

Use of darbepoetin alfa and epoetin alfa for anemia in clinical practice

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Origin of Study	USA
Type of Study	RETROSPECTIVE REVIEW OF HEALTHCARE CLAIMS
Objectives	Compare dosing of darbepoetin alfa (Aranesp) with that of epoetin alfa (Procrit) in cancer patients according to information from a large, US healthcare claims database using methodology accounting for differences in the half-life of these agents.
Study Design	<p>From January 1, 2005, to June 30, 2005, claims data were obtained from PharMetrics' database of inpatient, professional, and outpatient pharmacy claims from approximately 70 health plans and > 20 million lives covered annually.</p> <p>Subjects were identified on receipt of erythropoietins and with at least one encounter with diagnoses of cancer or receipt of chemotherapy on or before the first noted erythropoietin claim.</p> <p>Information related to erythropoietin dosing included billed units (for professional claims) and quantity dispensed and dose dispensed (pharmacy claims). "Questionable" claims were defined on the basis of billed units < 10 or > 80 and reimbursed amount \geq \$50 and \leq \$4,000.</p> <p>The team constructed episodes of care (EOCs) to account for the episodic nature of erythropoietin therapy in cancer and differences in product half-lives based on information from paid claims during the study period.</p> <p>The weekly dose of darbepoetin alfa and epoetin alfa was calculated based upon billed units for professional claims and therapy days and dose for pharmacy claims. Numerous sensitivity analyses were conducted to assess the robustness of the methodology.</p>
Patients	<p>Compared with those given epoetin alfa, patients receiving darbepoetin alfa were younger and more likely to have breast cancer and higher mean Charlson comorbidity scores and less likely to have cancers other than those of the breasts and lungs and non-Hodgkin's lymphoma (NHL).</p> <p>Patients with renal disease were excluded.</p> <p>Overall, 593 patients (mean age, 54.6 years) were given epoetin alfa and 1,194 (mean age, 53.4 years) were given darbepoetin alfa.</p>
Observations	<p>The darbepoetin alfa EOCs averaged 3.8 administrations over 54.8 days (mean weekly dose, 99 μg). The epoetin alfa EOCs averaged 5.6 administrations over 51.3 days (mean weekly dose, 42,634 IU). The epoetin alfa/darbepoetin alfa dose ratio was 431:1. The mean number of days between consecutive administrations in an EOC was 11.5 for epoetin alfa and 16.8 for darbepoetin alfa; the median duration of an EOC was 7.9 and 1.0, respectively.</p> <p>The effect of eliminating duration of clinical benefit from the epoetin alfa claim, but retaining single-dose EOCs, substantially increased the estimated mean weekly doses and decreased the epoetin alfa/darbepoetin alfa dose ratio. The effect of eliminating the duration of clinical benefit was more pronounced for darbepoetin alfa than for epoetin alfa. The effects of varying other assumptions were more modest.</p> <p>After adjusting for potentially confounding differences in patient demographic and clinical characteristics, the estimated mean weekly dose of epoetin alfa decreased, whereas that of darbepoetin alfa increased. The adjusted weekly dose for epoetin alfa was 39,922 IU and for darbepoetin alfa was 100 μg.</p>

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As a result, the epoetin alfa/darbepoetin alfa dose ratio declined.

Limitations of this study included analyses of administrative claims data being subject to various forms of bias, administrative claims data lacking information on patient clinical outcomes of erythropoietin therapy, and the lack of robust information regarding comparative effectiveness.

Conclusions

This analysis showed that patients treated with epoetin alfa received a mean weekly dose of 99 μg of darbepoetin alfa or 42,634 IU of epoetin alfa, resulting in a dose ratio of 431:1, based on an EOC approach that includes a duration of clinical benefit.

The average weekly doses are highly sensitive to assumptions concerning the inclusion/exclusion of duration of clinical benefit, with all analyses including a duration of clinical benefit that resulted in dose ratios $\geq 330:1$.

The median time between erythropoietin administrations supports the use of product-specific duration of clinical benefit in an EOC.

Discussion

Anemia is common among patients with cancer and may arise from myelosuppressive treatment or from other factors, such as bleeding or bone marrow infiltration. Anemic patients may experience marked fatigue, leading to impaired quality of life. A cornerstone of the treatment of anemia is recombinant erythropoietin, which stimulates red blood cell production. Two erythropoietic agents are available: darbepoetin alfa and epoetin alfa.

The doses at which these agents are administered may have implications in terms of efficacy, safety, and cost. Various doses have been set forth by the manufacturers, outlined in guidelines, and tested in trials; however, actual doses given in routine clinical practice are unknown. This study aimed to assess and compare doses of darbepoetin alfa and epoetin alfa administered in real-world settings.

Using a health insurance database, the investigators identified 1,787 patients with cancer who were treated with darbepoetin alfa or epoetin alfa. An EOC was defined as spanning from the day of first administration through the last estimated day of benefit from the last administration. Analyses were based on 1,323 episodes of darbepoetin alfa use and 683 episodes of epoetin alfa use.

On average, episodes were of nearly the same duration for both agents, lasting about 55 days for darbepoetin alfa and 52 days for epoetin alfa. The corresponding average numbers of administrations were 3.8 and 5.6 per episode. Finally, the respective mean doses per administration were 200 μg and 40,000 U.

Key Points

- Comparisons of darbepoetin alfa and epoetin alfa dosing should account for differences in duration of clinical benefit for these two agents.

Reference

Berger A, Kallich J, Oster G. Use of darbepoetin alfa and epoetin alfa for anemia in clinical practice. Presented at the 18th Annual Symposium of the Multinational Association of Supportive Care in Cancer; June 22–24, 2006; Toronto, Canada. Abstract 02-007.