Identify patients with non-radiographic axial spondyloarthritis (nr-axSpA)

cimzia® (certolizumab pegol)
FIRST & ONLY
FDA-approved TNF inhibitor for non-radiographic axial spondyloarthritis (nr-axSpA)

ASAS classification criteria were developed to identify patients with axSpA (nr-axSpA and AS)[1]*

nr-axSpA criteria in patients with back pain for ≥3 months and age of onset <45 years[1,2]

Imaging criteria

Sacroiliitis on imaging and ≥1 SpA feature

Active inflammation on MRI highly suggestive of sacroiliitis associated with SpA

OR

Clinical criteria

HLA-B27+ and ≥2 other SpA features

SpA features

- Inflammatory Back Pain (IBP)
- Arthritis
- Enthesitis (heel)
- Uveitis
- Dactylitis
- Psoriasis
- CD/UC
- Good response to NSAIDs
- Family history of SpA
- HLA-B27+
- Elevated CRP

It is important to note that diagnostic criteria for nr-axSpA have not been established. The classification criteria are standardized definitions, primarily intended to create well-defined, relatively homogeneous cohorts for clinical research; they are not intended to capture the entire universe of possible patients in the community.

*Derived from full ASAS axSpA Classification Criteria, which differentiates criteria for nr-axSpA and AS.

AS: Ankylosing Spondylitis; ASAS: Assessment of SpondyloArthritis international Society; axSpA: axial spondyloarthritis; CD: Crohn's disease; CRP: C-reactive protein; HLA-B27: human leukocyte antigen-B27; IBP: inflammatory back pain; MRI: magnetic resonance imaging; NSAID: nonsteroidal anti-inflammatory drug; SpA: spondyloarthritis; UC: ulcerative colitis.

The clinical diagnosis of axSpA (nr-axSpA and AS) relies upon a combination of SpA features and imaging[3]

Probability of nr-axSpA diagnosis[1,3,4]

14% Presence of IBP[1,3†]

35-70% Presence of one or two additional SpA features[1,3†]

>90% HLA-B27(+) (80%-90%[3†]) MRI SIJ (+) = nr-axSpA[5]

†Probability varies based on number of SpA features present.

For patients with active disease despite treatment with NSAIDs and physical therapy, the ACR/SAA/SPARTAN treatment guidelines strongly recommend TNFi as the first-line biologic therapy[6‡]

‡Recommendations are from the ACR/SAA/SPARTAN 2019 guidelines. Recommendations for nr-axSpA extrapolated from evidence in AS due to limited literature available for nr-axSpA.

ACR: American College of Rheumatology; AS: Ankylosing Spondylitis; axSpA: axial spondyloarthritis; IBP: inflammatory back pain; HLA-B27: human leukocyte antigen-B27; MRI: magnetic resonance imaging; NSAID: nonsteroidal anti-inflammatory drug; SAA: Spondylitis Association of America; SIJ: sacroiliac joint; SpA: spondyloarthritis; SPARTAN: The Spondyloarthritis Research and Treatment Network; TNFi: tumor necrosis factor inhibitor.

Indication

CIMZIA is indicated for the treatment of adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation.

Important Safety Information

Serious and sometimes fatal side effects have been reported with CIMZIA, including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens (such as Legionella or Listeria). Patients should be closely monitored for the signs and symptoms of infection during and after treatment with CIMZIA. Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which CIMZIA is a member. CIMZIA is not indicated for use in pediatric patients.

Please see additional Important Safety Information on next page. Please see full Prescribing Information at CIMZIAhcp.com.

References: 1. Rudwaleit M, van der Heijde D, Landewé R, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis.* 2009;68(6):777-783. **2.** van Tubergen A, Weber U. Diagnosis and classification in spondyloarthritis: identifying a chameleon. *Nat Rev Rheumatol.* 2012;8(5):253-261. **3.** Rudwaleit M, van der Heijde D, Khan M, Braun J, Sieper J. How to diagnose axial spondyloarthritis early. *Ann Rheum Dis.* 2004;63(5):535-543. **4.** Sieper J, Rudwaleit M, Baraliakos X, et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. *Ann Rheum Dis.* 2009;68(suppl 2):ii1-ii44. **5.** Braun J, Sieper J. Classification, diagnosis, and referral of patients with axial spondyloarthritis. *Rheum Dis Clin North Am.* 2012;38(3):477-485. **6.** Ward MM, Deodhar A, Gensler LS, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol.* 2019;71(10):1599-1613.

Indication

CIMZIA® (certolizumab pegol) is indicated for the treatment of adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation.

Important Safety Information

Contraindications

CIMZIA is contraindicated in patients with a history of hypersensitivity reaction to certolizumab pegol or to any of the excipients. Reactions have included angioedema, anaphylaxis, serum sickness, and urticaria.

Serious Infections

Patients treated with CIMZIA are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

Discontinue CIMZIA if a patient develops a serious infection or sepsis.

Reported infections include:

- **Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Test patients for latent TB before CIMZIA use and during therapy. Initiate treatment for latent TB prior to CIMZIA use.**
- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Consider empiric anti-fungal therapy in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella and Listeria.**

Carefully consider the risks and benefits of treatment with CIMZIA prior to initiating therapy in the following patients: with chronic or recurrent infection; who have been exposed to TB; with a history of opportunistic infection; who resided in or traveled in regions where mycoses are endemic; with underlying conditions that may predispose them to infection. Monitor patients closely for the development of signs and symptoms of infection during and after treatment with CIMZIA, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

- Do not start CIMZIA during an active infection, including localized infections.
- Patients older than 65 years, patients with co-morbid conditions, and/or patients taking concomitant immunosuppressants may be at greater risk of infection.
- If an infection develops, monitor carefully and initiate appropriate therapy.

Malignancy

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which CIMZIA is a member. CIMZIA is not indicated for use in pediatric patients.

- Consider the risks and benefits of CIMZIA treatment prior to initiating or continuing therapy in a patient with known malignancy.
- In clinical trials, more cases of malignancies were observed among CIMZIA-treated patients compared to control patients.
- In CIMZIA clinical trials, there was an approximately 2-fold higher rate of lymphoma than expected in the general U.S. population. Patients with rheumatoid arthritis, particularly those with highly active disease, are at a higher risk of lymphoma than the general population.
- Malignancies, some fatal, have been reported among children, adolescents, and young adults being treated with TNF blockers. Approximately half of the cases were lymphoma, while the rest were other types of malignancies, including rare types associated with immunosuppression and malignancies not usually seen in this patient population.
- Postmarketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers, including CIMZIA. These cases have had a very aggressive disease course and have been fatal. The majority of reported TNF blocker cases have occurred in patients with Crohn's disease or ulcerative colitis, and the majority were in adolescent and young adult males. Almost all of these patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with a TNF blocker at or prior to diagnosis. Carefully assess the risks and benefits of treating with CIMZIA in these patient types.
- Cases of acute and chronic leukemia were reported with TNF blocker use.

Heart Failure

- Worsening and new onset congestive heart failure (CHF) have been reported with TNF blockers. Exercise caution and monitor carefully.

Hypersensitivity

- Angioedema, anaphylaxis, dyspnea, hypotension, rash, serum sickness, and urticaria have been reported following CIMZIA administration. If a serious allergic reaction occurs, stop CIMZIA and institute appropriate therapy. The needle shield inside the removable cap of the CIMZIA prefilled syringe contains a derivative of natural rubber latex which may cause an allergic reaction in individuals sensitive to latex.

Hepatitis B Virus Reactivation

- Use of TNF blockers, including CIMZIA, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers. Some cases have been fatal.
- Test patients for HBV infection before initiating treatment with CIMZIA.
- Exercise caution in patients who are carriers of HBV and monitor them before and during CIMZIA treatment.
- Discontinue CIMZIA and begin antiviral therapy in patients who develop HBV reactivation. Exercise caution when resuming CIMZIA after HBV treatment.

Neurologic Reactions

- TNF blockers, including CIMZIA, have been associated with rare cases of new onset or exacerbation of central nervous system and peripheral demyelinating diseases, including multiple sclerosis, seizure disorder, optic neuritis, peripheral neuropathy, and Guillain-Barré syndrome.

Hematologic Reactions

- Rare reports of pancytopenia, including aplastic anemia, have been reported with TNF blockers. Medically significant cytopenia has been infrequently reported with CIMZIA.
- Consider stopping CIMZIA if significant hematologic abnormalities occur.

Drug Interactions

- Do not use CIMZIA in combination with other biological DMARDS.

Autoimmunity

- Treatment with CIMZIA may result in the formation of autoantibodies and, rarely, in development of a lupus-like syndrome. Discontinue treatment if symptoms of a lupus-like syndrome develop.

Immunizations

- Patients on CIMZIA should not receive live or live-attenuated vaccines.

Adverse Reactions

- The most common adverse reactions in CIMZIA clinical trials (≥8%) were upper respiratory infections (18%), rash (9%), and urinary tract infections (8%).

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