

# Medication for axial spondylitis with Celebrex

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## ABSTRACT

A crippling kind of chronic inflammatory arthritis that mostly affects the spine is called ankylosing spondylitis. The two main forms of treatment are pharmaceutical therapy (non-steroidal anti-inflammatory drugs, or NSAIDs) and non-pharmacological therapy, which primarily consists of exercise. Celecoxib, a cyclooxygenase-2 selective nonsteroidal anti-inflammatory drug, is one of the most researched pharmaceutical treatments for patients with ankylosing spondylitis. This succinct summary emphasises how crucial inflammation is to the pathophysiology of the illness. The safety and effectiveness of celecoxib in patients with ankylosing spondylitis are examined based on data from randomised, controlled clinical trials. Furthermore, more recent data from longer-term trials point to the possibility of celecoxib's ability to modify disease. Furthermore, more recent data from longer-term trials indicate that celecoxib may have the ability to modify disease, with potential benefits being more noticeable in individuals with syndesmophytes and higher than normal levels of inflammation, which are signs of a more serious illness. Patients with syndesmophytes and higher inflammatory levels, which are symptomatic of more severe illness, may benefit more from this treatment.

**Keywords :** *Ankylosing spondylitis; Celecoxib; Disease modification*

## INTRODUCTION

A type of chronic inflammatory arthritis that mostly affects the spine is called ankylosing spondylitis [1]. Ankylosing spondylitis is estimated to affect between 0.1% and 1.4% of people [1]. It is a disease that primarily affects young people, with a median presentation age of 26 years old [2]. Men are more likely than

women to get it, with one study finding a 2.4:1 male to female ratio [3]. The goals of treatment are to lessen symptoms, preserve posture and flexibility, and postpone structural damage [4, 5]. Although there is no known cure, physical therapy and exercise along with non-steroidal anti-inflammatory medications (NSAIDs), such as COX-2 selective inhibitors, are advised as first-line treatment according to European and North American treatment guidelines [4, 5]. This article describes the crucial role that inflammation plays in ankylosing spondylitis and summarises the information that is currently known regarding the safety and effectiveness of celecoxib, a COX-2 selective inhibitor that is one of the NSAID therapies for the condition that has received the greatest research. Lastly, celecoxib's possible ability to change disease is explored.

## Inflammation Is A Key Component Of Ankylosing Spondylitis

Sacroiliac joint, vertebral facet joint, and intervertebral disc fusion can result in ankylosing spondylitis, which is characterised by inflammatory back pain that impairs movement and causes spinal stiffness [1]. Controlling inflammation early in the disease process may prevent ongoing structural damage, as chronic inflammation is likely a direct cause of stiffness and bone fusion [6].

## Celecoxib Is An Effective Treatment Option For Patients With Ankylosing Spondylitis Guidelines

Guidelines from the European League Against Rheumatism (EULAR) [5] state that the course of treatment should be determined by the disease's current manifestations, including the severity and status of symptoms. Patient education and consistent exercise should serve as the foundation for non-pharmacological treatment, while disease monitoring (on an individual basis) should involve the patient's history, clinical parameters, laboratory tests, and imaging [5]. As first-line medication therapy, continued NSAID use—including COX-2 selective inhibitors—is advised. If NSAIDs prove ineffective, alternative pharmacological interventions, such as analgesics, directed corticosteroid injections, and anti-tumor necrosis factor [TNF] therapy, should be explored [5]. In patients who are more severe and do not respond, surgery may also be considered [5].

Similar recommendations are made by the American College of Rheumatology (ACR) guidelines [4], which also strongly support

continued NSAID and physical therapy treatment. The American College of Radiology (ACR) guidelines strongly advise against the use of systemic glucocorticoids and highly encourage anti-TNF medication for those who do not respond to NSAIDs or surgery for more severely affected patients [4].

### Clinical data

Celecoxib has been the subject of five randomised, controlled trials (Table 1) [7–11] for the treatment of ankylosing spondylitis. The trials showed non-inferiority when compared to non-selective NSAIDs and significantly better outcomes when compared with placebo. There were no recorded deaths while a patient was receiving active treatment; however, in one trial, a patient passed away after stopping celecoxib for ineffectiveness, but this was deemed unrelated to the medication [8]. Celecoxib was associated with severe decreased blood pressure, severe renal calculus, angina pectoris, dyspnea, sudden hearing loss, deterioration of ankylosing spondylitis, and familial Mediterranean fever, among other reported serious adverse events; however, the overall incidence was similar to controls [7–11].

In line with the demonstrated higher gastrointestinal safety of COX-2 selective inhibitors [12], celecoxib was generally well tolerated in these trials and was generally linked to numerically fewer gastrointestinal adverse events than the non-selective NSAID comparators [7–11]. Despite the trials' short duration and relatively young patient population, there was no discernible variation in cardiovascular adverse events (Table 1) [13]. Patients with ankylosing spondylitis would almost certainly have a lower risk of gastrointestinal and cardiovascular complications because they are typically younger and have fewer comorbidities than most other patients treated with celecoxib [13]. However, as compared to non-selective NSAIDs like ibuprofen and naproxen, celecoxib is not linked to an elevated cardiovascular risk, according to data currently available from individuals with osteoarthritis and rheumatoid arthritis [14, 15].

A 52-week randomised, controlled trial has also investigated etoricoxib, an alternative COX-2 selective inhibitor [16]. In this trial, etoricoxib at 90 or 120 mg once daily was compared with placebo and naproxen at 500 mg twice daily for a total of 46 weeks, with a 6-week placebo-controlled period [16]. Over the course of the one-year active-comparator phase, the mean change in pain score at six weeks was -12.6 with a placebo, compared with -33.7 with naproxen and -41.5 and -41.6 with etoricoxib 90 mg and 120 mg, respectively [16]. Health authorities first suggested a daily dose of 90 mg of etoricoxib; however, recent regulatory actions have caused some nations to lower their initial recommendation of etoricoxib for ankylosing spon-

dylitis [17]. It is now advised to begin at a dose of 60 mg per day, while some people may benefit from a higher dose of 90 mg per day. After patients have reached a state of clinical stability, the labelling suggests that they may resume taking 60 mg per day [18].

### Disease Modification In Ankylosing Spondylitis

Ankylosing spondylitis has no known cure, and standard disease-modifying anti-rheumatic medications (like methotrexate and sulfasalazine) have not been demonstrated to be efficacious in treating the condition [1,5]. At first, it was thought that NSAIDs would only be able to alter the symptoms of ankylosing spondylitis, having no impact on the disease's course. On the other hand, compared to patients receiving treatment on demand, patients from one celecoxib randomised controlled trial [7] had a lower rate of radiological progression during their 2-year period of continuous treatment [19]. This decrease revealed that NSAIDs might be able to change the course of a disease in addition to relieving symptoms. Patients with a high NSAID intake over a two-year period demonstrated a similar reduction in radiographic progression [20], with the impact being especially noticeable in patients with increased C reactive protein (CRP). It has been demonstrated that NSAID therapy lowers CRP levels, which are linked to more severe illness [21].

Additional acute phase reactants have also been linked to this process, with patients with elevated erythrocyte sedimentation rate (ESR), high Ankylosing spondylitis disease activity score (ASDAS)-CRP, or high ASDAS-ESR experiencing a more marked slowing of radiographic progression when on continuous NSAID treatment [22]. It is noteworthy that 2-year continuous diclofenac treatment [23] did not affect radiographic progression when compared with controls in studies similar to the ones previously described. This suggests that the effects of disease-modifying agents may be restricted to COX-2 selective inhibitors or to celecoxib alone.

The Wnt signalling pathway, which interacts with the prostaglandin signalling pathway and plays a significant regulatory role in the processes of fracture repair and cartilage cell regeneration, may be linked to the inhibition of new bone formation caused by NSAIDs [24]. The prostaglandin E receptor 4 gene (PTGER4) was linked to both the severity and susceptibility to ankylosing spondylitis, according to a recent genome-wide association study [25]. NSAIDs, specifically COX-2 selective inhibitors, may have an impact on this process. Ankylosing spondylitis patients with syndesmophytes and baseline elevated inflammatory levels are at risk for radiographic progression; these patients have been demonstrated to benefit more from continuous NSAID

use [20, 22]. This indicates that NSAIDs are most beneficial in patients at risk for delayed radiographic progression and new bone formation.

## Conclusions

With a good amount of data supporting both its safety and effectiveness, celecoxib is one of the NSAIDs that patients with ankylosing spondylitis have received the most research. It might also have the ability to modify disease, according to recent research. Even after experiencing the notable improvements in clinical symptoms that are frequently noted in clinical trials of this class of medications, patients with a high risk of radiographic progression may benefit from continuing to take celecoxib.

## Declarations

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