Acute Hepatic Porphyrias (AHP) • Rare, serious, life-threatening metabolic disorder caused by a genetic mutation in heme biosynthesis, leads to accumulation of toxic intermediates porphobilinogen (PBG) and 5-aminolevulinate (ALA) (Figure 1) • Includes acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), and variegate porphyria (VP) • Characterized by occurrence of both acute disabling neurological attacks, requiring hospitalizations (mean length of stay 5-7 days) • Chronic debilitating disease symptoms impacting patients daily functioning and quality of life Healthcare Utilization and Expenditures in AHP • Given nature of attacks and chronic nature of disease it is important to understand healthcare utilization and expenditures associated with AHP to understand burden on healthcare system • EXPLORE (NCT02407846) study is the first observational, multinational, prospective, ongoing study designed to characterize the natural history and clinical management of patients with AHP where data are collected on healthcare utilization

Objectives • Estimate healthcare resource utilization and expenditures associated with treatment of patients with AHP who experience recurrent attacks (>3 attacks/year) or who receive prophylaxis to prevent attacks from perspective of US payer

Methods • Healthcare resource utilization data from EXPLORE (Figure 2) and unit costs of resources (charges and economic costs) from publicly available sources (Table 1) were used to estimate annual expenditure per patient • EXPLORE analysis included data for hospitalizations (including length of stay), ER visits, and GP/Specialist visits • Frequency of prophylaxis use was noted by health care provider and obtained from current medication log • Attack rate and duration during study period calculated • Use of hemin to manage attacks estimated based on expert opinion depending on duration of attack • Probabilistic sensitivity analysis (PSA) conducted to quantify uncertainty in model estimates • Uncertainty in annual resource utilization inputs obtained from EXPLORE was quantified in terms of mean and standard errors • Standard errors calculated from reported standard deviation and study sample size or otherwise calculated from data

Results

Patient and Disease Characteristics • 112 patients (mean 39.3 years, 89% female, 85% white/Caucasian) enrolled from 13 countries (US: 44%, EU (12 countries): 56%) • AHP subtype: 93% AIP, 3% HCP, and 4% VP • Commonly observed medical conditions included renal/vascular disorders (38%), nervous system disorders (31%), psychiatric/sleep disorders (30%), and dermatological disorders (22%) • Patients reported annualized attack rate of 4.9 with average duration of 7 days. Patients with hemin prophylaxis had annualized attack rate of 4.1 and those without prophylaxis had an attack rate of 5.5

Healthcare Utilization Rates • Patients reported frequent health care utilization use with an average of 4.5 hospitalizations lasting an average of 6.6 days (Table 2)

Summary • Healthcare utilization and expenditures for management of patients with AHP was high, driven by hospitalizations and hemin use, both for attacks and prophylactically • Estimated average annual expenditure/patient was $398,463 (95% CI: $328,303 - $475,477) to $655,418 ($482,278 - $847,448) depending on whether hospital costs or charges were used • Limitations included: - Annual expenditure/patient is presented as both hospital cost and charge; charge may overestimate annual expenditure/patient and cost may underestimate annual expenditure/patient - ICD-9 code is not specific to prophylaxis; thus hospitalizations costs may be under-represented due to disease severity, both costs and charges are presented - Indirect costs and other treatment costs (e.g., treating disease complications and adverse events) were not captured - Variability of patient’s clinical presentation results in differences in costs and utilization; thus a PSA was conducted to account for uncertainty around sample mean • Use of hemin was based on expert’s opinion and future studies should look at actual use of hemin • Treatment options that reduce attacks and thereby hospitalizations may result in lower economic burden on US health care system

This is the first study to estimate expenditures associated with management of AHP and represents a significant burden to US healthcare system; future studies should evaluate expenditures from claims databases and expenditures associated with management of AHP in other countries.