Abbott Laboratories Ireland Ltd
4051 Kingswood Drive
Citywest Business Campus
Dublin 24
Ireland

Telephone: +353 1 469 1500
Fax: +353 1 469 1501

Important Safety Information

16 July 2008

Direct Healthcare Professional Communication on reports of hepatosplenic T-cell lymphoma in patients treated with HUMIRA® (adalimumab)

Dear Healthcare Professional,

Abbott would like to inform you of new safety information regarding HUMIRA® (adalimumab), which is a TNF alpha blocker authorised in adult patients for the treatment of rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease and psoriasis.

- From launch in December 2002, three postmarketing reports of hepatosplenic T-cell lymphoma (HSTCL), which is a rare aggressive form of non-Hodgkin lymphoma with a poor prognosis, have been reported in patients receiving HUMIRA®.

- Two of these three patients were young men also receiving azathioprine or 6-mercaptopurine for inflammatory bowel disease. A risk for the development of hepatosplenic T-cell lymphoma in patients treated with Humira cannot be excluded.

- HSTCL should be considered in the event that a patient receiving HUMIRA® develops symptoms of lymphomas and / or hepatosplenomegaly with or without peripheral lymphadenopathy or significant peripheral blood lymphocytosis.

- A warning will be added to the product information (SPC/Package Leaflet) as a risk minimization measure *(see attached/or below as appropriate).*

Further information on HSTCL

Hepatosplenic T-cell lymphoma (HSTCL) is a rare aggressive form of non-Hodgkin lymphoma with a poor prognosis that occurs most commonly in adolescent and young adult males. The median survival is estimated to be less than 2 years.

At the time of clinical presentation, patients typically have hepatosplenomegaly along with symptoms characteristic of lymphomas (fever, night sweats, and weight loss), but no lymphadenopathy. Peripheral blood smear evaluation in patients with HSTCL shows anemia, thrombocytopenia, and circulating lymphoma cells.

Published reports indicate HSTCL has occurred in patients receiving immunosuppressive therapy following organ transplantation, in patients taking azathioprine or 6-mercaptopurine monotherapy, as well as in Crohn's disease patients receiving infliximab and concomitant 6-mercaptopurine or azathioprine therapies.

Three cases have been reported post marketing during treatment with Humira. Two of those were young men also receiving azathioprine or 6-mercaptopurine for inflammatory bowel disease A causal relationship between HUMIRA® and HSTCL cannot be excluded.

HSTCL should be considered in the differential diagnosis in the event that a patient receiving HUMIRA® develops symptoms lymphomas and/or hepatosplenomegaly with or without peripheral lymphadenopathy or significant peripheral blood lymphocytosis. Appropriate specialist referral for investigation and management should be considered as clinically indicated.

Abbott has approximately 500,000 patient treatment years of experience across multiple indications with HUMIRA worldwide.

Call for reporting

Abbott will continue to monitor the safety profile of HUMIRA®. You can assist us by reporting occurrences of adverse reactions in patients receiving HUMIRA® in accordance with your local reporting requirements.

You may report an adverse event to the Abbott Ireland Medical Department on: 01-4691500 or to the Irish Medicines Board in the usual way.

Communication information

Should you have any questions or require additional information regarding the use of HUMIRA®, please contact the Abbott Ireland Medical Department on: 01-4691500.

Yours faithfully,

Dr. Michelle Costello-Smith.

Dr. Michelle Costello-Smith
Medical Director
Abbott Laboratories Ireland Limited

Please note the following additions to the relevant sections of the SmPC and PIL. The SmPC and PIL should be consulted for full information

SmPC

4.4 Special warnings and precautions for use

Malignancies and lymphoproliferative disorders

Rare postmarketing cases of hepatosplenic T-cell lymphoma have been identified in patients treated with adalimumab. This rare type of T-cell lymphoma has a very aggressive disease course and is usually fatal. Some of these hepatosplenic T-cell lymphomas with Humira have occurred in young adult patients on concomitant treatment with azathioprine or 6-mercaptopurine used for Crohn's disease. A risk for the development of hepatosplenic T-cell lymphoma in patients treated with Humira cannot be excluded (see sections 4.8).

4.8 Undesirable effects

Rare post-marketing cases of hepatosplenic T-cell lymphoma have been reported in patients treated with adalimumab (see section 4.4).

Undesirable Effects in Postmarketing Surveillance and Phase IV Clinical Studies

Undesirable Effects in Clinical Studies

Neoplasma benign and malignant (including cysts and polyps)	Hepatosplenic T-cell lymphoma

PIL

2. BEFORE YOU USE HUMIRA

Take special care with Humira:

On rare occasions, a specific and severe type of lymphoma, has been observed in patients taking Humira. Some of those patients were also treated with azathioprine or 6- mercaptopurine.

4. POSSIBLE SIDE EFFECTS

Other side effects that have been observed in patients taking Humira:

Hepatosplenic T-cell lymphoma