and medical claims data. Patients were required to have at least one pharmacy claim for topiramate between 1/1/00 and 11/30/05, and at least 12 units dispensed of any combination of migraine-specific acute therapy (triptan, ergotamine, or ergotamine combo) during the 6-month period preceding a first pharmacy claim for TPM (the index date). Headache-related inpatient and outpatient resource uses were compared: pre-index vs post-index period 1 (PIP1; months 1 through 6) and pre-index vs post-index period 2 (PIP2; months 7 through 12). Statistical analyses included McNemar’s and Wilcoxon signed-rank tests. RESULTS: A total of 3246 patients met the inclusion criteria. The mean ± SD age was 44 ± 10 years; 88% were female. The mean ± SD TPM dose was 106 ± 75 mg, and mean days on therapy were 144 days. Compared to pre-index period, use of abortive agents significantly decreased during PIP1 (13%, p < 0.00001) and PIP2 (25%, P < 0.0001). Percentage of patients using triptans and ergotamine combinations was significantly reduced (p < 0.0001) from pre-index (85% and 22%) to PIP1 (75% and 11%) and PIP2 (67% and 8%). Use of outpatient resources did not change significantly during PIP1, but decreased 33% during PIP2 for TPM patients. Diagnostic procedures (eg, CT scans and MRIs) decreased 48% during PIP1 and 74% during PIP2. ER visits decreased 7% during PIP1 and 27% during PIP2. Total cost was $2092 per patient in the pre-period, $2089 in PIP1 and $1765 in PIP2. CONCLUSION: TPM was associated with significantly lower health care resource use (ER visits, diagnostics, acute therapy) in the first six months of TPM treatment, with continuing decreases, including physician office visits, in months seven through twelve.