This is a summary of the American Academy of Neurology (AAN) practice advisory, “Etanercept for Poststroke Disability,” which was published in Neurology® online on June 6, 2016, and appears in the June 7, 2016, Neurology print issue.

Please refer to the full practice advisory at AAN.com/guidelines for more information, including the definitions of the classifications of evidence and recommendations.

Stroke is a leading cause of major disability. An inflammatory response may play an important role in ischemic stroke. Some authors have hypothesized that the cytokine tumor necrosis factor (TNF) may play a role in the mediation of inflammatory changes in the ischemic penumbra. Etanercept, a fusion protein consisting of the TNF receptor and the Fc portion of immunoglobulin G, inhibits TNF, thereby diminishing neurotoxic TNF-mediated microglia activation that might contribute to poststroke disability. Moreover, anti-TNF-α blockade has been reported to demonstrate efficacy in stroke animal models.

For adult patients with poststroke disability, does etanercept administered by any route (compared with no etanercept or placebo) improve functional status?

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<td>Clinicians should counsel patients considering etanercept for treatment of poststroke disability that there is insufficient evidence to determine its effectiveness and that the treatment may be associated with adverse outcomes and high cost.</td>
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Clinical Context

[The practice advisory authors] have very low confidence in the evidence for efficacy of etanercept for poststroke disability because of the high risk of bias of the relevant studies. The biological plausibility of benefit was judged to be low because of the reported immediate onset of benefit and single administration of a transiently acting medication. Explanations other than the effectiveness of the treatment for the observed improvements include observer expectation, performance motivation, regression to the mean, and the placebo effect.

Although adverse events of etanercept were not described in these studies, serious adverse events are described in studies of patients receiving etanercept for other conditions. Such events include injection site reactions, reactivation of tuberculosis, reactivation of hepatitis B virus infection, congestive heart failure, demyelinating neurologic disorders, vasculitis, and hematologic disorders such as aplastic anemia and pancytopenia. A recent randomized trial of subcutaneous etanercept 50 mg once weekly for 24 weeks for the treatment of Alzheimer disease reported no significant difference in the adverse event rates between patients treated with placebo and patients treated with etanercept. However, the study lacked the statistical precision to exclude uncommon, potentially serious adverse events. It is unclear whether the adverse event profile resulting from the recurrent use of etanercept can be generalized to the time-limited perispinal administration used for the treatment of poststroke disability. Given the limitations of the efficacy of the evidence and the potential for serious adverse events, [the practice advisory authors] judge the risk-benefit tradeoffs of etanercept for poststroke disability to be unfavorable.

As of this writing, the cost of a 25-mg vial of etanercept is about $440 in US currency. Additional costs associated with the pretreatment evaluation and administration of perispinal etanercept are likely to be substantially higher.
References


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