The impact of safety labeling changes on parathyroid hormone analog utilization and persistence

AUTHORS: Stefanie Pitts, PharmD[1] Douglas Mager, MS[2] Gail Bridges, PharmD[1] Timothy Dollear, PhD[2], Mary Dorholt, PharmD[1]
[1]ACCREDO, MEMPHIS, TENNESSEE, UNITED STATES
[2]EVERNORTH, BLOOMFIELD, CONNECTICUT, UNITED STATES

Accredo
By EVERNORTH

Background:

- Parathyroid hormone (PTH) analog black box warning for osteosarcoma risk limited class to two years lifetime exposure
- Additional safety data resulted in prescribing information (PI) changes
  - BBW removal in 2020 (teriparatide) and 2021 (abaloparatide)
  - Extended teriparatide use may be considered in those at high fracture risk.
- Limited osteoporosis treatment options, combined with safety and tolerability considerations may drive changes in PTH analog utilization
- Successful management seeks to balance adherence with evidence-based utilization

30% bisphosphonate intolerance or contraindication[1]

47% osteoporosis patients with high fracture risk[2]

PI updates may significantly influence PTH analog utilization

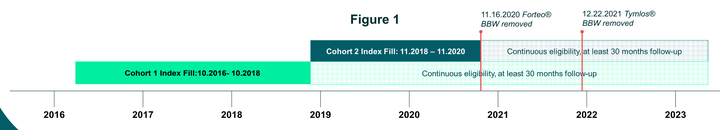
Objective:

- Evaluate whether PI changes altered PTH analog utilization
- Observe the impact of specialty management on PTH analog duration and 24-month persistence.

Methods:

- Retrospective pharmacy claims cohort analysis, using commercial PBM claims database.
- Patients continuously eligible for ≥30 months, having an index fill of a PTH analog, and no prior use in 6 months. Cox regression was used to control for variances (**Table 1)**
- Cohort assignment based on index fill relative to November 2020 PI update. Cohort one started ≥25 months before PI change, and cohort two started within 24 months of PI change (**Figure 1**)
- Utilization >24 months, persistence to 24 months, and follow-on treatment were measured

Figure 1



Results:

- Extended PTH analog use >24 months was significantly higher in cohort 2 (2.9% vs 4.5%, p < 0.01) (**Table 2)**
- Specialty-managed patients in cohort one had the lowest incidence of extended use (1.9% vs 4.5%, p < 0.01). Extended use did not significantly differ between cohorts in non-specialty channels **(Table 2)**
- After PI change, persistence up to 24-months increased 1.6% (p <0.01) and was better overall for specialty by 10.3%, controlling for age, gender and channel (p < 0.01) **(Figure 2)**
- Incidence of repeat PTH analog course did not differ between cohorts one and two (16.7% and 15.1%, p = 0.09) (**Table 3)**

Table 1

Demographics	Age, in yrs* (SD)	% Female†	% specialty managed‡
Cohort 1 (n=3571)	69.3 (±11.3)	85.1%	48.6%
Cohort 2 (n=2480)	66.0 (±11.5)	82.3%	42.3%

*p<0.01, †p<0.01, ‡p<0.01

Table 2

Treatment Duration > 24 months					
Incidence by cohort "pre-" vs "post-" PI change					
	N	Pct	N	Pct	P-value
Overall population	Cohort 1 (n=3571)		Cohort 2 (n=2480)		
	102	2.9%	112	4.5%	p=0.0006
Bi-variate by cohort & channel					
	N	Pct	N	Pct	P-value
Specialty-managed	Cohort 1 (N=1834)		Cohort 2 (N=1430)		
	34	1.9%	65	4.5%	p < 0.0001
Non-specialty	Cohort 1 (N=1737)		Cohort 2 (N=1050)		
	68	3.9%	47	4.5%	p=0.4703

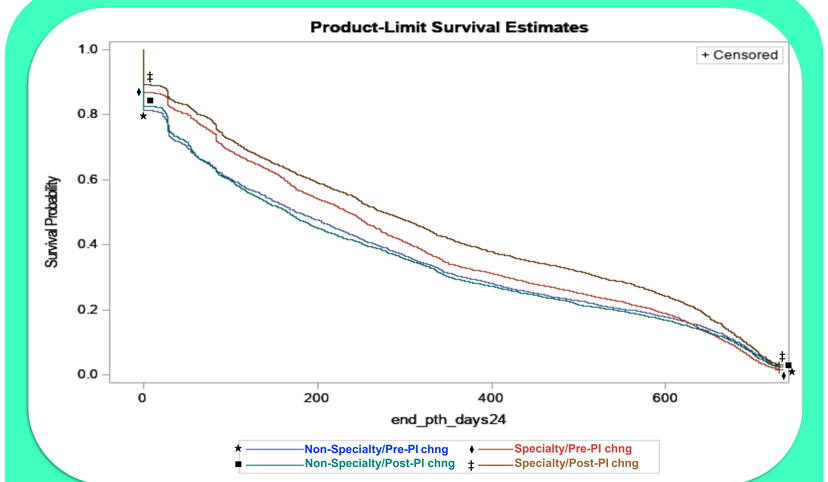
Table 3

Follow-on Osteoporosis treatment by Cohort					
	Cohort 1 (pre-)		Cohort 2 (post-)		
	N	Pct	N	Pct	P-value
PTH Analog (repeat course)	581	16.7%	357	15.1%	0.09
Bisphosphonate	377	10.9%	288	12.2%	0.13
Hormone replacement tx	320	9.2%	220	9.3%	0.93
RANKL Inhibitor	185	5.3%	91	3.8%	<0.01
Sel. estrogen receptor modifier	29	0.8%	15	0.6%	0.38
Calcitonin	30	0.9%	18	0.8%	0.66
SERM/Estrogen Combo	6	0.2%	0	0.0%	0.04
Sclerostin inhibitor	2	0.1%	7	0.3%	0.02
Total continuing any treatment	**3469**	**44.1%**	**2368**	**42.1%**	

Limitations:

- Follow-on treatment analysis is limited to pharmacy benefit claims.

Figure 2



Cohort/Channel Interaction Cox Regression

Parameter	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
Specialty/Pre-PI change	0.0696	0.0345	4.0779	0.0434	1.0720
Non-Specialty/Pre-PI change	-0.0313	0.0402	0.6050	0.4367	0.9690
Specialty/Post-PI change	**-0.1091**	**0.0376**	**8.4079**	**0.0037**	**0.8970**
Age	0.0011	0.0012	0.8730	0.3501	1.0010
Male	-0.0522	0.0360	2.0967	0.1476	0.9490

Conclusions:

- PTH analog PI changes were associated with more extended use >24 months.
- Pharmacy claims indicate that a repeat PTH analog course was common before and after the label changes.
- Specialty-managed patients were less likely to exceed two-year use limits before PI changes, but matched other channels' rate of extended use afterward.
- After PI changes, fewer specialty-managed patients stopped therapy early, demonstrating better persistence at 24 months compared to non-specialty channels.
- Specialty management of PTH analogs reflects labeled use over time, and balances treatment persistence with use limits.

References:

1. Adler RA, El-Hajj Fuleihan G, Bauer DC, et al. Managing Osteoporosis in Patients on Long-Term Bisphosphonate Treatment: Report of a Task Force of the American Society for Bone and Mineral Research [published correction appears in J Bone Miner Res. 2016 Oct;31(10):1910]. *J Bone Miner Res*. 2016;31(1):16-35. doi:10.1002/jbmr.2708
2. Diffenderfer BW, Wang Y, Pearman L, Pyrih N, Williams SA. Real-World Management of Patients With Osteoporosis at Very High Risk of Fracture. *J Am Acad Orthop Surg*. 2023;31(6):e327-e335. doi:10.5435/JAAOS-D-22-00476