



**Therapeutic Class Review<sup>SM</sup>**  
**Self-Injectable Target Immune Modulators**  
**in Rheumatoid Arthritis**  
**December 2005**

**Executive Summary**

- Target immune modulators, anakinra (Kineret), etanercept (Enbrel) and adalimumab (Humira) are marketed for their potential benefit in reducing pain and inflammation in RA and “slowing the progression of the disease”.
- Efficacy of these medications is difficult to compare due to:
  - Absence of direct head-to-head trials.
  - Individual studies that include patients with different disease severities (i.e. early disease  $\leq$  3 years duration versus longstanding, treatment-resistant disease).
  - Use of these medications alone or in combination with methotrexate.
- Although the evidence shows that anakinra (Kineret) (combined with methotrexate) is effective for pain and inflammation in RA, rheumatologists report that this combination is inferior to etanercept (Enbrel) or adalimumab (Humira) based on their experience.
- The utilization of anakinra (Kineret) is a fraction (1.2 %) of the overall utilization of the self-injectable target immune modulators.
- For treatment of RA, the net cost of etanercept (Enbrel) is less than for anakinra (Kineret) or adalimumab (Humira).

**Evidence**

- The greatest benefit with anakinra (Kineret), etanercept (Enbrel) and adalimumab (Humira) is observed when used concomitantly with methotrexate.
- Among anakinra (Kineret), etanercept (Enbrel), or adalimumab (Humira), there is no useful evidence to differentiate which agent is the most optimal in RA.
- There are no harms data to support any differences in safety between anakinra (Kineret), etanercept (Enbrel), or adalimumab (Humira).
- Ongoing concerns about risks of lymphoma or serious infections are based on post-marketing adverse event reporting and retrospective data analysis from clinical trials, prompting updates to prescribing information for anakinra (Kineret), etanercept (Enbrel) and adalimumab (Humira).

**Decision**

- Maintain etanercept (Enbrel) as formulary/preferred because etanercept (Enbrel) provides the best value compared to anakinra (Kineret) and adalimumab (Humira).
- Change anakinra (Kineret) to non-formulary/non-preferred because of:
  - Limited utility in clinical practice relative to other biologic agents used for rheumatologic conditions.
  - Maintaining anakinra (Kineret) as preferred/formulary will increase overall costs.
  - Changing anakinra (Kineret) to non-formulary/non-preferred will have minimal impact on members and prescribers.
- Maintain adalimumab (Humira) as non-formulary/non-preferred because there is
  - No evidence of better safety/efficacy.
  - Potentially higher (double) cost with higher dosing.

**Products** <sup>13,22-23</sup>

Drug Product	Date of FDA Approval	FDA Approved Indications					Dosing/Route	Potential Off-Label Uses
		Rheumatoid Arthritis (RA)	Juvenile RA (JRA)	Psoriatic Arthritis (PsA)	Ankylosing Spondylitis (AS)	Plaque Psoriasis (Ps)		
etanercept (Enbrel)	11/2/98	X	X	X	X		25mg SQ 2x/week 50mg SQ Q week	Crohns disease, Sjogrens Syndrome
						X	50mg SQ 2x/week for first 3 months, then 50mg SQ every week, thereafter.	
anakinra (Kineret)	11/14/01	X					100mg SQ Q week	JRA, PsA, AS, Ps
adalimumab (Humira)	12/31/02	X		X			40mg SQ every 2 weeks 40mg SQ every week	JRA, AS, Ps, Crohns disease

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