

CASE SERIES

# Retreatment with Pegloticase after a Gap in Therapy in Patients with Gout: A Report of Four Cases

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## ABSTRACT

**Introduction:** Pegloticase, a potent uricolytic biologic enzyme, has been shown to be an effective therapeutic option in patients with uncontrolled gout. However, there are limited data on clinical response after a gap in therapy and retreatment with pegloticase.

**Case Series:** This report describes four patients with chronic gout who were successfully managed with pegloticase and were retreated following a gap in therapy. Patient charts from a practice-based rheumatology clinic were retrospectively analyzed; four male patients, aged 70–75 years, with chronic gout and a more than 4-week gap in pegloticase therapy were reviewed. Before pegloticase treatment, patients had received allopurinol or febuxostat, but they

continued exhibiting symptoms, including visible tophi and serum uric acid (SUA) levels of 5.2–10.2 mg/dL (309–607  $\mu\text{mol/L}$ ), despite oral urate-lowering therapy. The first pegloticase treatment (8-mg infusion every 2 weeks) lasted 22–124 weeks. Pegloticase resolved tophi and improved SUA to below 1.5 mg/dL (less than 89  $\mu\text{mol/L}$ ); however, patients discontinued pegloticase because of symptom resolution, poor adherence, or personal reasons. Following treatment gaps (12–156 weeks), symptoms and SUA levels increased and patients were retreated with pegloticase (4–147 weeks). In three of four patients, reinitiating pegloticase lowered SUA levels to below 1.0 mg/dL (less than 59  $\mu\text{mol/L}$ ) and resolved symptoms. One patient experienced an infusion reaction and discontinued; no infusion reactions, gout flares, or adverse events occurred among the other three patients. **Conclusion:** Retreatment with pegloticase after a gap in therapy appears to be an effective and tolerated option in prior responders.

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**Keywords:** Chronic gout; Pegloticase; Retreatment; Therapy gap

## INTRODUCTION

Chronic gout is one of the most common forms of inflammatory arthritis in the USA [1]. Patients with uncontrolled gout often

experience painful flares, resulting from elevated serum uric acid (SUA) levels and significant urate deposition [2]. Patients with gout often have numerous comorbid conditions requiring medical management, and many patients may require referral to a rheumatologist for gout management [3].

In clinical practice, many factors influence the resolution and remission of gout. A retrospective analysis linking medical records with patient questionnaire responses demonstrated that adherence to urate-lowering therapy (ULT) was associated with achieving SUA goals and symptomatic improvement [4]. However, patient adherence to ULT regimens is a particular challenge. One exploratory study found that some patients cited increased frequency of gout flares during initial treatment with allopurinol as the reason for treatment discontinuation [5]. Educating patients about the occurrence of flares at the onset of therapy is an important component of gout management but is not always sufficiently explained [6]. In addition, it often requires years of remaining adherent on ULT to resolve tophi and improve symptoms over time [7].

Some patients with chronic gout do not adequately respond to conventional ULT [8] and, therefore, have limited treatment options for lowering urate levels. Pegloticase (PEGylated recombinant mammalian uricase enzyme) is a potent uricolytic biologic enzyme therapy that rapidly converts existing uric acid into the more soluble and easily eliminated substrate allantoin [9]. Pegloticase is an effective therapeutic option in patients with uncontrolled gout and has been shown to decrease SUA levels within 24 h of the first infusion [10]. Treatment with pegloticase markedly decreases urate burden and promotes tophi clearance [10–13]. Notably, patients treated with pegloticase may experience a high gout flare rate during the first 3 months of therapy with a subsequent decline in the frequency of flares thereafter.

There are limited data on the clinical response to pegloticase following a gap in therapy. Two replicate, 6-month, randomized, placebo-controlled trials found that 42% of patients initially treated with pegloticase responded to therapy (defined as maintaining a

plasma uric acid level less than 6.0 mg/dL [less than 357  $\mu\text{mol/L}$ ] for at least 80% of the treatment period) [10]. In a 2.5-year open-label extension of these studies, patients continued on pegloticase following a 12- to 223-day gap in therapy [14]. This open-label extension study demonstrated that, among patients who responded to pegloticase in the original trial, treatment continuation reduced SUA levels, tophi burden, and gout flares [13], with 29 of 34 responders (85%) meeting criteria for gout remission [14, 15]. An additional analysis of pegloticase responders, with a gap of at least 28 days from the last dose in the pivotal trials to the first dose in the open-label extension, demonstrated that most of these patients maintained an SUA-lowering response to pegloticase upon retreatment [16]. However, it is unknown if patients in a real-world clinical setting can successfully reinstate pegloticase therapy after a gap in treatment.

The present case series retrospectively evaluated the clinical outcomes of four patients with chronic gout who, after initial successful treatment with pegloticase, were retreated with pegloticase following a gap in therapy at a single rheumatology clinic. A secondary objective was to determine if retreatment with pegloticase after a gap in therapy was associated with any adverse outcomes.

Deidentified patient charts were retrospectively reviewed to identify patients with (1) chronic gout and (2) a prolonged (more than 4-week) lapse in pegloticase treatment. Before pegloticase initiation, the patients had ongoing symptoms of gout despite oral ULT. Demographics and disease characteristics of selected patients were recorded at baseline, including relevant comorbidities (diabetes mellitus, hypertension, coronary artery disease, hyperlipidemia, and chronic kidney disease), presence or absence of visible tophi, and duration of gout. Incidence of symptoms, adverse events (AEs), and laboratory profiles (serum creatinine [sCR], estimated glomerular filtration rate [eGFR], and SUA) were collected throughout the duration of therapy; reasons for treatment discontinuation were recorded when possible. Informed consent was obtained from all patients in the case series.

## CASE SERIES

### Baseline Characteristics and Disease History

Four male patients, aged 70–75 years, with chronic gout and a prolonged gap (more than 4 weeks) in pegloticase therapy were selected for review. A schematic overview of each patient's treatment and gaps in therapy is presented in Fig. 1.

At baseline evaluation, three patients (patients 1, 2, and 3) had comorbid coronary artery disease and two patients each had hypertension (patients 1 and 2) and chronic kidney disease (patients 2 and 3); all other comorbidities occurred in only one patient (Table 1). Before pegloticase treatment, patients were typically managed with allopurinol 300 mg daily, with the exception of patient 3 who received allopurinol 300 mg daily and then switched to febuxostat 80 mg (Table 2). Patients had also received at least 6 months of prophylaxis with colchicine 0.6 mg once or twice daily, depending on tolerance, and/or prednisone 5 mg daily. All patients had ongoing manifestations of uncontrolled gout, despite oral ULT (Table 1). SUA levels before the initial course of pegloticase therapy ranged from 5.2 to 10.2 mg/dL (309–607  $\mu\text{mol/L}$ ); eGFR and sCR levels ranged from 33 to greater than 60 mL/min/1.73 m<sup>2</sup> and 0.9 to 2.04 mg/dL (79.6–180.3  $\mu\text{mol/L}$ ), respectively (Table 3; Fig. 1). For patient 4, there was a gap of approximately 1 year between his initial evaluation and treatment initiation, as

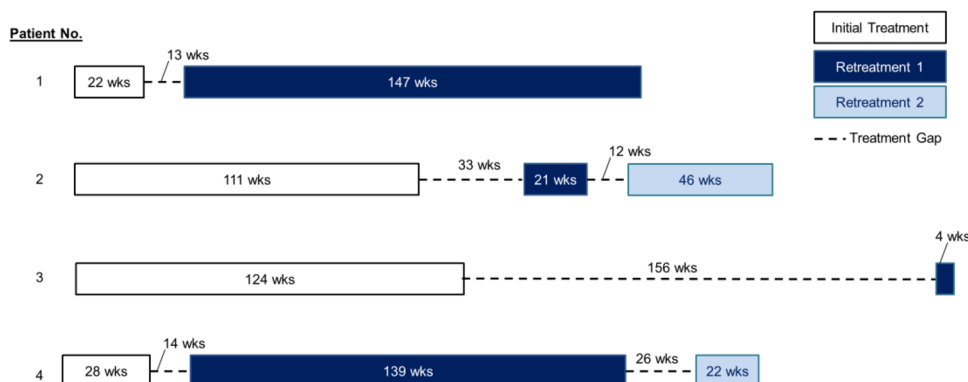
pegloticase was not yet available; both values are shown in Table 3.

### Initial Treatment

Consistent with standard of care, patients received pegloticase therapy (8-mg infusion every 2 weeks [Q2W]) after inadequate response to conventional oral ULT. To minimize the risk of anaphylaxis and infusion reactions (IRs), patients were pretreated with an antihistamine (diphenhydramine HCl 50 mg per os) and intravenously administered (IV) hydrocortisone 200 mg before pegloticase infusion. Patients also received concomitant prednisone 5 mg daily throughout the duration of pegloticase therapy.

Initial pegloticase treatment lasted 22–124 weeks (Table 2). As patient 3 spent 6 months of the year out of state, he underwent periods of treatment by another physician; therefore, the exact number of doses he received is not available. Patient 4 had low adherence; an occasional 3-week and one 5-week lapse occurred between treatments. During pegloticase treatment, patients' SUA levels improved to below 1.5 mg/dL (less than 89  $\mu\text{mol/L}$ ) (Fig. 2). eGFR and sCR levels were largely stable while on pegloticase therapy (Table 3). Two patients reported gout flares, one minor (patient 1) and one severe (patient 3, lasting 1 week). No patients experienced IRs or other AEs during the first pegloticase treatment (Table 4).

Two patients discontinued pegloticase because of physician's assessment following



**Fig. 1** Schematic of each patient's pegloticase treatment periods and gaps in pegloticase therapy. wks weeks

**Table 1** Demographics and baseline characteristics

Parameter	Patient 1	Patient 2	Patient 3	Patient 4
Age, years	74	70	74	75
Sex	Male	Male	Male	Male
Weight, kg	140	76	112	85
Disease duration, years	30	40	15	> 30
Tophi status	Visible	Visible	Visible	Visible
Comorbidities	Hypertension, coronary artery disease, diabetes mellitus, obesity	Hypertension, coronary artery disease, chronic kidney disease	Coronary artery disease, chronic kidney disease, osteoarthritis	Increased lipids

resolution of symptoms (patients 2 and 3). Pegloticase was discontinued in patient 4 as a result of poor adherence with infusions and because gout-related symptoms had almost entirely resolved. Patient 1 discontinued pegloticase because of personal reasons (death of spouse) (Table 2).

### First Treatment Gap and Retreatment

The length of the first treatment gap ranged broadly between patients, with 13 to 156 weeks elapsing between doses. During the treatment gap, patients 2 and 3 received febuxostat 80 mg daily and patient 4 received allopurinol 500 mg daily; therapy during the pegloticase treatment gap for patient 1 was not available (Table 2). Following the gap in therapy, patients experienced ongoing symptoms of gout. Patients 1 and 2 developed tophi, patients 2 and 4 experienced gout flares, and patient 3 had fatigue (Table 4). Elevated SUA levels were observed in all patients, ranging from 8.3 to 10.8 mg/dL (494–642  $\mu\text{mol/L}$ ) (Table 3; Fig. 2); for patients 1, 3, and 4, eGFR ranged from 33 to 86 mL/min/1.73 m<sup>2</sup> and sCR ranged from 0.9 to 2.0 mg/dL (79.6–176.8  $\mu\text{mol/L}$ ) (Table 3).

Patients were reinitiated on pegloticase therapy at 8 mg Q2W concurrently with concomitant prednisone 5 mg daily. As during the initial pegloticase treatment, patients were

pretreated with oral diphenhydramine HCl 50 mg and IV hydrocortisone 200 mg. Retreatment with pegloticase lasted from 4 to 147 weeks (Table 2).

The duration of retreatment for patient 3 lasted only 4 weeks because of an IR following the second dose of pegloticase. Before his first retreatment infusion, patient 3 had an SUA of 8.6 mg/dL (512  $\mu\text{mol/L}$ ). Before his second dose, his SUA was 8.9 mg/mL (529  $\mu\text{mol/L}$ ) (Table 3; Fig. 2). Despite preinfusion treatment with oral diphenhydramine HCl 50 mg and IV hydrocortisone 200 mg, the resulting IR caused chest discomfort and decreased blood pressure, neither of which required an emergency department visit. The patient discontinued pegloticase treatment and continues to be treated with febuxostat 80 mg daily. As of his last evaluation, the patient had an SUA of 4.6 mg/dL (274  $\mu\text{mol/L}$ ) (Table 3).

With the exception of patient 3, SUA levels were low during pegloticase retreatment, and patients 1, 2, and 4 did not experience IRs, gout flares, or other AEs (Table 4; Fig. 2). Patient 1 discontinued pegloticase because of resolution of gout-related symptoms. He continues to be treated with allopurinol 300 mg and lesinurad 200 mg daily. Approximately 3 months after discontinuation of pegloticase, his SUA was 6.5 mg/dL (387  $\mu\text{mol/L}$ ); his eGFR and sCR levels were 62 mL/min/1.73 m<sup>2</sup> and 1.21 mg/dL

**Table 2** Summary of pegloticase treatment

	Patient 1	Patient 2	Patient 3	Patient 4
Initial pegloticase treatment				
Treatment before pegloticase	Allopurinol 300 mg QD	Allopurinol 300 mg QD	Allopurinol 300 mg QD; febuxostat 80 mg QD	Allopurinol 300 mg QD
Duration of initial pegloticase treatment, weeks (doses)	22 (11)	111 (56)	124 <sup>a</sup>	28 (14) <sup>b</sup>
Reason for discontinuation	Patient choice <sup>c</sup>	Resolution of symptoms	Resolution of symptoms	Patient choice <sup>d</sup>
First pegloticase retreatment				
Length of pegloticase treatment gap, weeks	13	33	156	14
Treatment regimen during pegloticase treatment gap	Unknown	Febuxostat 80 mg QD	Febuxostat 80 mg QD	Allopurinol 500 mg QD
Duration of pegloticase retreatment, weeks (doses)	147 (70)	21 (11)	4 (2)	139 (64)
Reason for discontinuation	Resolution of symptoms	Patient choice <sup>e</sup>	Adverse event <sup>f</sup>	Patient choice <sup>g</sup>
Second pegloticase retreatment				
Length of pegloticase treatment gap, weeks	NA	12	NA	26
Treatment regimen during pegloticase treatment gap	NA	Febuxostat 80 mg QD	NA	Unknown
Duration of pegloticase retreatment, weeks (doses)	NA	46 (24)	NA	22 (9)
Reason for discontinuation	NA	Resolution of symptoms	NA	Resolution of symptoms

**Table 2** continued

	Patient 1	Patient 2	Patient 3	Patient 4
After final pegloticase treatment				
Treatment regimen	Allopurinol 300 mg + lesinurad 200 mg QD	Allopurinol 100 mg BID	Febuxostat 80 mg + lesinurad 200 mg QD	Allopurinol 300 mg QD

*BID* twice daily, *NA* not applicable, *QD* once daily

<sup>a</sup> Number of doses could not be confirmed as patient was treated at another office during two periods over the course of treatment

<sup>b</sup> Patient was frequently nonadherent to treatment plan; an occasional 3-week and one 5-week lapse occurred between doses

<sup>c</sup> Death of spouse

<sup>d</sup> Poor treatment adherence

<sup>e</sup> Insurance complications

<sup>f</sup> Infusion reaction with chest discomfort and decreased blood pressure, neither of which required an emergency department visit

<sup>g</sup> Patient preferred to be treated during the summer and discontinued in the winter because of poor veins

(107.0  $\mu\text{mol/L}$ ), respectively (Table 3). Patients 2 and 4 discontinued pegloticase because of patient choice; patient 2 experienced insurance complications and patient 4 indicated that his veins were poor during the winter and chose to discontinue pegloticase treatment until the summer (Table 2).

### Second Treatment Gap and Retreatment

Patients 2 and 4 reinitiated pegloticase after a second gap in therapy of 12 and 26 weeks, respectively. During the gap, patient 2 received febuxostat 80 mg daily; treatment for patient 4 during this time was not available (Table 2). After the second gap in treatment, patient 2 developed tophi and patient 4 experienced a gout flare. SUA levels before retreatment for patients 2 and 4 were 2.4 mg/dL (143  $\mu\text{mol/L}$ ) and 11.9 mg/dL (708  $\mu\text{mol/L}$ ), respectively (Table 3; Fig. 2).

Treatment with pegloticase resumed at 8 mg Q2W with concomitant prednisone 5 mg daily. As during previous pegloticase treatments, patients were pretreated with diphenhydramine HCl 50 mg per os and hydrocortisone 200 mg IV before pegloticase infusion. Retreatment lasted 46 weeks for patient 2 and 22 weeks for patient

4 (Table 2). During this time, neither patient experienced IRs, flares, or other AEs, and SUA levels for both patients were below 1.0 mg/dL (less than 59  $\mu\text{mol/L}$ ) (Table 4; Fig. 2).

Both patients ultimately discontinued pegloticase treatment because of symptom resolution (Table 2). One month after his last infusion with pegloticase, patient 2 had an SUA of below 1.0 mg/dL (less than 59  $\mu\text{mol/L}$ ); his eGFR and sCr levels were 42 mL/min/1.73 m<sup>2</sup> and 1.70 mg/dL (150.3  $\mu\text{mol/L}$ ), respectively, and he reported no gout flares (Tables 3, 4; Fig. 2). He continues to be treated with allopurinol 100 mg twice daily (Table 2). Similarly, patient 4 reported no flares 4 months after his last treatment and he continues to be treated with allopurinol 300 mg daily (Table 2).

## DISCUSSION

Gout affects approximately 8.3 million people in the USA and is associated with poor quality of life, increased hospitalization, and morbidity [1, 2, 17, 18]. While treatment options such as allopurinol and febuxostat are typically used as first-line therapies, some patients with gout do not adequately respond to traditional ULTs and continue to have elevated SUA, tophi, and gout

**Table 3** SUA and markers of kidney function over time

Parameter	Patient 1	Patient 2	Patient 3	Patient 4
Initial pegloticase treatment				
Before pegloticase treatment				
SUA, mg/dL	10.2	5.9	10.0	6.0 <sup>a</sup> (5.2 <sup>b</sup> )
eGFR, mL/min/1.73 m <sup>2</sup>	63	33	58.5	> 60
sCR, mg/dL	1.15	2.04	1.3	0.9
During pegloticase treatment				
SUA, mg/dL	< 0.5	< 1.5	< 0.5–1.6	< 0.5
eGFR, mL/min/1.73 m <sup>2</sup>	54.6	39–49	53–58	–
sCR, mg/dL	1.3	1.50–1.76	1.3–1.4	0.9
End of first pegloticase treatment				
SUA, mg/dL	< 0.5	< 1.0	< 0.5	< 0.5
eGFR, mL/min/1.73 m <sup>2</sup>	–	–	–	–
sCR, mg/dL	–	–	–	–
First pegloticase retreatment				
Before pegloticase retreatment				
SUA, mg/dL	10.8	8.3	8.6	8.3
eGFR, mL/min/1.73 m <sup>2</sup>	66.0	–	33	86
sCR, mg/dL	1.1	–	2.0	0.9
During pegloticase retreatment				
SUA, mg/dL	< 1.0	< 1.0	8.9	< 1.0
eGFR, mL/min/1.73 m <sup>2</sup>	59.5–72	43–44	–	63–128
sCR, mg/dL	1.07–1.2	1.65–1.68	–	0.5–1.20
Follow-up				
SUA, mg/dL	< 1.0 <sup>c</sup> (6.5) <sup>d</sup>	NA	7.3 <sup>e</sup> (4.6) <sup>f</sup>	NA
eGFR, mL/min/1.73 m <sup>2</sup>	61 <sup>c</sup> (62) <sup>d</sup>	NA	59.5 <sup>e</sup> (49.7) <sup>f</sup>	NA
sCR, mg/dL	1.23 <sup>c</sup> (1.21) <sup>d</sup>	NA	1.2 <sup>e</sup> (1.4) <sup>f</sup>	NA
Second pegloticase retreatment				
Before pegloticase retreatment				
SUA, mg/dL	NA	< 1.0 <sup>g</sup> (2.4) <sup>h</sup>	NA	2.7 <sup>i</sup> (11.9) <sup>j</sup>
eGFR, mL/min/1.73 m <sup>2</sup>	NA	39	NA	–
sCR, mg/dL	NA	1.84	NA	–
During pegloticase retreatment				
SUA, mg/dL	NA	< 1.0	NA	< 1.0

**Table 3** continued

Parameter	Patient 1	Patient 2	Patient 3	Patient 4
eGFR, mL/min/1.73 m <sup>2</sup>	NA	43–52	NA	–
sCR, mg/dL	NA	1.43–1.67	NA	–
Follow-up				
SUA, mg/dL	NA	< 1.0 <sup>k</sup>	NA	–
eGFR, mL/min/1.73 m <sup>2</sup>	NA	42	NA	–
sCR, mg/dL	NA	1.70	NA	–

To convert mg/dL to  $\mu\text{mol/L}$  for SUA, multiply by 59.485. To convert mg/dL to  $\mu\text{mol/L}$  for sCR, multiply by 88.4  
 – Indicates not available, *eGFR* estimated glomerular filtration rate, *NA* not applicable, *sCR* serum creatinine, *SUA* serum uric acid

<sup>a</sup> Taken approximately 1 year before initiating therapy

<sup>b</sup> Taken approximately 6 months before initiating therapy

<sup>c</sup> Taken approximately 1 week after the last infusion

<sup>d</sup> Taken approximately 13 weeks after the last infusion

<sup>e</sup> Taken approximately 6 weeks after the last infusion

<sup>f</sup> Taken approximately 15 weeks after the last infusion

<sup>g</sup> Taken approximately 11 weeks after the last infusion

<sup>h</sup> Taken approximately 12 weeks after the last infusion

<sup>i</sup> Taken approximately 10 weeks after the last infusion

<sup>j</sup> Taken approximately 24 weeks after the last infusion

<sup>k</sup> Taken approximately 4 weeks after the last infusion

flares, leaving them with few treatment options [17, 19, 20]. Pegloticase has been shown to decrease SUA levels and tophi burden and increase health-related quality of life in patients with an inadequate response to other therapies [8–10, 13, 14, 16].

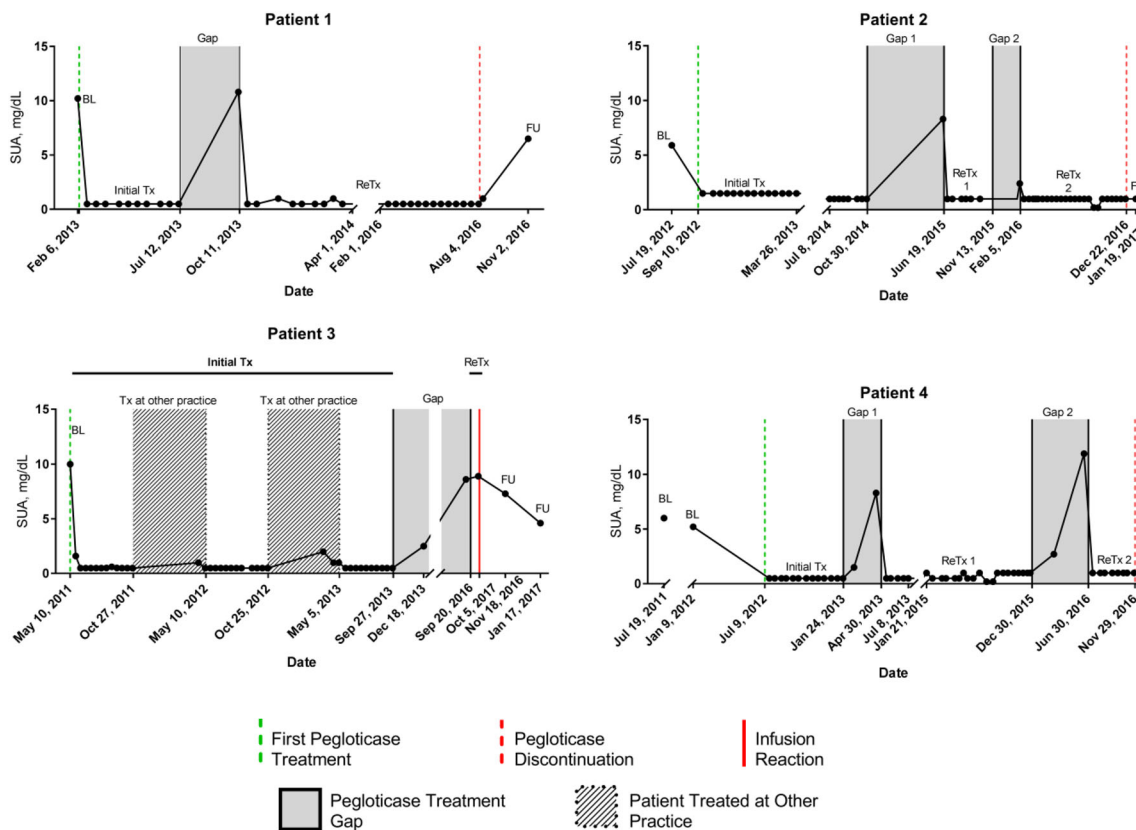
A particular challenge in the treatment of gout is patient adherence. In this rheumatology practice, the treating physician is a solo practitioner with over 35 years in practice; gout therapy at his practice involves patient education to improve adherence to the treatment regimen. A number of factors can lead to poor adherence, including AEs at treatment onset, concerns about future AEs, or financial difficulties related to the cost of therapy [21]. However, evidence suggests that patient education concerning the temporary increase in gout flares at the onset of ULT is lacking and may be a contributing factor to low compliance and

adherence [6, 22]. Importantly, patients with poor adherence are less likely to achieve or maintain an SUA level of below 6.0 mg/dL (less than 357  $\mu\text{mol/L}$ ) compared with adherent patients [23, 24].

Pegloticase is an option for patients with uncontrolled gout who cannot take traditional oral ULT or in whom these medications are contraindicated. However, the dosing regimen of pegloticase requires infusions Q2W, with preinfusion SUA checks before each infusion. For a variety of reasons, patients such as the four cases presented here missed doses and experienced gaps during their pegloticase treatment course.

As patients may reinstate pegloticase treatment after missing doses or upon re-emergence of their gout signs and symptoms, it is important to understand how a temporary gap may affect subsequent retreatment. In a subanalysis





**Fig. 2** SUA levels over time during treatment with pegloticase, pegloticase treatment gaps, and retreatment(s) with pegloticase in each patient. BL baseline, FU follow-up, ReTx retreatment, SUA serum uric acid, Tx

treatment. To convert mg/dL to  $\mu\text{mol/L}$  for SUA, multiply by 59.485

**Table 4** AEs and disease symptoms during pegloticase therapy

Parameter	Patient 1	Patient 2	Patient 3	Patient 4
Initial pegloticase treatment				
AEs during initial treatment	Mild flare	None	Severe flare (lasting 1 week)	None
First pegloticase retreatment				
Symptoms after gap in therapy	Tophi	Tophi and gout flares	Fatigue	Gout flares
AEs during retreatment	None	None	Infusion reaction <sup>a</sup>	None
Second pegloticase retreatment				
Symptoms after gap in therapy	NA	Tophi	NA	Gout flare
AEs during retreatment	NA	None	NA	None

AEs adverse events, NA not applicable

<sup>a</sup> Infusion reaction with chest discomfort and decreased blood pressure, neither of which required an emergency department visit

of two randomized clinical trials, most pegloticase responders with at least a 28-day gap in therapy ( $n = 10/14$  [71%]) maintained an SUA below 6.0 mg/dL (less than 357  $\mu\text{mol/L}$ ) upon retreatment; furthermore, logistic regression indicated that the length of the treatment gap did not correlate with any urate-lowering effects upon reinitiation [16]. Therefore, in the clinical trial setting, it appears that discontinuation of pegloticase did not diminish its effectiveness or raise any new safety signals upon retreatment.

In this case series, the efficacy of pegloticase in four patients with varying gaps in therapy (12–156 weeks) was retrospectively evaluated in routine clinical practice. The responder rate to retreatment was similar to that observed in clinical trials; in three of four patients (75%) who reinitiated therapy, pegloticase effectively reduced SUA levels and resolved tophi with no gout flares, IRs, or other AEs. One patient experienced an IR, which was resolved without emergency medical intervention and led to discontinuation of pegloticase retreatment. Renal function remained relatively stable for each patient during treatment with pegloticase. Patients also self-reported improvements in quality of life to the physician while receiving pegloticase therapy.

Without application of the preinfusion SUA stopping rules, which suggest ceasing treatment in the event of an SUA increase (at least 6.0 mg/dL [at least 357  $\mu\text{mol/L}$ ]) following pegloticase infusion, 26% of patients in clinical trials experienced IRs [25]. However, when the SUA stopping rule was applied, this incidence dropped by nearly one-half, to 14% of patients. IRs from pegloticase treatment commonly include chest discomfort, flushing, and dyspnea during or immediately following an infusion. The development of high titers of anti-pegloticase antibodies, which are believed to interfere with enzymatic function of pegloticase, can precipitate an IR. Therefore, while on pegloticase therapy, an increase in preinfusion SUA can reflect a decrease in pegloticase efficacy and can be used as a biomarker for the risk stratification of an IR [25, 26]. In the case of the IR experienced by patient 3, his elevated SUA before his last infusion (SUA = 8.9 mg/dL [529  $\mu\text{mol/L}$ ]) would have ideally deterred the subsequent

infusion, potentially preventing the IR that occurred. While anti-pegloticase antibodies were not measured in these patients (aged 70–75 years), a previous analysis of two clinical trials found that low titers of antibodies and older age were both associated with higher response rates to pegloticase, suggesting that age may influence the development of anti-pegloticase antibodies and treatment responsiveness [26]. Further study of the effect of repeated treatment on the immunogenicity of pegloticase is needed but logistically challenging.

This report describes the pegloticase retreatment experience of one single-practitioner rheumatology clinic and, as such, several limitations may be considered. There are similarities between the cases, although all data points are purely observational. Given the indication and best-practice use with pegloticase as a Q2W medication, a controlled study on retreatment with pegloticase after a gap in therapy is unlikely to occur.

## CONCLUSIONS

In three of the four cases presented here, retreatment with pegloticase in prior responders was as effective and safe as during initial treatment. The goal of this publication was to provide a real-world look at the retreatment experience with pegloticase following a gap in therapy at one rheumatology clinic. When treating patients with uncontrolled gout with pegloticase who were SUA responders but discontinued therapy for any reason, it appears that retreatment may be an effective and tolerable therapeutic option.

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**Compliance with Ethics Guidelines.** Informed consent was obtained from all patients in the case series. We thank the participants of the study.

**Data Availability.** The data sets analyzed during the current study are not publicly available, as they contain protected health information, but are available from the corresponding author on reasonable request.

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