



**TITLE:** Increased Dose or Decreased Dosing Interval of Biologics: Clinical Effectiveness

**DATE:** 28 July 2010

**RESEARCH QUESTION:**

What is the clinical effectiveness of an increased dose or a decreased dosing interval of biologics for the treatment of conditions other than rheumatoid arthritis?

**METHODS:**

A limited literature search was conducted on key health technology assessment resources, including PubMed, OVID EMBASE, the Cochrane Library (Issue 7 2010), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI (Health Devices Gold), EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between January 1, 2005 and July 14, 2010. Filters were applied to limit the retrieval to health technology assessments, systematic reviews, meta-analyses and randomized controlled trials. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

**RESULTS:**

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials.

Nine relevant randomized controlled trials were identified pertaining to the clinical effectiveness of an increased dose or a decreased dosing interval of biologics for the treatment of conditions other than rheumatoid arthritis. No relevant health technology assessment reports, systematic reviews, or meta-analyses were identified. Additional information that may be of interest has been included in the appendix.

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**OVERALL SUMMARY OF FINDINGS:**

Overall, evidence for the clinical effectiveness of an increased dose or a decreased dosing interval of biologics for the treatment of conditions other than rheumatoid arthritis is varied.

For patients with Crohn’s disease:

- shorter dosing interval of certolizumab<sup>2</sup> was no more effective than conventional dosing in terms of treatment response and remission
- two studies found fewer Crohn’s-related surgeries and hospitalizations for patients taking adalimumab with shorter dosing intervals<sup>3,4</sup> and one study did not find a difference in response rates.<sup>5</sup>

In patients with psoriasis:

- higher doses of adalimumab<sup>6</sup> and shorter dosing interval for entercept<sup>7</sup> were associated with higher response rates
- higher doses of golimumab were more effective for those with more severe disease (3% surface area or more) than for those with more mild cases.<sup>8</sup>

For patients with psoriatic arthritis:

- shorter dosing interval with entercept resulted in similar efficacy to the conventional schedule<sup>7</sup>
- increased doses of golimumab resulted in slightly better American College of Rheumatology 20% improvement criteria in patients with psoriatic arthritis.<sup>8</sup>

For patients with akylosing spondylitis<sup>1</sup> and psoriatic arthritis taking Infliximab,<sup>9</sup> no conclusions regarding dosing increases were presented in the included abstracts but could potentially be reported in the full text articles. No relevant information pertaining to the treatment of ulcerative colitis was identified. Further details of the included studies can be found in Table 1.

**Table 1: Details of included studies**

Patient Group	Study type	Biologic Drug, Dosing	Results and Conclusions
Crohn’s disease	RCT	Certolizumab 400 mg every 2 or 4 weeks after induction dosing.	In patients with secondary failure to infliximab, maintenance doses of 400 mg certolizumab delivered at 2 week or 4 week intervals had similar efficacy. <sup>2</sup>
	RCT	Adalimumab 40 mg every other week, or 40 mg every week after induction dosing.	Continuous treatment with 40 mg adalimumab weekly or every other week had similar efficacy and both were more effective than induction therapy followed by placebo. <sup>3</sup>
	RCT	Adalimumab 40 mg every other week or 40 mg every	Weekly treatment with 40 mg adalimumab has associated with higher relative reductions in 12 month all-cause hospitalizations and 12 month risk of Crohn’s related hospitalizations than 40 mg every other week. <sup>4</sup>

**Table 1: Details of included studies**

Patient Group	Study type	Biologic Drug, Dosing	Results and Conclusions
		week after induction dosing.	
	RCT	Adalimumab 40 mg every other week or 40 mg every week after induction dosing.	No significant differences observed between treatment outcomes in patients receiving 40 mg adalimumab weekly or every other week. <sup>5</sup>
Akylosing spondylitis	RCT	Infliximab 5 mg/kg every six weeks or up to 7.5 mg/kg every six weeks after first 6 weeks.	Patients starting at 5 mg/kg infliximab every 6 weeks received dose escalations to 7.5 mg/kg and showed significant increases in bone mineral density after 2 years. No specific conclusions regarding the dose escalations were presented in the abstract. <sup>1</sup>
Psoriasis	RCT	Adalimumab 40 mg every other week or 80 mg every other week after induction dosing.	Patients receiving adalimumab 80 mg every other week had higher response rates (as per the Psoriasis Area and Severity Index) than those receiving 40 mg every other week. <sup>6</sup>
Psoriasis and psoriatic arthritis	RCT	Entercept 50 mg twice weekly or 50 mg weekly.	For patients with psoriasis, 50 mg entercept twice weekly was more effective than 50 mg once weekly. For patients with psoriatic arthritis, response rate was similar between 50 mg weekly and 50 mg twice per week. <sup>7</sup>
	RCT	Golimumab 50 mg every 4 weeks or 100 mg every 4 weeks.	Response rate after 14 weeks in patients with psoriatic arthritis was slightly higher for those taking 50 mg golimumab every 4 weeks than 100 mg every 4 weeks. For patients with at least 3% body surface area with psoriasis, response rates were higher in the 100 mg group than in the 50 mg group. <sup>8</sup>
Psoriatic arthritis	RCT	Infliximab 5 mg/kg every 8 weeks or 10 mg/kg after	Patients receiving 5 mg/kg infliximab could escalate dose to 10 mg/kg if response was lost. No specific conclusions regarding dose escalation presented in the abstract but infliximab was found to have high clinical

**Table 1: Details of included studies**

Patient Group	Study type	Biologic Drug, Dosing	Results and Conclusions
		induction dosing or lost response.	efficacy. <sup>9</sup>

mg = milligram; mg/kg = milligram per kilogram; RCT = randomized controlled trial

**REFERENCES SUMMARIZED:**

**Health technology assessments**

No literature identified.

**Systematic reviews and meta-analyses**

No literature identified.

**Randomized controlled trials**

*Ankylosing spondylitis*

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*Psoriasis and Psoriatic arthritis*

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9. Kavanaugh A, Krueger GG, Beutler A, Guzzo C, Zhou B, Dooley LT, et al. Infliximab maintains a high degree of clinical response in patients with active psoriatic arthritis through 1 year of treatment: results from the IMPACT 2 trial. *Ann Rheum Dis* [Internet]. 2007 Apr. [cited 2010 Jul 14]; 66(4):498-505. Available from:  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1856065> [PubMed: PM17114188](#)

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## **APPENDIX – FURTHER INFORMATION:**

### **Health technology assessments**

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Subscription required.  
*Note: Reprinted with edits in 2009, no change to search dates or to conclusions*

### **Economic information**

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