

# Emerging Drug List

## MYCOPHENOLATE MOFETIL



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**Generic (Trade Name):** Mycophenolate mofetil (MMF) (CellCept®)

**Manufacturer:** Roche Pharmaceuticals, Inc.

**Indication:** MMF is indicated for the prevention of organ transplant rejection.<sup>1</sup> Since the early 1990s, MMF has been used as a treatment option for severe psoriasis.<sup>2-4</sup>

**Current Regulatory Status:** MMF is approved in Canada and the US. Canada approved MMF for the prevention of kidney transplant rejection in 1996, then for the prophylaxis of heart transplant rejection in 1998.<sup>5</sup> The US Food and Drug Administration approved it in 1995 for the prevention of acute organ transplant rejection.<sup>6</sup>

**Description:** MMF is an immunosuppressant that inhibits purine synthesis, which is required for the replication of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). In turn, this induces a selective inhibition of lymphocyte proliferation and antibody formation.<sup>2,6</sup> Psoriasis is considered to be an autoimmune disease that is induced by T-cells and proinflammatory cytokine.<sup>7-9</sup> MMF selectively suppresses these cells by blocking the purine synthesis pathway.<sup>2,10,11</sup>

**Current Treatment:** Chronic plaque psoriasis, which is the most common form of psoriasis, affects about one million Canadians.<sup>12,13</sup> Psoriasis is treated by using topical or immunobiological drugs. Topical treatments include phototherapy [ultraviolet B (UVB), and ultraviolet A plus psoralen (PUVA)], systemic drugs (methotrexate, retinoids, and cyclosporine), and topical agents (corticosteroids, dithranol, and vitamin D<sub>3</sub> analogues).<sup>13-18</sup> Topical drugs are the first-line treatment for mild psoriasis, but are also effective in treating severe psoriasis.<sup>13</sup> Most of these drugs are associated with side effects such as irritation, bone marrow suppression, hypertension, elevated serum lipids, photosensitivity, and skin cancer.<sup>13,15</sup>

Immunobiological drugs, such as monoclonal antibodies and fusion proteins,<sup>15</sup> are designed to target specific components of the immune system. These second-line drugs are prescribed when systemic and topical treatments fail.<sup>13</sup> Alefacept (Amevive®), efalizumab (Raptiva™), and etanercept (Enbrel®) are approved in Canada for psoriasis treatment.<sup>13,15,16,19</sup> Reports show that these drugs, when compared with topical drugs, are effective with less severe side effects.<sup>8,20,21</sup> Most of these drugs, however, are new and lack long-term safety profiles.

**Cost:** The cost for treatment with an MMF dosage of two grams per day for one month averages C\$560.<sup>6</sup>

**Evidence:** The efficacy and safety of MMF in treating psoriasis are yet to be demonstrated in large randomized clinical trials. Nevertheless, therapeutic benefits have been shown in small clinical trials and case reports. In a two-centre, open-label clinical trial,<sup>4</sup> 23 patients with mod-

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erate to severe psoriasis [mean psoriasis area and severity index (PASI) of 21.7] were treated with two to three grams of MMF a day for three months. Eighteen of the 23 completed the trial. In six weeks, the mean PASI declined by 24% ( $p < 0.001$ ), and by 47% ( $p < 0.001$ ) in three months. At the end of the trial, 61% of the patients had their PASI reduced by >50%, and 22% of the patients had >75% reduction in their PASI. Five patients (27%) experienced nausea.

In another trial,<sup>7</sup> 11 patients with severe psoriasis and a mean PASI of 30.5 received one gram of MMF twice daily for three weeks, and 0.5 gram twice daily for another three weeks. In three weeks, seven patients had their PASI reduced by 40% to 70%, and three patients experienced a reduction in PASI by 25% to 39%. Further improvement was observed in six patients after six weeks. One patient experienced a side effect of muscle pain.

Several case reports supporting the use of MMF in treating severe psoriasis have also been published.<sup>2,3,17,18,22-25</sup>

### Adverse Effects:

The profile of adverse reactions associated with the administration of MMF in organ transplant rejection is available. The adverse event profile associated with the use of MMF in treating psoriasis, however, has not been established because of the lack of large, randomized controlled clinical trials. The principal side effects include vomiting, leukopenia, sepsis, and a high incidence of opportunistic infections such as herpes zoster, urinary tract infections, tissue invasive infections, and Candida infections.<sup>1</sup> These largely dose-dependent side effects are usually observed in organ transplant patients on dosages that exceed two grams per day.<sup>2</sup>

### Commentary:

The evidence that shows MMF to be an effective therapy for psoriasis comes from small clinical trials and several case reports. It would be optimal to have evidence from large, randomized, controlled clinical trials to establish the efficacy and safety of this emerging therapy. Given that severe psoriasis affects about one million Canadians,<sup>12</sup> the monthly cost of C\$560 per patient may have a significant impact on the health care system. In addition, there is no approved standard dosage or optimal treatment duration with MMF. All this suggests cost implications and complexity in prescription decisions.

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This series highlights medical technologies that are not yet in widespread use in Canada and that may have a significant impact on health care. The contents are based on information from early experience with the technology; however, further evidence may become available in the future. These summaries are not intended to replace professional medical advice. They are compiled as an information service for those involved in planning and providing health care in Canada.

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