OBJECTIVES: Progressive multifocal leukoencephalopathy (PML) is an infrequent but serious adverse event associated with natalizumab in the treatment of patients with relapsing-remitting multiple sclerosis (RRMS). The objective is to evaluate the risks and benefits of natalizumab treatment across three PML risk sub-groups against comparator agent interferon-β and no treatment. **METHODS:** The risk-benefit analysis was conducted using an adaptation of the original natalizumab model submitted to the National Institute for Health and Clinical Excellence that simulates natural disease progression and potential treatment impact on outcomes. A PML risk stratification component was incorporated to define PML risk by anti-JC virus (JCV) antibody status, previous immunosuppressant (IS) history, and duration of exposure to natalizumab therapy. A disutility score was applied to PML and post-PML states, as well as disease states defined by EDSS scores. **RESULTS:** Over a 20-year time horizon, treating anti-JCV antibody negative patients with natalizumab resulted in a total of 6.49 quality-adjusted-life-years (QALYs) per patient. Treatment with natalizumab in the anti-JCV antibody positive sub-groups, with and without previous IS history resulted in 6.27 and 6.43 QALYs per patient, respectively. Interferon-β treatment resulted in 6.05 QALYs per patient across all PML risk groups, whereas no treatment led to 5.82 QALYs per patient. In the highest risk group (anti-JCV antibody positive with prior IS use), utility decrement due to PML was small compared to the lowest risk anti-JCV antibody negative group (0.22), and overall QALYs were higher than interferon-β and no treatment. When considering the overall RRMS patient population, the risk of PML associated with natalizumab had to be more than 10.43 times higher in order to result in equivalent QALYs with interferon-β. **CONCLUSIONS:** The risk of PML associated with natalizumab treatment is offset by the benefit of natalizumab across all patient groups compared to interferon-β and no treatment.

PND2

DOPAMINE AGONISTS AND DYSKINESIA IN ADVANCED PARKINSON'S DISEASE: A NETWORK META-ANALYSIS OF ROTIGOTINE, PRAMIPEXOLE AND ROPINIROLE AS ADJUNCT THERAPY TO LEVODOPA

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OBJECTIVES: The development of dyskinesia in Parkinson's disease (PD) patients may be associated with pulsatile stimulation of dopamine receptors, especially when using short-acting dopaminergic agents such as levodopa. Adjunctive therapy to levodopa with dopamine agonists may increase the risk of dyskinesia. This study quantitatively assessed the short-term incidence of dyskinesia in patients with advanced PD when treated with rotigotine transdermal patch (RTG) compared with ropinirole (ROP) and pramipexole (PPX) immediate-release (IR) and extended-release (ER). **METHODS:** A systematic review of randomized controlled comparative trials of RTG, ROP, PPX and placebo (PBO) on a background of levodopa therapy in advanced PD patients was performed, followed by a network meta-analysis. Trials published up to September 2011 were included. Incidence of dyskinesia was assigned as reported in each study. Study-level relative treatment effects were combined using both random-effect (base case) and fixed-effect models (sensitivity analysis) within a Bayesian framework using Markov Chain Monte Carlo methods in WinBUGS. **RESULTS:** Sisteen trials and 4446 patients were incorporated in the meta-analysis, which included 20 direct pair-wise comparisons. Patient characteristics were similar in terms of mean age at baseline, disease duration and severity (UPDRS III); however, average levodopa dosage differed across studies (range 272.9-843.4 mg/day). Under the base case assumption, odds of dyskinesia occurrence were comparable across dopamine agonists; odds numerically favored RTG over ROP-IR (OR: 0.70 [95% CI: 0.31, 1.59]), ROP-ER (0.33 [0.09, 1.15]) and PPX-IR (0.86 [0.49, 1.58]), but not PPX-ER (1.02 [0.42, 2.43]). The sensitivity analysis suggested that patients receiving RTG were estimated to experience fewer dyskinesias than those receiving ROP-ER (0.32 [0.11, 0.88]). **CONCLUSIONS:** This meta-analysis suggests that in levodopa-treated patients with advanced PD, dopamine agonists were comparable in terms of short-term odds of experiencing dyskinesia, with a numerical trend favoring RTG over ROP-ER. Further large-scale, confirmatory randomized clinical trials are required.

PND3

INDIRECT TREATMENT COMPARISON (ITC) ANALYSIS OF THERAPIES THAT ARE OFTEN CONSIDERED FOR TREATMENT-EXPERIENCED PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS

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OBJECTIVES: Relapsing-remitting multiple sclerosis (RRMS) is the most common form of MS and is characterised by inflammatory episodes in the brain followed by periods of remission. Damage caused by relapses accumulates over time and many patients will develop some form of permanent disability after 10 years. Natalizumab 300mg, fingolimod 0.5mg and INFβ-1a 44mcg are typically considered for treatment-experienced patients with RRMS. This meta-analysis aimed to assess the efficacy of natalizumab versus other potential treatments for RRMS. **METHODS:** Electronic searches of Medline, Embase and the Cochrane library were undertaken to identify potential studies conducted in adults with RRMS treated with natalizumab, fingolimod or INFβ-1a. Direct meta-analysis was conducted in STATA version 12 using the metan package. Indirect comparisons between treatments via common comparators were made using the Bucher method. **RESULTS:** Out of 2512 records obtained from systematic searches, forty studies were included in the final data set. Analysis of evidence suggested that patients treated with natalizumab were twice as likely to remain free from disease activity (ie free from both clinical and radiological activity) at 24 months compared with fingolimod (OR=2.05, 95% CI: 1.127, 3.735). Progression of disability (i.e. increase in EDSS score) was lower in patients treated with natalizumab compared with fingolimod (mean difference in EDSS score change= -0.69, 95% CI: -0.882,-0.498). Patients treated with natalizumab had a 50% lower chance of relapse per year compared with INFβ-1a (OR=0.5, 95% CI: 0.391, 0.640). Likewise, patients receiving fingolimod were less likely to have a relapse in a year compared with INFβ-1a (OR=0.64, 95% CI: 0.477, 0.867). Analysis of additional outcomes based on limited data, showed directional favour towards natalizumab compared with fingolimod and INFb-1a without reaching statistical significance. **CONCLUSIONS:** Compared with fingolimod and IFNb-1a, natalizumab was shown to be a more effective treatment alternative for RRMS patients in this analysis.

PND4

TRENDS OF Z-DRUGS PRESCRIPTIONS IN TAIWANESE ADULT POPULATIONS

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OBJECTIVES: Those non-benzodiazepine hypnotics (Z-drugs) were introduced for the short-term management of insomnia due to its advantage of favorable safety profiles. It is inconclusive about its benefits of long-term use and risks of dependence concerning Z-drugs. This study was to examine the trends of Z-drugs prescriptions stratified by elderly and non-elderly adult populations across times in Taiwan. **METHODS:** We conducted a secondary data analysis using 2000 and 2005 Longitudinal Health Insurance Database (2 million random samples). During the observation period (2003 to 2009), we defined adult outpatient users as those NHI adult beneficiaries (aged ≥18 year-old) ever made outpatient visits and Z-drug users as those ever prescribed with Z-drugs (zolpidem, zopiclone and zaleplon) in each year. The prescription prevalence rate of Z-drugs, its average number of defined daily dose (DDD) and prescriber specialties were stratified by age (elderly vs. non-elderly) and gender and compared across years. **RESULTS:** Among adult outpatient users, the prescription prevalence rate of Z-drugs was increased from 2003 to 2005, decreased in 2006 but maintained from 2007 to 2009. Female and non-elderly patients were predominant (all about 61%) across years. The average DDD within one year were increased over 7-year period (exception in 2006) and that among elderly users was always higher than non-elderly users. There were up to 8.3% of Z-drug users prescribed with over 365 DDD yearly (9.0% in elderly group). While 36% were prescribed by more than two specialties, the top 4 prescriber specialties were general/family medicine, internal medicine, psychiatry and neurology, regardless of age groups and years. **CONCLUSIONS:** Except in 2006, the Z-drugs prescription was gradually increased but maintained from 2003 to 2009 in Taiwan. Those common prescribers of Z-drugs should be warrant about its long-term uses for whole year, especially among the elderly.

NEUROLOGICAL DISORDERS – Cost Studies

PND5

BUDGET IMPACT ANALYSIS OF FINGOLIMOD FOR THE TREATMENT OF MULTIPLE SCLEROSIS IN COLOMBIA

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BACKGROUND: Multiple sclerosis (MS) is a neurodegenerative disease associated with long-term disability and significant social economic impact. Available first-line disease modifying treatments for MS (interferons and glatiramer acetate) have moderate efficacy and must be administered in daily or weekly injections. The introduction of fingolimod, a new molecule which superior efficacy in reducing MS relapses compared to interferon-beta 1a im justifies a budget impact analysis from the Colombian health system perspective. **OBJECTIVES:** To develop a budget impact analysis, for years 2012 to 2016, of the introduction of fingolimod in the Colombian health system, for the treatment of remitting relapsing multiple sclerosis (RRMS). **METHODS:** Using the perspective of the Colombian health system, we designed a budget impact model to compare costs of illness with and without the introduction of fingolimod for patients with RRMS. Clinical data and prevalence were obtained from published literature, costs were collected from local sources. A Monte Carlo simulation was performed as part of the sensitivity analysis. Exchange rate used was 1.786 Colombian pesos per US dollar (Jun 2011). No discount rate was used. **RESULTS:** Total annual net costs (from 2012 to 2016) for the scenario without fingolimod were, in million USD, $11.44, $12.16, $12.75, $13.47, and $14.18. In the fingolimod scenario net costs were: $11.46, $12.23, $12.83, $13.59 and $14.41. On the other hand, fingolimod was associated with 91 relapses averted in this five year period. Monte Carlo simulation did not show significant differences in costs between both scenarios. **CONCLUSIONS:** Under these assumptions, the introduction of fingolimod in the Colombian health care system does not imply a significant budget impact but represents an important reduction in the number of relapses.

PND6

BUDGET IMPACT ANALYSIS OF ANTIEPILEPTIC DRUGS IN THE TREATMENT OF LENNOX-GASTAUT SYNDROME

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OBJECTIVES: Lennox-Gastaut syndrome (LGS) is a debilitating form of epilepsy characterized by developmental disorders and high frequency of drop attacks that are often refractory to antiepileptic drug (AED) therapy. Clobazam was approved by the FDA in October 2011 for adjunctive treatment of seizures associated with LGS. We developed a model to compare the budget impact of adding clobazam to an AED portfolio containing topiramate, lamotrigine, and rufinamide in a hypothetical