# Secukinumab dose optimization in adult psoriasis patients: A retrospective, multicenter case series

Michelle Phung, BMSc,[a] Jorge R. Georgakopoulos, BSc,[b] Arvin Ighani, BMSc,[c] Lyne Giroux, MD, FRCPC,[d] and Jensen Yeung, MD, FRCPC[e,f]
*Toronto, London, Sudbury, and Waterloo, Canada*

***Key words:*** dose escalation; dose optimization; psoriasis; secukinumab.

## INTRODUCTION

Secukinumab is an interleukin-17A monoclonal antibody approved in 2015 in Canada and the United States for the treatment of moderate-to-severe psoriasis in adult patients.[1,2] The current approved dosing regimen is 300 mg subcutaneous at weeks 0, 1, 2, 3, and 4, followed by monthly maintenance dosing starting at week 8.[3] In clinical practice, some patients only partially respond to this dosing schedule or display disease relapse during the interim between maintenance injections. Some clinicians treat these patients by using off-label secukinumab dosing regimens, which involves increasing the frequency of maintenance dosing. There are scant data on off-label regimens for secukinumab; therefore, this case series aims to evaluate the effectiveness and safety of secukinumab dose optimization.

We performed a retrospective chart review of adult patients treated with an off-label secukinumab up-dose regimen for psoriasis at 3 dermatology clinics in Ontario, Canada. Research Ethics Board approval was obtained at Sunnybrook Health Sciences Centre in Toronto. Effectiveness after dose optimization was measured using a 75% reduction from baseline in the Psoriasis Area and Severity Index (PASI-75), or a Physician Global Assessment (PGA) score of 0 (clear) or 1 (almost clear) if PASI scores were not provided. To assess safety, adverse events (AEs) were recorded.

*Abbreviations used:*

| | |
|---|---|
| AE: | adverse event |
| PASI: | Psoriasis Area and Severity Index |
| PASI-75: | 75% reduction from baseline PASI score |
| PGA: | Physician Global Assessment |

## CASES

Case summaries are presented in Table I.

### Case 1

Case 1 was a 50-year-old woman with psoriasis on the arms, legs, and trunk. She did not achieve PASI-75 after 12 weeks of secukinumab treatment. At week 52, she had a PASI of 5.1, and her dose was optimized to 300 mg every 3 weeks. Complete clearance was achieved 12 weeks following optimization. No AEs were reported throughout treatment.

### Case 2

Case 2 was a 60-year-old man with a baseline PASI of 11.4, with psoriasis affecting the arms, legs, trunk, and scalp. Despite achieving PASI-75 at week 12, his disease relapsed at week 52, and his dose was optimized to 300 mg every 3 weeks. PASI-75 (PASI 1.2) was achieved after 12 weeks. No AEs were reported throughout treatment.

From the Department of Pharmacology and Toxicology, University of Toronto[a]; Schulich School of Medicine and Dentistry, Western University, London[b]; Faculty of Medicine, University of Toronto[c]; Department of Dermatology, The Northern Ontario School of Medicine, Sudbury[d]; Division of Dermatology, Faculty of Medicine, University of Toronto[e]; and Probity Medical Research, Waterloo.[f]

Funding sources: None.

Conflicts of interest: Dr Yeung has been a speaker, consultant, and investigator for AbbVie, Allergan, Amgen, Astellas, Boehringer Ingelheim, Celgene, Centocor, Coherus, Dermira, Eli Lilly, Forward, Galderma, Janssen, Leo, Medimmune, Merck, Novartis, Pfizer, Regeneron, and Takeda. Ms Phung, Mr Georgakopoulos, Mr Ighani, and Dr Giroux have no conflicts of interest to declare.

Correspondence to: Jensen Yeung, MD, FRCPC, Division of Dermatology, Faculty of Medicine, Medical Sciences Building, University of Toronto, 27 King's College Cir, Toronto, ON M5S 1A1, Canada. E-mail: jensen.yeung@utoronto.ca.

JAAD Case Reports 2018;4:310-3.
2352-5126



https://doi.org/10.1016/j.jdcr.2017.11.006

**Table I.** Case demographics and clinical features before and after secukinumab dosage optimization

| | | | | | Approved dosing regimen | | | | Optimized dosing regimen | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Sex | Age, y | Weight, kg | Previously failed biologics | Baseline score | Follow-up week; score | PASI-75 achieved | Treatment duration, weeks | Scores before optimized regimen | Dosing regimen | Follow-up week; score | PASI-75 achieved | Concomitant systemic medications |
| 1 | F | 50 | 79.0 | Adalimumab | PASI 10.8 | 12; PASI 2.8 | N | 52 | PASI 5.1 | 300 mg q3w | 12; PASI 0 | Y | None |
| 2 | M | 60 | 96.0 | Adalimumab | PASI 11.4 | 12; PASI 2.4 | Y | 52 | PASI 6.8 | 300 mg q3w | 12; PASI 1.2 | Y | None |
| 3 | M | 34 | 89.0 | None | PASI 10.6 | 12; PASI 0.6 | Y | 35 | PASI 5.2 | 300 mg q3w | 12; PASI 1.2 | Y | None |
| 4 | F | 68 | 49.0 | Etanercept, ustekinumab | PASI 14.6 | 12; PASI 7.9 | N | 12 | PASI 7.9 | 300 mg q3w | 12; PASI 1.6 | Y | None |
| 5 | F | 52 | 77.0 | Efalizumab, adalimumab, etanercept, infliximab, ustekinumab | PASI 14.5 | 12; PGA 1 | NA | 65 | NA | 300 mg q2w | 12; PGA 1 | NA | Methotrexate |
| 6 | M | 52 | 62.0 | Etanercept | PASI 13.5 | 12; PGA 0 | NA | 65 | NA | 300 mg q2w | 12; PGA 0 | NA | None |
| 7 | M | 63 | 109.1 | Ustekinumab | PGA 3 | 5; improved | NA | 26 | PGA 3 | 300 mg/w for 2 weeks, then q3w thereafter | 30.5; PGA 3 | NA | Allitretinoin |
| 8 | M | 66 | NA | Alefacept, etanercept, adalimumab, ustekinumab | NA | 12; PGA 4 | NA | 48 | PGA 4 | 300 mg q3w | 12; PGA 3 | NA | Apremilast |
| 9 | M | 66 | NA | Adalimumab | PGA 4 | 26; PGA 3 | NA | 52 | PGA 2 | 300 mg q3w | 8; PGA 1 | NA | None |
| 10 | F | 38 | NA | Ustekinumab, adalimumab | NA | 26; improved | NA | 30.5 | PGA 4 | 300 mg q2w | 22; PGA 1 | NA | Methotrexate |
| 11 | M | 18 | NA | None | NA | 12; PGA 0 | NA | 12 | PGA 0 | 300 mg q2w | 17; PGA 0 | NA | None |
| 12 | M | 60 | 90.9 | Ustekinumab, adalimumab | PGA 2 | 12; PGA 2 | NA | 82.5 | PGA 2 | 300 mg q3w | 12; PGA 2 | NA | None |
| 13 | F | 53 | NA | Etanercept, ustekinumab, adalimumab | PGA 0 | NA | NA | 35 | PGA 2 | 300 mg q2w | 12; PGA 0 | NA | None |
| Mean | | 52.3 | 81.5 (n = 8) | | | | | 43.6 | PASI 6.25 (n = 4) | | | | |

*N*, No; *NA*, data not available; *PASI*, Psoriasis Area and Severity Index; *PASI-75*, 75% reduction from baseline PASI score; *PGA*, Physician Global Assessment; *q2w*, every 2 weeks; *q3w*, every 3 weeks; *Y*, yes.

**Case 3**

Case 3 was a 34-year-old man with a baseline PASI of 10.6 who achieved PASI-75 at week 12. After 35 weeks, the patient was optimized to 300 mg every 3 weeks because he experienced a disease relapse (PASI 5.2). Twelve weeks following optimization, he once again achieved PASI-75 (PASI 1.2). No AEs were reported throughout treatment.

**Case 4**

Case 4 was a 68-year-old woman who displayed suboptimal response after 12 weeks of treatment; she was subsequently optimized to 300 mg every 3 weeks. She achieved PASI-75 (PASI 1.6) after 12 weeks taking this dosing regimen. No AEs were reported throughout treatment.

**Case 5**

Case 5 was a 52-year-old woman with psoriasis on the soles of her feet and elbow. The patient was taking 15 mg methotrexate for psoriatic arthritis concurrently with secukinumab; a superficial skin bacterial infection developed. She was almost clear after 12 weeks. At week 65, she relapsed with scattered, erythematous, scaly plaques on the knees; she was optimized to the drug regimen 300 mg secukinumab every 2 weeks with methotrexate. After 12 weeks taking this regimen, only thin plaques on the elbows persisted. No AEs were reported throughout treatment.

**Case 6**

Case 6 was a 52-year-old man who completely cleared after 12 weeks on secukinumab. At week 65, the patient showed a minor disease relapse with guttate-like plaques on the right lower leg (body surface area 2.5%). He was optimized to 300 mg every 2 weeks, and after 12 weeks, he had complete skin clearance. No AEs were reported throughout treatment.

**Case 7**

Case 7 was a 63-year-old man with palmoplantar psoriasis with notable improvement after 5 weeks on secukinumab. He experienced fatigue for 2 days postinjection. At week 26, both of his heels were cracking and bleeding. The loading dose reduced lesion thickness on the hands, but did not clear them completely. Nail ridging was also present. He was then prescribed the regimen of 300 mg secukinumab weekly for 2 weeks (because he missed a dose); thereafter he took secukinumab every 3 weeks and alitretinoin (10 mg) once daily. His psoriasis improved slightly after 30.5 weeks taking this dosing regimen. No AEs were reported after dose optimization.

**Case 8**

Case 8 was a 66-year-old man with no improvement of psoriasis after 12 weeks on secukinumab. Apremilast was added to the regimen at this time. After 48 weeks, dry scaly plaques were noted on his hands, forearms, elbow, and lower legs, affecting >10% of his body surface area. He was then optimized to 300 mg secukinumab every 3 weeks in combination with apremilast. After 12 weeks, his psoriasis was still not adequately controlled. No AEs were reported throughout treatment.

**Case 9**

Case 9 was a 66-year-old man with a severe psoriatic flare after failing adalimumab. AEs included minor paronychia and fatigue while on secukinumab. After 26 weeks, there was improvement, but large plaques remained on his shins and knees. Recalcitrant plaques persisted after 52 weeks. Following optimization to 300 mg every 3 weeks, almost complete skin clearance was achieved at week 8. No AEs were reported after dose optimization.

**Case 10**

Case 10 was a 38-year-old woman with psoriatic arthritis treated with secukinumab and methotrexate (15 mg) concurrently, which was tapered and stopped at week 6. Her arthritis worsened on this treatment. After 26 weeks on secukinumab, the patient achieved significant skin clearance. She flared 2 weeks later with small lesions on the scalp and scaly, thick plaques on the elbows and legs. After 30.5 weeks of treatment, the patient dose was optimized to 300 mg every 2 weeks. After 22 weeks of treatment on the optimized dosing regimen, her scalp and ears were clear, but residual plaques to the lower legs, feet, and elbows remained. No AEs were reported throughout treatment.

**Case 11**

Case 11 was an 18-year-old man with guttate psoriasis who experienced significant skin clearance on secukinumab despite delaying the fifth loading injection due to a common cold. At week 12, he achieved complete clearance but was flaring in between maintenance injections. His dosage was optimized to 300 mg every 2 weeks, and after 17 weeks on this dosing regimen, his skin was clear. No AEs were reported throughout treatment.

**Case 12**

Case 12 was a 60-year-old man who had small, scaly lesions on the lower legs before taking secukinumab therapy. After 12 weeks of this treatment,

he would flare 3 weeks after his maintenance injection, and experienced pruritus 3 days before the next dose. This remained an issue after 82.5 weeks of treatment. Pruritic, dry, scaly patches remained on the back and popliteal fossa. His dosing regimen was then optimized to 300 mg every 3 weeks. After 12 weeks on this regimen, uncomfortable lesions persisted on his back. No AEs were reported throughout treatment.

### Case 13

Case 13 was a 53-year-old woman who began secukinumab for psoriatic arthritis but did not have psoriasis at the start of therapy. After 12 weeks, there was less swelling in her joints, but after 35 weeks, she experienced psoriatic flaring in her abdomen and groin folds. She was then optimized to secukinumab 300 mg every 2 weeks, during which time she had a common cold. After 12 weeks taking the optimized dose, her skin was clear.

## DISCUSSION

Understanding current literature on the effectiveness and safety of off-label biologics dosing regimens is imperative to decision-making and clinical care for psoriasis patients. This case series provides evidence of clinical benefit and minimal AEs during secukinumab dose optimization for psoriasis. The most common reasons for optimization included incomplete clearance of psoriasis in recalcitrant areas and flaring before the next maintenance dose. Because no guidelines are currently available, the rationale behind the chosen regimens included disease severity and the clinician's comfort in prescribing 300 mg every 2 or 3 weeks. The optimal alternative regimen should be investigated in large-scale clinical trials.

In 10 of 13 (76.9%) cases, a significant improvement was experienced after dose optimization: 3 achieved PGA 0, 3 achieved PGA 1, and 4 achieved PASI-75. The remaining 3 cases (23.1%) did not show an adequate response to alternative dosing based on our study endpoints (Table I). Failures might be attributable to the indication, considering 1 patient was given secukinumab to treat palmoplantar psoriasis, rather than plaque psoriasis. Patients with severe or therapy-resistant psoriasis, as indicated by high baseline scores or numerous previous failures on biologics, might also fail to benefit from the increased secukinumab dosage.

Combination therapy with systemic agents, such as methotrexate, was not considered as an alternative to dose escalation because most patients already failed or have a contraindication for these therapies. However, at this time, it is unclear why some patients respond suboptimally to secukinumab and, therefore, elect to increase their dosage. Through our clinical experience in combination with the limited data available on biologic therapy failures, we believe that factors such as weight or body mass index might contribute to biologic therapy failures.[4]

The safety findings of this case series are similar to those reported in secukinumab phase 3 clinical trials.[5] Aside from case 13 who developed a common cold after optimization, there seems to be no apparent dose-related difference in incidences of adverse events. The present work suggests that AEs following secukinumab dose optimization are uncommon. However, it is challenging to draw conclusions due to low event rates and the small number of cases included in our analysis.

### Conclusion

These preliminary findings suggest that most patients using off-label higher-dose secukinumab regimens for psoriasis experience a significant clinical improvement. AEs were uncommon, and we expect AE rates on the higher dosing regimen to parallel those reported for the approved dosing regimen used in secukinumab clinical trials. Before discontinuing secukinumab or switching to another therapy, dose optimization can be considered by clinicians to manage patients who inadequately respond to the currently approved regimen. This case series necessitates larger studies of longer duration to better understand the effectiveness and long-term safety of using higher dosages of secukinumab.

### REFERENCES

1. Health Canada. Summary Basis of Decision - Cosentyx - Health Canada. Available at: https://hpr-rps.hres.ca/reg-content/summary-basis-decision-detailTwo.php?lang=en&linkID=SBD00178. Accessed October 27, 2017.
2. US Food and Drug Administration. FDA approves new psoriasis drug Cosentyx. Available at: www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm430969.htm. Accessed October 27, 2017.
3. Novartis Pharmaceuticals Canada Inc. Dorval, QC. Cosentyx (secukinumab). Available at: https://pdf.hres.ca/dpd_pm/00040683.PDF. Accessed September 6, 2017.
4. Edson-Heredia E, Sterling KL, Alatorre CI, et al. Heterogeneity of response to biologic treatment: perspective for psoriasis. *J Invest Dermatol*. 2013;134:18-23.
5. Langley RG, Elewski BE, Lebwhol M, et al. Secukinumab in plaque psoriasis — results of two phase 3 trials. *N Engl J Med*. 2014;371(4):326-338.