EULAR guidelines currently recommend methotrexate (MTX) as first line treatment of rheumatoid arthritis (RA). Treatment should be start at 10-15 mg/week, with escalation of 5 mg every 2-4 weeks up to 20-30 mg/week, depending on clinical response and tolerability. However the bioavailability of higher oral dose of MTX in adult patients with RA is highly variable and, on average, is two-thirds that of subcutaneous (sc) or intramuscular. Besides, its clinical benefit is often limited by gastrointestinal side effects. The enhanced bioavailability of sc MTX may make this route of administration preferable to the oral in some patients and a useful strategy to gain the full benefit of MTX therapy.

Several studies have compared the clinical efficacy and safety of sc versus oral administration of MTX. In a study conducted by Braun et al (Arthritis Rheum 2008) in 384 patients with active RA, sc MTX was significantly more effective (ACR 20 and 70) than oral MTX at the same dosage, especially in patients with a disease duration of ≥ 1 year, who respond earlier to sc MTX than to oral MTX. The safety profile was not significantly different between both application routes.

In a study by Rutkowska-Sak et al (Reumatologia 2009) 70 patients with RA were switched from oral to the same dose of sc MTX because of gastro-intestinal (GI) side effects. Switching from oral to s.c. MTX had reduced intensity of GI side effects in all enrolled patients. Some side effects like vomiting and diarrhea were completely eliminated by sc MTX.

Nevertheless, Bharadway et al, (Rheumatology 2008) have shown in a retrospective study that switching from oral to sc MTX can delay the necessity for biologics.

In summary, there is now a wealth of evidence about sc MTX superior efficacy vs. oral application, faster onset of action, less gastro-intestinal side-effects, better/reproducible bioavailability, which results in increase use of sc MTX seen throughout Europe.

**Key words:** rheumatoid arthritis, treatment, subcutaneous methotrexate