

CYP450 substrates with a narrow therapeutic index, monitoring of the effect (e.g., warfarin) or drug concentration (e.g., cyclosporine or theophylline) is recommended and the individual dose of the drug product may be adjusted as needed.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category B

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction and developmental studies are not always predictive of human response, HUMIRA should be used during pregnancy only if clearly needed.

Pregnancy Registry: To monitor outcomes of pregnant women exposed to HUMIRA, a pregnancy registry has been established. Physicians are encouraged to register patients by calling 1-877-311-8972.

Nursing Mothers

It is not known whether adalimumab is excreted in human milk or absorbed systemically after ingestion. Because many drugs and immunoglobulins are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from HUMIRA, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and efficacy of HUMIRA in pediatric patients for uses other than juvenile idiopathic arthritis (JIA) have not been established.

Juvenile Idiopathic Arthritis

In the JIA trial, HUMIRA was shown to reduce signs and symptoms of active polyarticular JIA in patients 4 to 17 years of age. HUMIRA has not been studied in children less than 4 years of age, and there are limited data on HUMIRA treatment in children with weight <15 kg.

The safety of HUMIRA in pediatric patients in the JIA trial was generally similar to that observed in adults with certain exceptions [see *Adverse Reactions*].

Post-marketing cases of malignancies, some fatal, have been reported among children, adolescents, and young adults who received

treatment with TNF-blockers including HUMIRA [see *Warnings and Precautions*].

Geriatric Use

A total of 519 RA patients 65 years of age and older, including 107 patients 75 years of age and older, received HUMIRA in clinical studies RA-I through IV. No overall difference in effectiveness was observed between these subjects and younger subjects. The frequency of serious infection and malignancy among HUMIRA treated subjects over 65 years of age was higher than for those under 65 years of age. Because there is a higher incidence of infections and malignancies in the elderly population, use caution when treating the elderly.

OVERDOSAGE

Doses up to 10 mg/kg have been administered to patients in clinical trials without evidence of dose-limiting toxicities. In case of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions or effects and appropriate symptomatic treatment instituted immediately.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies of HUMIRA have not been conducted to evaluate the carcinogenic potential or its effect on fertility. No clastogenic or mutagenic effects of HUMIRA were observed in the *in vivo* mouse micronucleus test or the *Salmonella-Escherichia coli* (Ames) assay, respectively.

PATIENT COUNSELING INFORMATION

Patient Counseling

Provide the HUMIRA "Medication Guide" to patients or their caregivers, and provide them an opportunity to read it and ask questions prior to initiation of therapy and prior to each time the prescription is renewed. If patients develop signs and symptoms of infection, instruct them to seek medical evaluation immediately.

Advise patients of the potential benefits and risks of HUMIRA.

• Infections

Inform patients that HUMIRA may lower the ability of their immune system to fight infections. Instruct patients of the importance of contacting their doctor if they develop any symptoms of infection,

including tuberculosis, invasive fungal infections, and reactivation of hepatitis B virus infections.

• Malignancies

Counsel patients about the risk of malignancies while receiving HUMIRA.

• Allergic Reactions

Advise patients to seek immediate medical attention if they experience any symptoms of severe allergic reactions. Advise latex-sensitive patients that the needle cap of the prefilled syringe contains latex.

• Other Medical Conditions

Advise patients to report any signs of new or worsening medical conditions such as congestive heart failure, neurological disease, autoimmune disorders, or cytopenias. Advise patients to report any symptoms suggestive of a cytopenia such as bruising, bleeding, or persistent fever.

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LÉXICO MÉDICO

Biología sintética


Pocas veces un científico puede vanagloriarse de haber sido el centro de la creación de una nueva rama de la ciencia. Ese es el caso del norteamericano George Church, nacido en 1954, profesor de genética molecular en Harvard y de biotecnología en MIT, figura descollante y pionero de la Biología Sintética.

La Biología Sintética estudia y crea en el laboratorio biomoléculas y sistemas biológicos inéditos que no provienen de la naturaleza. Son entidades biológicas completas que pueden ejercer labores útiles para el ser humano y vivir, independientemente.

Inicialmente, se han escogido determinadas bacterias, que son seres vivos con un genoma que puede ser modificado para inducirlo a fabricar proteínas sintéticas. Esto se encuentra aún en su etapa inicial y busca identificar los genes mínimos o los genes imprescindibles para que la célula bacteriana "viva". Cuando esto se logre plenamente, dispondremos de bacterias "básicas" que pueden ser transformadas en productoras de nuevas

proteínas. Esto lleva al concepto, que parece ciencia ficción, de "evolución dirigida", que está cerca de demostrar su practicidad.

La biología sintética se basa en dos logros de la ciencia: la genética molecular y la informática, que al unirse facilitan la predicción del comportamiento de los genomas mínimos. Sus aplicaciones futuras y sus ramificaciones modificarán radicalmente a la Medicina y las ciencias. La producción en el cuerpo de medicamentos y componentes fisiológicos faltantes (insulina, aminoácidos esenciales), la sustitución hormonal a pedido, la reparación de genes dañados, la regeneración tisular y la reprogramación de células comunes en células madre.

Fuera del campo de la Medicina están la descontaminación bacteriana de sistemas, la fabricación de biosensores, de biomateriales y de bioenergía, rama en la que lleva la delantera el genetista Craig Venter, copartícipe de la decodificación del genoma humano hace unos años. 

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