Dear Healthcare Professional,

Abbott is pleased to announce the FDA has approved HUMIRA® (adalimumab) for the treatment of moderate to severe polyarticular Juvenile Idiopathic Arthritis (JIA). HUMIRA is now indicated to reduce the signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients 4 years of age and older. This represents another key milestone for HUMIRA as the sixth FDA-approved disease indication since the launch of HUMIRA in 2002. With this indication and the recent approval for moderate to severe chronic plaque psoriasis, HUMIRA now has the most indications of any self-injectable TNF antagonist and is the only monoclonal antibody with an indication for polyarticular JIA.

Key Clinical Data:

The approval is based on data from a clinical trial containing 171 patients with polyarticular JIA. In the trial, patients were stratified into two groups, MTX treated and non-MTX treated and included four phases.

Phase	Description	Duration	HUMIRA Dosing*
1	Open Label Lead-In	16 weeks	BSA: 24mg/m^2 eow
2	Double-Blind Randomized Withdrawal	32 weeks	BSA: 24mg/m^2 eow
3	Open-Label BSA Extension	Up to 136 weeks	BSA: 24mg/m^2 eow
4	Open-Label Fixed-Dosed Extension	16 weeks	Patient<30kg: 20mg eow Patient ≥30kg: 40mg eow

*BSA= Body Surface Area

Key trial results[1]:

At the end of the 16 week open-label lead-in phase, 94% of the patients in the methotrexate group and 74% of the patients in the non-methotrexate group were Pediatric ACR 30 responders.

In the double blind phase, significantly fewer patients who received HUMIRA experienced disease flare compared to placebo, both without MTX (43% vs. 71%) and with methotrexate (37% vs. 65%).

Pediatric ACR responses were maintained for up to two years in the open label extension phase in patients who received HUMIRA throughout the study.

In general, the adverse reactions in juvenile idiopathic arthritis patients were similar in frequency and type to those seen in adult patients.

- Severe adverse reactions reported in the clinical trial in JIA included neutropenia, streptococcal pharyngitis, increased aminotransferases, herpes zoster, myositis, metrorrhagia and appendicitis.
- Serious infections were observed in 4% of patients within approximately 2 years of initiation of treatment with HUMIRA and included cases of herpes simplex, pneumonia, urinary tract infection, pharyngitis, and herpes zoster.

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Dosing and Administration:
The recommended dose of HUMIRA for patients 4 to 17 years of age with polyarticular JIA is 20 mg every other week for patients 15 kg (33 lbs) to <30 kg (66 lbs) and 40 mg every other week for JIA patients weighing ≥30 kg (66 lbs). Methotrexate, glucocorticoids, salicylates, NSAIDs or analgesics may be continued during treatment with HUMIRA. Limited data are available for pediatric patients with a weight below 15 kg. HUMIRA 40mg is currently available in a pre-filled syringe and pen device. HUMIRA 20mg is available only in a pre-filled syringe.

About HUMIRA:
More than 250,000 patients worldwide are currently being treated with HUMIRA.[2] HUMIRA is indicated to reduce the signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients 4 years of age and older. HUMIRA is also indicated in adults for the treatment of moderate to severe rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, moderately to severely active Crohn's disease in patients who have had an inadequate response to conventional therapy, and moderate to severe chronic plaque psoriasis.[1]

Enclosed for your reference is updated full Prescribing Information. For additional information about HUMIRA (adalimumab), please contact your Abbott sales representative. For patient support and injection training resources, please call 1-800-4HUMIRA.

Sincerely,

Jeffrey D. Kent, MD
Global Project Head
Global Pharmaceutical Research and Development
Abbott Immunology

References:
1. HUMIRA Package Insert
2. Data on File

Please see reverse side or next page for Important Safety Information. Refer to accompanying full Prescribing Information or visit HUMIRA.com.
Project # 64C-102213

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NOW APPROVED for moderate to severe polyarticular Juvenile Idiopathic Arthritis (JIA)

- The only anti-TNF monoclonal antibody approved for JIA
- HUMIRA, now approved for its 6th disease indication (JIA), has the most indications of any self-administered TNF antagonist

HUMIRA dosing for JIA in children 4 to 17 years of age

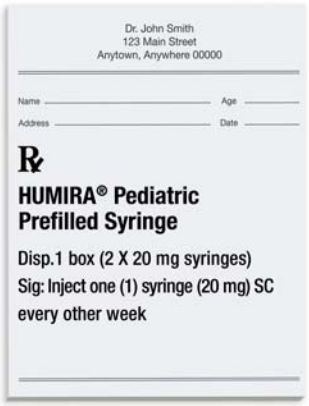
In children weighing **15 kg** (33 lbs) to **<30 kg** (66 lbs), dose **20 mg** HUMIRA every other week

In children weighing **≥30 kg** (66 lbs), dose **40 mg** HUMIRA every other week

- Methotrexate, glucocorticoids, salicylates, NSAIDs or analgesics may be continued during treatment with HUMIRA
- Limited data are available for HUMIRA treatment in pediatric patients with a weight below 15 kg

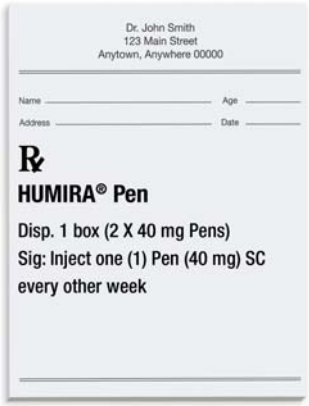
HUMIRA dosing regimens for polyarticular JIA

Children 15 kg (33 lbs) to <30 kg (66 lbs)



NDC 0074-9374-02

Children ≥30 kg (66 lbs)



NDC 0074-4339-02

HUMIRA 40 mg is also available in a prefilled syringe.

*Only available for children 15 kg (33 lbs) to <30 kg (66 lbs).
†Small, 27-gauge needle.

It is recommended that healthcare professionals train and supervise patients or caregivers during administration of the initial dose of HUMIRA. For self-injection assistance, please see accompanying Medication Guide or call 1-800-4HUMIRA (1-800-448-6472).

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Please see next page or reverse side for Important Safety Information and accompanying full Prescribing Information.

HUMIRA is indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients 4 years of age and older. HUMIRA can be used alone or in combination with methotrexate.

IMPORTANT SAFETY INFORMATION

Tuberculosis (TB), invasive fungal infections, and other opportunistic infections, have been observed in patients receiving HUMIRA. Some infections have been fatal. Anti-TB treatment of patients with latent TB infection reduces the risk of reactivation in patients receiving HUMIRA. However, active TB has developed in patients receiving HUMIRA whose screening for latent TB infection was negative. Patients should be evaluated for TB risk factors and be tested for latent TB prior to initiating HUMIRA and during therapy. When TB skin testing is performed, an induration size of 5mm or greater should be considered positive, even if vaccinated previously with Bacille Calmette-Guerin (BCG). Treatment of latent TB should be initiated prior to therapy with HUMIRA. Physicians should monitor patients receiving HUMIRA for signs and symptoms of active TB, including patients who tested negative for latent TB.

Serious infections and sepsis, including fatalities, have been reported with the use of TNF-blocking agents, including HUMIRA. Many of these infections occurred in patients predisposed to infections because of concomitant immunosuppressive therapy in addition to their underlying disease. Patients who develop a new infection while using HUMIRA should be monitored closely. Treatment should be discontinued if a patient develops a serious infection. Do not start HUMIRA in patients with active infection (including chronic or localized). Exercise caution in patients with a history of recurrent infection or with underlying conditions, which may predispose patients to infections, or patients who have resided in regions where TB and histoplasmosis are endemic.

More cases of malignancies have been observed among patients receiving TNF blockers, including HUMIRA, compared to control patients in clinical trials. These malignancies, other than lymphoma and non-melanoma skin cancer, were similar in type and number to what would be expected in the general population. In the controlled and open-label portions of HUMIRA clinical trials, there was an approximately 3 fold higher rate of lymphoma than expected in the general population. The potential role of TNF-blocking therapy in the development of malignancies is not known. Anaphylaxis and angioneurotic edema have been reported rarely following HUMIRA administration.

Use of TNF-blockers, including HUMIRA, may increase the risk of reactivation of hepatitis B (HBV) in patients who are chronic carriers. Some cases have been fatal. Patients at risk for HBV infection should be evaluated for prior evidence of HBV infection before initiating TNF blocker therapy. For patients identified as carriers of HBV, exercise caution when prescribing HUMIRA, with careful evaluation and monitoring prior to and during treatment. HUMIRA should be stopped and antiviral therapy should be initiated in patients who develop hepatitis B reactivation. TNF-blocking agents, including HUMIRA, have been associated in rare cases with new onset or exacerbation of demyelinating disease. Exercise caution when considering HUMIRA for patients with these disorders.

Rare reports of pancytopenia including aplastic anemia have been reported with TNF-blocking agents. Medically significant cytopenia (e.g. thrombocytopenia, leukopenia) has been infrequently reported with HUMIRA. The causal relationship of these reports to HUMIRA remains unclear. Worsening congestive heart failure (CHF) has been observed with TNF-blocking agents, including HUMIRA, and new onset CHF has been reported with TNF-blocking agents. Treatment with HUMIRA may result in the formation of autoantibodies and, rarely, in development of a lupus-like syndrome. Discontinue treatment if symptoms of lupus-like syndrome develop. Patients on HUMIRA should not receive live vaccines. It is recommended that juvenile idiopathic arthritis patients, if possible, be brought up to date with all immunizations in agreement with current immunization guidelines prior to initiating HUMIRA therapy. Serious infections were seen in studies with concurrent use of anakinra and another TNF-blocking agent, therefore, the combination of HUMIRA and anakinra is not recommended.

In the placebo-controlled clinical studies of adult patients with rheumatoid arthritis the most frequent adverse reactions vs placebo were injection site reactions (20% vs 14%), upper respiratory infection (17% vs 13%), injection site pain (12% vs 12%), headache (12% vs 8%), rash (12% vs 6%), and sinusitis (11% vs 9%). Discontinuations due to adverse events were 7% for HUMIRA vs 4% for placebo.

In HUMIRA clinical trials for ankylosing spondylitis, psoriatic arthritis, Crohn's disease and plaque psoriasis the safety profile for patients treated with HUMIRA was similar to the safety profile seen in patients with rheumatoid arthritis. In the placebo-controlled clinical trials in plaque psoriasis, the incidence of arthralgia was 3% in HUMIRA-treated patients versus 1% in controls.

In general, the adverse reactions in juvenile idiopathic arthritis (JIA) patients were similar in frequency and type to those seen in adult patients. Severe adverse reactions reported in the clinical trial in JIA included neutropenia, streptococcal pharyngitis, increased aminotransferases, herpes zoster, myositis, metrorrhagia and appendicitis. Serious infections were observed in 4% of patients within approximately 2 years of initiation of treatment with HUMIRA and included cases of herpes simplex, pneumonia, urinary tract infection, pharyngitis, and herpes zoster. The safety of HUMIRA in pediatric patients for uses other than JIA has not been established.

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Please see accompanying full Prescribing Information and/or go to www.HUMIRA.com

HUMIRA is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage and improving physical function in adult patients with moderately to severely active rheumatoid arthritis. **HUMIRA** is indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients 4 years of age and older. HUMIRA can be used alone or in combination with methotrexate. **HUMIRA** is indicated for reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage and improving physical function in adult patients with psoriatic arthritis. **HUMIRA** is indicated for reducing signs and symptoms in adult patients with active ankylosing spondylitis. **HUMIRA** is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy, and reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab. **HUMIRA** is indicated for the treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate. HUMIRA should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician.