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adalimumab (HUMIRA°) and plaque psoriasis in children

No better than other immunosuppressants

● **In a trial in 114 children, the efficacy of *adalimumab* was not notably different from that of *methotrexate*, and its adverse effects profile did not appear to be more favourable.**

Treatment of children with plaque psoriasis is based mainly on topical drugs, starting with emollients or possibly topical corticosteroids, or vitamin D derivatives. A short course of UVB phototherapy is an option for children with extensive or refractory psoriasis. Systemic immunosuppressive therapy should only be considered in very severe cases, because of its adverse effects and its limited evaluation in children (1). *Methotrexate* has long been used to treat other disorders in children, but this immunosuppressant carries a risk of infections, haematological disorders, liver injury and cancer (2). The harm-benefit balance of *etanercept*, a TNF-alpha antagonist, is uncertain in children with psoriasis (1,3).

Adalimumab (Humira°, Abbvie), another TNF-alpha antagonist authorised for the treatment of various paediatric disorders, has been approved for use in children with severe plaque psoriasis in whom local treatment or phototherapy has failed.

What is the harm-benefit balance of *adalimumab* in this setting?

About 50% of children improved, but frequent relapses after treatment discontinuation. Clinical evaluation of *adalimumab* in children with plaque psoriasis is mainly based on a randomised, double-blind trial versus *methotrexate* in 114 patients aged 4 to 17 years, 97 of whom were over 8 years old. Very few of the children had severe psoriasis, based on criteria taking into account the character and extent of lesions. All children had already received a local treatment, one-half had received phototherapy, and one-third had received a systemic treatment (10% with *etanercept*) (4). After randomisation, the children received *adalimumab* 0.4 mg/kg, *adalimumab* 0.8 mg/kg (the approved dosage), or *methotrexate* at a maximum dose of 0.4 mg/kg per week.

After 16 weeks, a marked reduction in the extent and severity of the lesions was observed in 58% of the 38 children who received *adalimumab* 0.8 mg/kg versus 32% of those who received *methotrexate* (p=0.027). The lesions disappeared or were considered "minimal" in about half of children, with no statistically significant difference between the groups (4).

At the end of treatment, psoriasis worsened in 83% of the children who received *adalimumab* 0.8 mg/kg versus 69% of those in the *methotrexate* group (4).

Infections, including herpes zoster and tuberculosis. *Adalimumab* has a burdensome adverse effect profile, including infections, hypersensitivity reactions, injection site reactions, haematological disorders, liver injury, and cancer (including some very aggressive lymphomas) (5,6).

In the paediatric trial, about one-quarter of the children developed infections possibly related to the treatment, with no difference between the groups (4). Three children in the *adalimumab* groups developed herpes zoster, and two had primary tuberculosis (4). Psoriasis worsened markedly in two children receiving *adalimumab* and in none of those treated with *methotrexate* (4). No cancers were reported during the trial, but follow-up was short (4).

Ten children in the *adalimumab* groups developed antibodies to *adalimumab*. The efficacy of *adalimumab* 0.8 mg/kg did not appear to be affected by the presence of these antibodies, but the number of patients was too small to reach firm conclusions (4).

In practice. *Adalimumab* has mainly been evaluated in children with moderate psoriasis. Overall, compared to *methotrexate*, *adalimumab* seemed slightly more effective on psoriatic lesions, but relapses after treatment withdrawal were more frequent. Because of its potentially serious adverse effects, including a risk of infections and cancer, *adalimumab*, like other immunosuppressants, should only be considered for children with very debilitating plaque psoriasis.

adalimumab solution for SC injection

HUMIRA°

• **40 mg** of *adalimumab* per syringe, pre-filled pen, or vial (0.8 ml)

immunosuppressant; TNF-alpha antagonist

■ **New indication:** *"(…) severe chronic plaque psoriasis in children and adolescents from 4 years of age who have had an inadequate response to or are inappropriate candidates for topical therapy and phototherapies".*
[EU centralised authorisation]

Selected references from Prescrire's literature search.

In response to our request for information, AbbVie provided us with published articles, administrative documents, and packaging items.

1- Prescrire Editorial Staff "Childhood psoriasis: often favourable outcome" *Prescrire Int* 2009; **18** (104): 275.
2- Prescrire Rédaction "20-1-4. Patients sous méthotrexate" *Rev Prescrire* 2015; **35** (386 suppl. interactions médicamenteuses).
3- Prescrire Rédaction "étanercept-Enbrel° et psoriasis en plaques chez les enfants. En dernier recours: beaucoup d'incertitudes" *Rev Prescrire* 2009; **29** (309): 486.
4- EMA - CHMP "Extension of indication variation assessment report for Humira. EMEA/H/C/000481/II/0134" 26 February 2015: 58 pages.
5- Prescrire Rédaction "adalimumab-Humira° et arthrite juvénile idiopathique. 2e anti-TNF alpha dès l'âge de 4 ans, sans progrès décisif" *Rev Prescrire* 2012; **32** (339): 15.
6- Prescrire Rédaction "adalimumab-Humira° et enfants atteints de maladie de Crohn sévère. Autant d'incertitudes qu'avec l'infliximab" *Rev Prescrire* 2014; **34** (364): 98.