EMA/174755/2023
EMEA/H/C/004760

Rinvoq (*upadacitinib*)

An overview of Rinvoq and why it is authorised in the EU

What is Rinvoq and what is it used for?

Rinvoq is a medicine that acts on the immune system (the body's natural defences) and is used to treat:

- adults with moderate to severe rheumatoid arthritis (a disease that causes inflammation of the joints) that cannot be controlled well enough with disease-modifying anti-rheumatic medicines (DMARDs) or if the patient cannot take these medicines. It can be used on its own or with methotrexate, another medicine that acts on the immune system;
- adults with active psoriatic arthritis (inflammation of the joints associated with psoriasis, a disease causing red, scaly patches on the skin) that cannot be controlled well enough with DMARDs, or if the patient cannot take these medicines. Rinvoq can be used on its own or with methotrexate;
- adults with active axial spondyloarthritis (inflammation of the spine causing back pain), including ankylosing spondylitis, when X-ray shows the disease, and non-radiographic axial spondyloarthritis, when there are clear signs of inflammation but X-ray does not show disease. It is used when other treatments do not work well enough;
- adults and children from 12 years of age with moderate to severe atopic dermatitis (also known as eczema, when the skin is itchy, red and dry) who can be treated with a medicine given by mouth or by injection;
- adults with ulcerative colitis (inflammation of the large intestine causing ulceration and bleeding) or Crohn's disease (an inflammatory disease affecting the gut). Rinvoq is used to treat moderately to severely active disease when other medicines, including biological medicines, do not or no longer work, or if the patient cannot take them.

Rinvoq contains the active substance upadacitinib.

How is Rinvoq used?

Rinvoq can only be obtained with a prescription and treatment should be started and supervised by a doctor experienced in diagnosing and treating the conditions for which the medicine is used.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Rinvoq is available as tablets to be taken by mouth once a day. The dose depends on the disease Rinvoq is used for and other factors including the patient's age and the severity of the disease. The doctor may interrupt treatment in case of certain side effects, including falls in blood cell counts. Treatment may also be stopped if the patient does not respond after a number of weeks, which depends on the condition Rinvoq is used for. For more information about using Rinvoq, see the package leaflet or contact your healthcare provider.

How does Rinvoq work?

In patients with rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis, atopic dermatitis, ulcerative colitis and Crohn's disease, the immune system attacks healthy tissue, causing inflammation, pain and other symptoms.

Upadacitinib, the active substance in Rinvoq, is an immunosuppressant. This means that it reduces the activity of the immune system. Upadacitinib works by blocking the action of enzymes called Janus kinases. These enzymes are involved in setting up processes that lead to inflammation, and blocking their effect brings symptoms of the conditions under control.

What benefits of Rinvoq have been shown in studies?

Rheumatoid arthritis

Five studies involving a total of nearly 4,400 patients found Rinvoq effective in reducing symptoms in patients with moderate to severe rheumatoid arthritis. These studies involved rating disease activity in 28 joints in the body on a standard scale. They showed that Rinvoq was effective at clearing the symptoms or achieving low disease activity in 43 to 48% of patients; this compared with a reduced disease activity in 14 to 19% of patients given placebo (a dummy treatment) or methotrexate.

Psoriatic arthritis

Two studies involving over 2,000 patients with active psoriatic arthritis despite prior treatment showed that Rinvoq, used on its own or with methotrexate, was more effective than adalimumab (another medicine used for psoriatic arthritis) or placebo at reducing the symptoms of the disease. Between 57 and 71% of patients on Rinvoq at a dose of 15 mg per day achieved a reduction in symptoms after 12 weeks of treatment, compared with 65% of patients treated with adalimumab and 24 to 36% of patients on placebo.

Axial spondyloarthritis

For ankylosing spondylitis a 14-week study involving 187 patients whose disease could not be controlled well enough with other treatments showed that Rinvoq was effective at reducing symptoms of the disease. Of the patients who received Rinvoq, around 52% had a reduction in the number and severity of symptoms, compared with 26% of patients on placebo.

In addition, a study involving around 300 patients with non-radiographic axial spondyloarthritis whose diseases could not be controlled well enough with other treatments showed that Rinvoq improved symptoms of the disease: symptoms improved by at least 40% after 14 weeks in 45% of patients taking Rinvoq compared with 23% of patients on placebo.

Atopic dermatitis

Rinvoq was effective at clearing up the skin and reducing disease extent and severity in patients with moderate to severe atopic dermatitis in three main studies involving a total of 2,584 adults and children from 12 years of age. The studies compared the effects of two doses of Rinvoq (15 and 30 mg a day), used with or without corticosteroids applied to the skin, with placebo.

Treatment with Rinvoq on its own led to reduced extent and severity of the disease in 60 to 70% of patients taking the 15 mg dose and in 73 to 80% of those taking 30 mg, compared with 13 to 16% of patients given placebo. Clear or almost clear skin was achieved in 39 to 62% of patients taking Rinvoq, compared with 5 to 8% of patients on placebo.

Similar results were observed when Rinvoq was used with corticosteroids: extent and severity of the disease were reduced in 65 to 77% of patients taking Rinvoq versus 26% of patients on placebo; skin cleared or almost cleared in 40 to 59% of patients taking Rinvoq, compared with 11% of patients in the placebo group.

Ulcerative colitis

Two main studies involving 988 patients showed that Rinvoq was effective at clearing symptoms and improving the inflammation in the lining of the bowel of moderately to severely active ulcerative colitis in patients whose disease had not responded to other treatment or who could not tolerate other treatment. After eight weeks of treatment during which patients took Rinvoq 45 mg or placebo once a day, the proportion of patients on Rinvoq whose symptoms were gone or almost gone, along with normal or mild inflammation in the lining of the bowel, was 26% in the first study and 34% in the second study, compared with almost 5% and 4% for those taking placebo.

In a third study, a total of 451 patients from the first two studies whose ulcerative colitis condition had improved with Rinvoq went on to receive 15 or 30 mg of the medicine once daily, or placebo. After 52 weeks of treatment, symptoms of ulcerative colitis were gone or almost gone in 42% of patients on 15 mg Rinvoq and in 52% of patients on 30 mg Rinvoq, compared with around 12% of patients on placebo.

Crohn’s disease

Two main studies involving a total of 1,021 patients with moderately to severely active Crohn’s disease showed that Rinvoq was effective at improving symptoms of the disease. After 12 weeks of treatment during which patients took Rinvoq 45 mg or placebo once a day, the proportion of patients on Rinvoq whose symptoms were gone or almost gone in the two studies was 40% and 51%, compared with 14% and 22% for those taking placebo. Inflammation of the gut lining was reduced by more than half in 35% and 46% of patients given Rinvoq, compared with 4% and 13% in patients given placebo.

A third study involved 502 patients from the first two studies whose Crohn’s disease had improved with Rinvoq. Patients took 15 or 30 mg of the medicine once daily, or placebo. After 52 weeks of treatment, symptoms of Crohn’s disease were gone or almost gone in 36% of patients on 15 mg Rinvoq and in 46% of patients on 30 mg Rinvoq, compared with 14% of patients on placebo. Inflammation of the gut lining was reduced by more than half in 28% and 40% of patients given Rinvoq 15 mg and 30 mg, respectively, compared with 7% of patients on placebo.

What are the risks associated with Rinvoq?

For the complete list of side effects and restrictions with Rinvoq, see the package leaflet.

The most common side effects with Rinvoq seen in the rheumatoid arthritis, psoriatic arthritis and axial spondyloarthritis studies (which may affect more than 2 in 100 people) are upper respiratory tract infections (nose and throat infections), increased blood levels of the enzymes creatine phosphokinase (CPK, an enzyme released into the blood when a muscle is damaged), alanine transaminase or aspartate transaminase (indicating possible liver damage), bronchitis (inflammation of the airways in the lungs), nausea (feeling sick), cough and hypercholesterolaemia (high blood cholesterol levels).

In the atopic dermatitis studies, the most common side effects (which may affect more than 2 in 100 people) were upper respiratory tract infection, acne, herpes simplex (a viral infection that causes cold sores), headache, increased blood levels of CPK, cough, folliculitis (inflammation of hair follicles), abdominal (belly) pain, nausea, neutropenia (low levels of neutrophils, a type of white blood cell), fever and influenza (flu).

In the ulcerative colitis and Crohn's disease studies, the most common side effects (which may affect more than 3 in 100 people) were upper respiratory tract infection, fever, increased blood levels of CPK, anaemia (low levels of red blood cells), headache, acne, herpes zoster (a painful, blistering rash in one part of the body), neutropenia, rash, pneumonia, hypercholesterolaemia, bronchitis, tiredness, increased levels of liver enzymes, folliculitis, herpes simplex, and influenza.

The most common serious side effects are serious infections.

Rinvoq must not be used in patients with tuberculosis or serious infections. It must also not be used in patients with severe liver problems or during pregnancy.

Rinvoq should only be used if no suitable treatment alternatives are available in patients aged 65 years or above, in patients with a history of cardiovascular disease (such as heart attack or stroke) or with risk factors for such a disease (such as current or previous long-term smokers), or in patients at increased risk of cancer.

Why is Rinvoq authorised in the EU?

Rinvoq was effective at controlling moderate to severe rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis, atopic dermatitis, ulcerative colitis and Crohn's disease in patients whose disease had not improved enough with, or could not take, other treatments. Studies found that it reduced disease activity when used alone or combined with other medicines, depending on the condition treated. Patients treated with Rinvoq may have side effects that include infection, neutropenia, and blood tests that suggest liver or muscle damage and raised blood lipids (fats). However, these side effects are considered manageable.

The European Medicines Agency therefore decided that Rinvoq's benefits are greater than its risks and that it can be authorised for use in the EU.

What measures are being taken to ensure the safe and effective use of Rinvoq?

The company that markets Rinvoq will provide educational materials to healthcare professionals and patients with information about the risks with the medicine, particularly the risk of serious infections, blood clots, major cardiovascular events, cancer or gastrointestinal perforation in certain patients. They will also include a reminder that Rinvoq should not be taken during pregnancy and that women taking Rinvoq must use contraception during treatment and for four weeks after stopping treatment.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Rinvoq have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Rinvoq are continuously monitored. Side effects reported with Rinvoq are carefully evaluated and any necessary action taken to protect patients.

Other information about Rinvoq

Rinvoq received a marketing authorisation valid throughout the EU on 16 December 2019.

Further information on Rinvoq can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/rinvoq

This overview was last updated in 04-2023.