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DMARDs for Juvenile Idiopathic Arthritis

A Review of the Research for Parents and Caregivers

John M. Eisenberg Center for Clinical Decisions and Communications Science.

Baylor College of Medicine, Houston, Texas

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Is This Information Right for Me?

Yes, if

- A doctor said your child has “juvenile idiopathic arthritis” (JIA) (formerly known as “juvenile rheumatoid arthritis” or JRA).
 - Systemic arthritis
 - Oligoarthritis
 - Psoriatic arthritis
 - Enthesitis-related arthritis
 - Undifferentiated arthritis
 - Polyarthritis—rheumatoid factor negative
 - Polyarthritis—rheumatoid factor positive
- The doctor suggested a type of medicine called a “disease-modifying anti-rheumatic drug” (DMARD).

No, if

- Your child is over the age of 16.
- Your child has joint pain, but a doctor has not said that it is JIA.
- The doctor has not suggested a DMARD.

What does this summary cover?

This summary describes the research about the effectiveness and safety of DMARDs to treat JIA. It explains what research shows about how DMARDs help children with JIA, their side effects, and how much they cost. It is written to help you talk with your doctor when deciding if a DMARD is best for your child.

Where does the information come from?

This information comes from a report that reviewed 56 research studies on DMARDs to treat JIA. The report was funded by the Agency for Healthcare Research and Quality (AHRQ), a Federal government research agency, and reviewed by clinicians, researchers, experts, and the public. You can read the report at www.effectivehealthcare.ahrq.gov/dmardsjia.cfm.

Understanding Your Child's Condition

What is JIA?

Juvenile Idiopathic Arthritis (JIA) is a chronic (ongoing) disease that causes children to have swelling, pain, and stiffness in their joints. The ankles, knees, hips, elbows, jaw, and joints in the wrists, hands, and feet are most often affected. JIA occurs before the age of 16.

- JIA affects each child differently. Symptoms range from mild to severe, and the number of joints affected may be different for each child.

- JIA can also cause fever, rash, swollen glands, and eye inflammation. Pain, sensitivity to light, or blurry vision can be signs of eye inflammation, but often it has no symptoms.
- Rarely, JIA can also cause irritation around the heart and lungs.
- Some children with JIA may develop destructive joint disease. JIA can cause life-long pain and disability
- The growth of some children with JIA may be delayed or slowed. Also, the bones around their joints may grow at different rates, causing their arms or legs to be different lengths.

How common is JIA?

Although JIA is rare, it is the most common childhood joint disease. About 1 in 1,000 children have JIA. It affects children of all races.

What causes JIA?

The immune system normally protects the body from disease by destroying bacteria or viruses. In children with JIA, the immune system targets and destroys healthy tissue in their joints. Doctors are not sure why this happens.

What else should I know about JIA?

- JIA is not usually life threatening. Although there is no cure for JIA, there are medicines that can control the symptoms of the disease and help prevent long-term disability.
- Children with JIA may go through periods with no joint pain or swelling, called “remission.” While some children achieve long periods of remission, others will have their symptoms come back or “flare.” The goal of treatment is to keep children in remission and minimize flares.
- Most children with JIA can play sports and exercise when their symptoms are not flaring.
- Your child's primary care physician or pediatrician may suggest you take your child to a doctor who specializes in treating children with joint problems. This type of doctor is called a “pediatric rheumatologist” (pronounced roo-mah-TOL-o-jest).

Understanding Your Options

How is JIA treated?

Before any treatment is started, the doctor will ask many questions to understand your child's symptoms and activities. Sometimes doctors use questionnaires to collect this information. Doctors and nurses use this information to decide what kind of medicines will be best for your child and to measure the success of treatment.

The doctor may recommend medicines that help your child by:

- Lessening the pain and swelling when these symptoms “flare.”
- Reducing the number of times the child has symptoms, with the goal of taking away all symptoms for long periods of time (“remission”).
- Preventing long-term painful joint damage.

The way JIA is treated depends on how severe your child's symptoms are and how well your child responds to the different treatments that are available. Most children with JIA will start with one or both of these medicines that treat pain and inflammation:

- Nonsteroidal anti-inflammatory drugs (NSAIDs).
- Corticosteroids injected into the painful joint or sometimes taken by mouth.

For some children, NSAIDs and corticosteroids will be all that is needed to relieve the symptoms of JIA and to reduce the risk of long-term problems. Other children may need a third kind of drug called a “disease-modifying anti-rheumatic drug,” or DMARD.

What are DMARDs?

DMARDs are a family of medicines that slow or stop the immune system from destroying the joints. Several of these medicines have been approved by the United States Food and Drug Administration (FDA) for use in children with JIA.

There are two types of DMARDs — nonbiologic and biologic. Nonbiologic DMARDs are produced from chemicals, like most drugs. Biologic DMARDs are antibodies that are similar to those made in the body but

these antibodies are created in laboratories.

- The most common DMARD given to children with JIA is a nonbiologic called “methotrexate” (pronounced meth-oh-TREK-sate). Many doctors prescribe methotrexate as standard treatment for JIA.
- Both nonbiologic and biologic DMARDs can be added to standard treatment for children with more severe symptoms of JIA or when they are not getting enough relief from their symptoms. DMARDs may be taken with each other and with NSAIDs and corticosteroids.

What's the difference between nonbiologic and biologic DMARDs?

- Nonbiologic DMARDs can be given as pills or as shots. Biologic DMARDs must be given through an IV (intravenous) tube or as a shot. The IV treatment must be given in a clinic or doctor's office, but the shot may be given in a clinic or doctor's office or at home.
- Because nonbiologic and biologic DMARDs work in different ways, they have different safety concerns. There is not enough research yet to know what all of the differences may be or how important they are.

<i>Generic Name</i>	<i>Brand Name</i>
Nonbiologic DMARDs	
Azathioprine	Azasan[®]; Imuran[®]
Cyclosporine A	Neoral[®]; Gengraf[®]
Penicillamine	Depen[®]; Cuprimine[®]
Leflunomide	Arava[®]
Methotrexate*	Methotrexate LPF[®]
Sulfasalazine*	Azulfidine[®]; Sulfazine[®]
Biologic DMARDs	
Abatacept*	Orencia[®]
Adalimumab*	Humira[®]
Anakinra	Kineret[®]
Etanercept*	Enbrel[®]
Infliximab	Remicade[®]
Intravenous immunoglobulin (IVIG)	BayGam[®]; Carimune[®] NF; Flebogamma[®] 5% DIF; Gammagard[®] S/D; Gammagard[®] Liquid 10%; Gammar-P[®]; Gamunex[®] 10%; Iveegam EN[®]; Octagam[®] 5%; Panglobulin[®]; Polygam[®] S/D; Privigen[®] 10%; Vivaglobin[®]
Tocilizumab	Actemra[®]

All of the medicines in this list have been studied on children with JIA. Those followed by an * have been approved by the United States Food and Drug Administration (FDA) for treating JIA. This list of DMARDs may not include newer medicines that are being studied and used for JIA. Ask your doctor about the names of other DMARDs that may be available to you.

What does the research say about the benefits of DMARDs?

Researchers know much more about using DMARDs in adults than they know about using them in children. For this reason, researchers cannot say with much certainty how well these drugs work for children with JIA.

Researchers found that:

- Adding the nonbiologic DMARD methotrexate to treatment works better than NSAIDs and corticosteroids alone to improve the symptoms of JIA.
- Biologic DMARDs can improve the symptoms of JIA and reduce flares in some children.

A very small amount of research found:

- Children who took DMARDs had some improvement to their quality of life and abilities, but there is not enough research to know this for sure.
- Nonbiologic DMARDs may reduce symptoms and improve the health of children with JIA, but there is not enough research to know this for sure.

There is not enough research to know if:

- Any one of the nonbiologic or biologic DMARDs works better than any other to reduce pain and swelling or to protect against joint damage.

What does the research say about the side effects of DMARDs?

- The FDA warns that certain biologic DMARDs may rarely lead to the development of unusual infections like tuberculosis (called “TB”) and fungal infections like yeast. Children are usually tested for these infections before starting biologic DMARDs.
- Serious infections were seen most often in children taking methotrexate and the biologic DMARD infliximab at the same time.
- The FDA warns that certain biologic DMARDs called “TNF-alpha blockers” — adalimumab (Humira[®]), etanercept (Enbrel[®]), and infliximab (Remicade[®]) — have been associated with cancer in children, but this is rare. The cancer that usually occurs is lymphoma (cancer in the lymph glands, which are part of the immune system).
- There is not enough research to know if the side effects are different among DMARDs.

Making a Decision

What else should be considered when making a decision?

- Your child's symptoms can help you decide what treatment is best. Be sure to talk about all of your child's symptoms and your concerns when answering the doctor's questions. Also tell the doctor about the activities your child wants to be able to do.
- In reviewing all the treatment choices with your doctor, you may want to talk about the “trade-offs” between the benefits of certain treatments and the risks of possible side effects. In these discussions, you want to understand from your doctor the risk of crippling or destructive joint disease if your child is not treated or is not treated enough.

What are the costs of DMARDs?

The cost to you for these medicines depends on:

- The type of health insurance you have.
- The dose (amount) of medicine your child needs to take.
- Whether the medicine comes in a generic form.

The most commonly used nonbiologic DMARD is methotrexate. This drug comes in both generic and brand forms.

The cost of methotrexate can range widely, depending on the weight of your child. The average wholesale price of the medicine for a 65-pound child is around \$60 a month for generic methotrexate (tablets), around \$187 a month for the brand Rheumatrex[®], and around \$76 a month for the brand Trexall[®].

The cost of biologic DMARDs can range widely, depending on the weight of your child and the type of DMARD. For a child who weighs about 88 pounds, the cost of a 1-month supply of a biologic DMARD is between \$750 and \$2,500.

Ask Your Doctor

- What do you think about the research on DMARDs?
- Given my child's symptoms, which treatment option is best?
- What are the short-term and long-term side effects of the medicines?
- Is my child at risk for developing infections or cancer if he or she takes these medicines?
- What should I expect will happen to my child if no treatment is given?

Other questions for your doctor

Write the answers here

Source

The information in this summary comes from the report *Disease-Modifying Antirheumatic Drugs (DMARDs) in Children With Juvenile Idiopathic Arthritis (JIA)*. It was produced by the Duke University Evidence-based Practice Center with funding by the Agency for Healthcare Research and Quality (AHRQ). For a copy of the report, or for more information about AHRQ and the Effective Health Care Program, go to www.effectivehealthcare.ahrq.gov/dmardsjia.cfm. Additional information for this summary came from MedlinePlus® Web site, a service of the U.S. National Library of Medicine and the National Institutes of Health. This site is available at www.nlm.nih.gov/medlineplus.

This summary was prepared by the John M. Eisenberg Center for Clinical Decisions and Communications Science at Baylor College of Medicine, Houston, TX.



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