

OHTAC Recommendation

Ultraviolet Phototherapy Management of Moderate-to-Severe Plaque Psoriasis

*Presented to the Ontario Health Technology
Advisory Committee in June 2009*

November 2009

OHTAC Ontario
Health Technology
Advisory Committee

Background

The Ontario Health Technology Committee (OHTAC) met on June 26, 2009 to review the effectiveness and safety of ultraviolet phototherapy devices for the management of moderate-to-severe psoriasis, based on an evidence review produced by the Medical Advisory Secretariat (MAS).

Psoriasis is a common chronic, systemic inflammatory disease affecting the skin, nails and occasionally the joints and has a lifelong waning and waxing course. It has a worldwide occurrence with a prevalence of at least 2% of the general population, making it one of the most common systemic inflammatory diseases. The immune-mediated disease has several clinical presentations with the most common (85% - 90%) being plaque psoriasis.

Characteristic features of psoriasis include scaling, redness, and elevation of the skin. Patients with psoriasis may also present with a range of disabling symptoms such as pruritus (itching), pain, bleeding, or burning associated with plaque lesions and up to 30% are classified as having moderate-to-severe disease. Further, some psoriasis patients can be complex medical cases in which diabetes, inflammatory bowel disease, and hypertension are more likely to be present than in control populations and 10% also suffer from arthritis (psoriatic arthritis). The etiology of psoriasis is unknown but is thought to result from complex interactions between the environment and predisposing genes.

Management of psoriasis is related to the extent of the skin involvement, although its presence on the hands, feet, face or genitalia can present challenges. Moderate-to-severe psoriasis is managed by phototherapy and a range of systemic agents including traditional immunosuppressants such as methotrexate and cyclosporin. Treatment with modern immunosuppressant agents known as biologicals, which more specifically target the immune defects of the disease, is usually reserved for patients with contraindications and those failing or unresponsive to treatments with traditional immunosuppressants or phototherapy.

Treatment plans are based on a long-term approach to managing the disease, patient's expectations, individual responses and risk of complications. The treatment goals are several fold but primarily to:

- 1) improve physical signs and secondary psychological effects,
- 2) reduce inflammation and control skin shedding,
- 3) control physical signs as long as possible, and to
- 4) avoid factors that can aggravate the condition.

Approaches are generally individualized because of the variable presentation, quality of life implications, co-existent medical conditions, and triggering factors (e.g. stress, infections and medications). Individual responses and commitments to therapy also present possible limitations.

Ultraviolet phototherapy units have been licensed since February 1993 as a class 2 device in Canada. Units are available as hand held devices, hand and foot devices, full-body panel, and booth styles for institutional and home use. Units are also available with a range of ultraviolet A, broad and narrow band ultraviolet B (BB-UVB and NB-UVB) lamps. After establishing appropriate ultraviolet doses, three-times weekly treatment schedules for 20 to 25 treatments are generally needed to control symptoms.

MAS and OHTAC Findings

The MAS conducted a systematic literature review using bibliographic databases and employing keywords and subject headings to capture the concepts of 1) phototherapy and 2) psoriasis, for literature published between January 1999 and March 31, 2009, followed by search alerts until June 2009. A 2000 health technology evidence report by the NHS R&D HTA Programme on the overall management of psoriasis was identified in the MAS evidence-based review. The report included 109 RCT studies published between 1966 and June 1999 involving four major treatment approaches – 51 RCTs on phototherapy, 32 RCTs on oral retinoids, 18 RCTs on cyclosporine and five RCTs on fumarates. The absence of RCTs on methotrexate was noted as original studies with this agent had been performed prior to 1966.

Of the 51 RCT studies involving phototherapy, 22 involved UVA, 21 involved UVB, five involved both UVA and UVB, and three involved natural light as a source of UV. The RCT studies included comparisons of treatment schedules, ultraviolet source, addition of adjuvant therapies and comparisons between phototherapy and topical treatment schedules. Due to heterogeneity across the studies, no synthesis or meta-analysis was performed. Overall the reviewers concluded that the efficacy of only five therapies could be supported from the RCT-based evidence review: photochemotherapy or phototherapy, cyclosporin, systemic retinoids, combination topical vitamin D₃ analogues (calcipotriol), and corticosteroids in combination with phototherapy and fumarates. Although there was no RCT evidence supporting methotrexate, its efficacy for psoriasis is well known and continues to be a mainstay in the treatment of psoriasis.

Although the conclusion of the evidence review was that both photochemotherapy and phototherapy were effective treatments for clearing psoriasis, their comparative effectiveness was unknown. The authors concluded that phototherapy and photochemotherapy had important roles in psoriasis management and are standard therapeutic options for psoriasis offered in dermatology practices.

Despite the conclusions on efficacy of phototherapy for psoriasis a number of issues were identified in the evidence review:

- Outcome measures reported in the trials were highly variable and often presented in forms that would not allow cross-study comparison.
- The definition and measurement of “severe” psoriasis was not uniform and the clinical measures of severity commonly employed were generally inadequate, often representing an underestimate of disease severity.
- Many trials were under-powered and lacked relevant treatment or comparator arms.
- The follow-up or surveillance of treatments was short, if not absent, and reporting of side-effects, even in the short term periods of the studies, was generally poor.

Several areas for future research were discussed to address these limitations. Trials focusing on comparative effectiveness, either between ultraviolet sources or between classes of treatment (e.g. methotrexate versus phototherapy), were recommended to refine treatment algorithms. The need for better assessment of cost-effectiveness of those therapies that consider systemic drug costs and costs of surveillance as well as drug efficacy, was also noted.

The MAS evidence-based review was performed as an update to the 2000 systematic review of treatments for severe psoriasis and focused on the RCT trial evidence for ultraviolet phototherapy management of

moderate-to-severe plaque psoriasis. In the MAS review, 26 reports were identified involving RCT studies involving phototherapy or photochemotherapy. Among them were two RCTs comparing ultraviolet wavelength source, five RCTs comparing different forms of phototherapy, four RCTs combining phototherapy with prior spa saline bathing, nine RCTs combining phototherapy with topical agents, two RCTs combining phototherapy with systemic immunosuppressive agents methotrexate and alefacept, one RCT comparing phototherapy with an additional light source (the excimer laser), and one RCT comparing the simultaneous psychosocial intervention on mindfulness and stress reduction audio tape. Two trials examined the effect of treatment setting on the effectiveness of phototherapy, specifically, inpatient versus outpatient treatment and outpatient versus home treatment.

The conclusions on these trials are summarized below.

Table 1: Summary of the RCT evidence for ultraviolet phototherapy treatment of moderate-to-severe plaque psoriasis

Conclusion	Evidence Level
<ul style="list-style-type: none"> Phototherapy is an effective treatment for moderate-to-severe plaque psoriasis 	Moderate quality and adequate study evidence
<ul style="list-style-type: none"> Narrow band PT is more effective than broad band PT for moderate-to-severe plaque psoriasis 	High quality but limited study evidence
<ul style="list-style-type: none"> Oral-PUVA has a greater clinical response, requires less treatments and has a greater cumulative UV irradiation dose than UVB to achieve treatment effects for moderate-to-severe plaque psoriasis 	High quality and adequate study evidence
<ul style="list-style-type: none"> Spa salt water baths prior to phototherapy did increase short term clinical response of moderate-to-severe plaque psoriasis but did not decrease cumulative UV irradiation dose 	High quality and adequate study evidence
<ul style="list-style-type: none"> Addition of topical agents (vitamin D3 calcipotriol) to NB-UVB did not increase mean clinical response or decrease treatments or cumulative UV irradiation dose 	High quality and adequate study evidence
<ul style="list-style-type: none"> Methotrexate prior to NB-UVB in high need psoriasis patients did significantly increase clinical response, decrease number of treatment sessions and decrease cumulative UV irradiation dose 	High quality study but limited study evidence
<ul style="list-style-type: none"> Phototherapy following alefacept did increase early clinical response in moderate-to-severe plaque psoriasis 	Inadequate study evidence
<ul style="list-style-type: none"> Effectiveness and safety of home NB-UVB phototherapy was not inferior to NB-UVB phototherapy provided in a clinic to patients with psoriasis referred for phototherapy. Treatment burden was lower and patient satisfaction was higher with home therapy and patients in both groups preferred future phototherapy treatments at home 	High quality study but limited study evidence

Many of the evidence gaps identified in the 2000 evidence review persisted in the MAS update. In particular, the lack of evidence on comparative effectiveness or cost-effectiveness between the major treatment options for moderate-to-severe psoriasis remains. The evidence of the effectiveness of longer-term strategies for disease management has also not been addressed.

OHTAC Recommendations

Based on the above evidence, OHTAC recommends the following with regard to ultraviolet phototherapy management of moderate-to-severe plaque psoriasis:

1. Access to phototherapy should be supported and encouraged for patients with moderate-to-severe plaque psoriasis or those unresponsive to topical therapies.
2. Local Health Integration Network (LHIN) authorities should review the availability of phototherapy services for patients in their regions.

OHTAC noted that technological advances have enabled changes in phototherapy treatment regimens from lengthy hospital inpatient stays to outpatient clinic visits and, more recently, to an at-home basis – although evidence for the effectiveness, safety and cost-effectiveness of phototherapy delivered in the latter setting is limited.

Finally, OHTAC noted that because psoriasis is a chronic disease, strategies for disease control and improvements in self-efficacy employed in other chronic disease management strategies should be investigated.