

## Corticosteroid Dosing for Flares in Relapsing Remitting Multiple Sclerosis

### Pearl for Practice

Short courses of high doses of oral prednisone (up to 1250 mg/day) may be prescribed off-label for multiple sclerosis flares.

Flares (i.e. acute relapses / exacerbations) in multiple sclerosis (MS) may be defined as<sup>1</sup>:

- The appearance of any new symptom or any worsening of existing symptoms for more than 24 hours.
- These symptoms must be preceded by a 30-day period of stability.

Whether or not to treat a flare with steroids depends on clinical judgment of a healthcare professional specializing in MS.<sup>1</sup> If treatment is initiated it should be within 14 days of symptom onset.<sup>1</sup> The ideal corticosteroid, route of administration, dose, and duration of therapy have yet to be established. Table 1 provides regimens that have been recommended in various resources.<sup>1-4</sup> Interestingly, a 2009 survey of physicians practicing in Canadian MS clinics found the most commonly prescribed regimen to be oral prednisone 500-1250 mg once daily for 3-5 days.<sup>5</sup>

**Table 1: Recommended / Common Dosing of Corticosteroids for MS Flares:**

Corticosteroid	Dose	Duration
<b>Intravenous methylprednisolone (IVMP)</b>	1000 mg once daily	3-5 days <sup>1*</sup>
	500-1000 mg once daily	3-5 days <sup>2</sup>
<b>Oral methylprednisolone (OMP)</b>	500 mg once daily	5 days <sup>1,2†</sup>
<b>Oral prednisone (OP)</b>	500-1250 mg once daily	3-7 days <sup>3-5</sup>

\* National Institute for Health Care and Excellence (NICE) guidelines recommend IVMP as an alternate for people who cannot tolerate/ have failed oral steroids, or for patients who require hospital admission.<sup>1</sup>

† NICE<sup>1</sup> and European Federation of Neurological Societies (ENFS)<sup>2</sup> guidelines recommend flare treatment to be no less than 500 mg MP for 5 days (IV or oral).

### Equivalency and Efficacy

In a pharmacokinetic study, serum levels of the participants were measured at 1, 2, 4, 8, 24, and 48 hours.<sup>6</sup> By the 8<sup>th</sup> hour there were no statistically significant differences in serum levels between the 1000mg IVMP group and the 1250mg OP group.

A Cochrane Review concluded there is no significant difference between oral vs. IV corticosteroids for treatment of acute exacerbations of MS.<sup>7</sup> Two small trials found the oral route non-inferior to IV administration.<sup>8,9</sup>

One non-inferiority trial compared 1000 mg once daily for three days for each of OMP and IVMP.<sup>8</sup> OMP was shown to be non-inferior to IVMP in the improvement of Extended Disability Status Scale (EDSS) scores one month after treatment and was not associated with more frequent or new relapses over the next six months.

The other non-inferiority trial used bioequivalent doses of steroids: 1250 mg OMP once daily vs. 1000 mg IVMP once daily for three days.<sup>9</sup> To assess efficacy the researchers used the EDSS and measured lesions on magnetic resonance imaging (MRI). At the end of the study, OMP was shown to be non-inferior to IVMP in reducing EDSS; MRI lesions were also similar at 4 weeks.

### **Should there be a Taper?**

Based on the Canadian survey, the use of tapering in practice is highly variable.<sup>5</sup> NICE guidelines do not mention tapering at all.<sup>1</sup> The MS Society suggests tapering is optional, based on the clinician's experience and judgment.<sup>3</sup> A retrospective chart review compared the EDSS scores at 3, 6, and 12 months after treatment of relapse with either IVMP alone (1g once daily for five days) or IVMP plus an oral prednisone taper (starting at 80 mg per day and tapered over 14-18 days).<sup>10</sup> There were no differences in the scores between the two groups at any time point. However, it bears emphasis that this is not a randomized trial and neither baseline MS severity scores nor MRI results are available to more confidently determine the similarity between groups.

### **Adverse Effects**

All in all the adverse effects seen in corticosteroid therapy are very similar between oral and intravenous therapy. Statistical differences have been noted for dysgeusia<sup>7</sup> and insomnia,<sup>8</sup> which were more common after oral treatment. Other adverse effects that have been reported with steroid therapy are: mood disorder, headache, palpitations, nausea, stomach pain, diarrhea, and rash.<sup>8,9</sup> It is not surprising then that the Canadian MS specialists also reported frequent co-prescription of gastric protectants and sedatives to accompany the steroid regimen.<sup>5</sup>

A more serious, and potentially fatal, adverse effect that has been associated with high-dose steroid therapy is hepatotoxicity (based on 26 case reports from 11 countries).<sup>11</sup> "High-dose" was defined as a cumulative dose of >2000mg over no more than 31 days. Practitioners using high-dose steroid therapy should consider steroid induced hepatotoxicity when investigating liver damage; delayed onset of hepatotoxicity can be several weeks or longer.<sup>11</sup>

### **New Guidelines Expected Soon**

Europe and the United States are currently working on updating their guidelines; these are expected to come out later this year.<sup>12</sup> The new guidelines may offer more direction in treating MS flares.

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