1. ABSTRACT

- **Title:** Burden of Illness Among Patients with Gout and Treated with Pegloticase
- **Keywords:** Gout, Pegloticase, Burden of Illness, Flare, Real-World Data
- **Rationale and Background:** In the United States, recent estimates indicate that up to 5.2% of the adult population is affected by gout[1,2] with a rise in prevalence occurring due to increasing obesity rates, dietary factors, and metabolic syndrome.[3] Annual healthcare costs for gout patients range from $11,839 (patients with 0-1 flares) to $14,842 (patients with 3+ flares), with costs driven primarily by ambulatory and inpatient costs.[4] Long-term management aims to prevent painful flares and complications by maintaining serum urate levels below the saturation point for crystal formation.[5] This is achieved through urate-lowering therapies (ULT).[6] Adherence to ULT is critical for effective gout management, but many patients struggle with medication adherence due to side effects, complex dosing regimens, and misconceptions about the chronic nature of the disease.[7] Patients who do not respond to traditional ULT have the option of pegloticase (KRYSTEXXA®) as a third-line treatment for severe, treatment-refractory, chronic gout.[8] To support both the ongoing value of pegloticase given the scarcity of recent data on gout and flare-related healthcare utilization and costs, this retrospective database study leveraged Inovalon's MORE^2 Registry®, the 100% Medicare Fee-for-Service (FFS) claims database, and the Norstella Laboratory database.
- **Research Question and Objectives**
  - To describe patient characteristics of a sample of patients with gout who initiate pegloticase treatment
  - To examine treatment patterns among a sample of patients with gout pre- and post-pegloticase initiation
  - To assess rates of gout flares pre- and post-pegloticase initiation
  - To assess gout- and flare-related healthcare resource utilization and costs among a sample of patients pre- and post-pegloticase initiation
- **Study Design:** This retrospective cohort study described patient characteristics and treatment patterns and compared gout flares, laboratory measures, and HCRU and cost between the pre- and post- pegloticase initiation periods (see Table 1 for details)

among gout patients in a real-world setting using administrative claims data from the MORE^2 Registry® and the 100% Medicare FFS database.

- **Setting:** The full study period spanned from 01 January 2016 to 31 December 2022, and the patient identification window (i.e. index period) was from 01 January 2018 to 31 December 2021.
- **Subjects and Study Size, Including Dropouts:** The final study population consisted of 203 adults diagnosed with gout who were newly treated with pegloticase between January 1, 2018, and December 31, 2021. Of the 1,198 pegloticase treated gout patients, 278 were continuously treated for 180-days. Of the 278 patients, 203 were newly treated adults with 360-days of continuous enrollment prior to and after initiating pegloticase.
- **Data Source(s) and Methods:** This study used data from the Inovalon MORE^2 Registry® and the 100% Medicare FFS database. This study was descriptive in nature and results were presented overall and by data source. All outcomes (flare, laboratory results, and healthcare resource utilization and cost) were measured prior to pegloticase initiation, the first 180-days after pegloticase initiation, and after 180-days after pegloticase initiation (this time period ended at the earliest of disenrollment, death or 12/31/2023). As a sensitivity analysis, all outcomes were measured during the time from pegloticase discontinuation until the earliest of disenrollment, death or 12/31/2023.
- **Variables:** Patient demographics were assessed on the index date and clinical characteristics were measured during the 12-month pre-index period. Treatment patterns, laboratory values, flares, gout-related and flare-related HCRU and expenditures were examined during all time periods (baseline period, follow-up1, follow-up2 and post completion, see Table 1 for details).
- **Results:** Overall, only 203 newly treated pegloticase patients with gout met all study inclusion criteria. Patients were an average age of 67.1 years, insured through Medicare FFS insurance (75.4%) and male (76.4%). Patients had a high comorbidity burden, consistent with an aging population.

  The use of pegloticase was consistent with treatment guidelines and was associated with a reduced flare episode rate, decreased use of opioids and oral glucocorticoids. Additionally, the observed serum urate values were lower during and after pegloticase treatment. In contrast, the eGFR values were consistent before, during, and after pegloticase treatment.

  Overall, HCRU related to gout and flare decreased following the initiation of pegloticase and were below baseline levels after completing pegloticase treatment.

Flare-related costs, like flare-related HCRU, decreased from baseline to post-pegloticase completion. In contrast, gout-related cost actually increased from baseline to post-pegloticase completion. However, limitations inherent in claims data, including the inability to capture disease severity or clinical decision-making rationale, may affect interpretation of cost trends. Further research is needed to discern the impact of pegloticase on gout related cost in this patient population.

- **Discussion:** The study findings demonstrated the benefit of pegloticase use and showed pegloticase was associated with a reduction in flare episode rates without an observed change in kidney function. Although patients with gout continued to incur high economic burden after completing pegloticase treatment (mean gout related cost of $7,450 PPPY post pegloticase completion), flare-related cost decreased from $619 PPPY to $134 PPPY pre vs post pegloticase completion, respectively. Consistent with total gout-related cost, gout-related ED cost increased from baseline ($77) to post-completion ($170). In contrast, gout-related inpatient cost reduced from $290 in the baseline period to $13 in both the follow-up2 and post-completion periods. Flare-related inpatient and ED costs reduced from baseline to follow-up2 and post-completion, following the trend of flare-related total cost. These findings are consistent with prior literature reporting improvements in serum urate values and flare rates following pegloticase initiation. Additionally, the observed persistence of clinical benefits after treatment completion suggests that pegloticase may provide durable therapeutic effects. Additional research is needed to evaluate the long-term effectiveness, durability of response, and cost-effectiveness of pegloticase across broader patient populations.