

JANUS KINAZ (JAK) INHİBİTÖRÜ HK_EN

REPUBLIC OF TÜRKİYE MINISTRY OF HEALTH Türkiye Medicines and Medical Devices Agency

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Number: E-62820468-000-1134067 Subject: Products containing Janus kinase (JAK) inhibitors.

DOSSIER

Taking into account the EMA and FDA evaluations concerning products that contain Janus kinase (JAK) inhibitors (baricitinib, upadacitinib, tofacitinib, abrocitinib), our Agency's Clinical Evaluation Unit has re-evaluated the SmPC/PILs of the products in question. You are required to revise the approved indications in the indications section of the SmPC/PILs of products containing JAK inhibitors (baricitinib, upadacitinib, tofacitinib, abrocitinib) licensed in our country as follows: "Atopic dermatitis" ... is indicated for the treatment of moderate/severe atopic dermatitis in cases with contraindication or inadequate response to other systemic treatments (systemic steroids, cyclosporine, etc.). It is not suitable for use with other JAK inhibitors, biologic immunomodulators, or other immunosuppressants. "Rheumatoid arthritis (RA)" ... is indicated for moderate or severe active rheumatoid arthritis (RA) in adults with inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs) when there is inadequate response or intolerance to the use of one or more TNF (tumour necrosis factor) blockers. It is not suitable for use with other JAK inhibitors, biologic DMARDs, or potent immunosuppressants such as azathioprine and cyclosporine. "Psoriatic Arthritis (PsA)" ... is indicated for the treatment of active psoriatic arthritis (PsA) in adults with inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs) when there is inadequate response or intolerance to the use of one or more TNF blockers. It is not suitable for use with other JAK inhibitors, biologic DMARDs, or potent immunosuppressants such as azathioprine and cyclosporine. "Ankylosing spondylitis (AS)" ... is indicated for the treatment of ankylosing spondylitis (AS) in adults with no response to conventional therapy when there is inadequate response or intolerance to the use of one or more TNF blockers. It is not suitable for use with other JAK inhibitors, biologic DMARDs, or potent immunosuppressants such as azathioprine and cyclosporine. "Non-radiographic axial spondyloarthritis" ... is indicated for the treatment of ankylosing spondylitis (AS) in adults with no response to conventional therapy when there is inadequate response or intolerance to the use of one or more TNF blockers. It is not suitable for use with other JAK inhibitors, biologic DMARDs, or potent immunosuppressants such as azathioprine and cyclosporine. "Polyarticular juvenile idiopathic arthritis (pJIA)" ... is indicated for patients with active polyarticular juvenile idiopathic arthritis (pJIA) weighing 40 kg or more without response to methotrexate therapy when there is inadequate response or intolerance to the use of one or more TNF blockers and anti-interleukin-6. 12.06.2023

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It is not suitable for use with other JAK inhibitors, biologic DMARDs, or potent immunosuppressants such as azathioprine and cyclosporine. "Ulcerative colitis" ... is indicated for

the treatment of adult patients with moderate to severe active ulcerative colitis who have shown inadequate response, loss of response, or intolerance to conventional therapy and a biologic agent. It is not suitable for use with other JAK inhibitors, biologic therapies for ulcerative colitis, or potent immunosuppressants such as azathioprine and cyclosporine. You are required to add the following black boxed warning to the beginning of the SmPC/PILs of the products containing any of the JAK inhibitors (baricitinib, upadacitinib, tofacitinib, abrocitinib) in question:

WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCIES, MAJOR CARDIOVASCULAR ADVERSE EVENTS (MACE) AND THROMBOSIS

SERIOUS INFECTIONS Patients treated with have an increased risk of developing serious infections, which may lead to hospitalisation or death (see sections 4.4 and 4.8). Most patients who developed such infections were receiving concomitant immunosuppressants such as methotrexate or corticosteroids. If a serious infection develops, withhold until the infection is under control. Reported infections include the following: Active tuberculosis, which may manifest as pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before and during the use of Treatment of latent infection should be considered before using Invasive fungal infections, including cryptococcosis and pneumocytosis. Bacterial, viral, and other infections caused by opportunistic pathogens, including herpes zoster. In patients with chronic or recurrent infections, the risks and benefits of treatment with should be carefully evaluated before starting treatment. Patients should be closely monitored for the development of signs and symptoms during and after treatment with, including possible development of tuberculosis in patients who test negative for latent tuberculosis infection before starting treatment (see section 4.4).

MORTALITY A higher all-cause mortality rate, including sudden cardiovascular death, was observed with JAK inhibitor therapy in a large, randomised, post-marketing safety study comparing another Janus kinase (JAK) inhibitor with tumour necrosis factor (TNF) blockers in rheumatoid arthritis (RA) patients aged 50 years or older with at least one cardiovascular (CV) risk factor (see section 4.4).

MALIGNANCIES Lymphoma and other malignancies have been observed in patients treated with A higher rate of malignancy (excluding non-melanoma skin cancers, NMSCs) was observed in rheumatoid arthritis (RA) patients treated with another JAK inhibitor compared to TNF blocker therapy. Patients who are current or past smokers are at additionally increased risk (see section 4.4).

MAJOR CARDIOVASCULAR ADVERSE EVENTS A higher rate of major cardiovascular adverse events (MACE) (defined as cardiovascular death, myocardial infarction, and stroke) was observed in rheumatoid arthritis (RA) patients aged 50 years and older with at least one cardiovascular risk factor who were treated with another JAK inhibitor compared to TNF blocker therapy. Patients who are current or past smokers are at additionally increased risk. should be withheld in patients with a history of myocardial infarction or stroke (see section 4.4).

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THROMBOSIS Thrombosis-related events, including deep vein thrombosis (DVT), pulmonary embolism (PE), and arterial thrombosis occurred in patients treated with JAK inhibitors used to treat inflammatory conditions. Most of these adverse events are serious and some have resulted in fatal outcomes. A higher rate of thrombosis was observed in rheumatoid arthritis patients aged 50 years and older with at least one cardiovascular risk factor who were treated with another JAK inhibitor compared to TNF blocker therapy. Avoid using in patients at risk. should be withheld and a prompt evaluation should be made in patients with symptoms of thrombosis (see section 4.4).

You are required to add the statement, “should be used in the following patient groups only when there is no other suitable alternative treatment available” in section 4.4 “Warnings and Precautions” of the SmPC/PILs of JAK inhibitors (baricitinib, upadacitinib, tofacitinib, abrocitinib). - Patients aged 65 years and above, - Patients who are current smokers or have smoking history for a long time in the past, - Patients with other cardiovascular or malignancy risk factors, - Patients with VTE risk factors other than those listed above You are required to take into account the aforementioned considerations for JAK inhibitors for which a marketing authorisation application and indication extension will be submitted. You are requested to submit your opinions, recommendations and contributions, if any, in relation to the decision in question to the Clinical Evaluation Unit within 10 (ten) days of the union-association announcement date and not submit any applications concerning “products containing Janus kinase (JAK) inhibitors (baricitinib, upadacitinib, tofacitinib, abrocitinib)” to the Pharmacological Evaluation Unit and the Regulatory Affairs Unit within the specified time period.

Manolya KIVILCIM, PharmD. on behalf of the Agency President Deputy Head of Department

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