Infliximab and questionable efficacy of recommendations on tuberculosis screening

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Infliximab (Remicade®) is a TNF-alpha blocking agent, indicated for severe rheumatoid arthritis, Crohn's disease and ankylosing spondylitis. In December 2000, the EMEA recommended screening for latent and active TBC infections. In February 2002 , the EMEA limited the indications for use and recommended additional precautions against infections.
Despite these recommendations, the Netherlands Pharmacovigilance Centre Lareb still receives reports on TBC infections. The Swedish Medical Product Agency also reported 13 cases of tuberculosis in patients with TNF-alpha therapy and the FDA reported 335 cases until September 2002.
We are concerned whether the health professionals adhere to the recommendations and whether the recommendations for screening for TBC are effective. To answer these questions, the involved Lareb reports have been analysed. Since 16 May 2001 until 20 February 2004 Lareb received 19 reports (14 from Markeing Authorization Holders, 5 from medical specialists) concerning 13 patients (11 with indication rheumatoid arthritis, one with Crohn's disease, one with uveitis). Five of these patients died.

Together with literature data on this issue, these reports of tuberculosis in patients with TNF-alpha therapy raise three concerns:

1. The SPC recommendation is insufficiently implemented by health professionals
2. Different recommendations exist, which may be confusing
3. The recommendations for screening and prophylaxis may be insufficient to protect against TBC, and especially against TBC reactivation during or after prophylactic TBC therapy