Utilization and Cost in Clinical Practice of Darbepoetin Alfa and Epoetin Alfa for Anemia Concomitant With Chemotherapy

Ariel Berger, MPH[1]; Claudia Lord, BA[1]; Patricia K. Corey-Lisle, PhD[2]; G. Rhys Williams, ScD[2]; and Gerry Oster, PhD[1]

[1]*Policy Analysis Inc, Brookline, Massachusetts; and* [2]*Amgen, Inc, Thousand Oaks, California*

ABSTRACT

Background: In 2005, the mean weekly dose ratio of epoetin alfa (EA) to darbepoetin alfa (DA) in clinical practice was estimated to be ~400 to 1. In 2006, a 500-μg dose and new dosing schedule was approved for DA in the United States. In 2007, the warnings and dosing/administration sections were modified for both agents. All of these factors may have changed the way that physicians use EA and DA. Previous studies of the use of erythropoiesis-stimulating agents (ESAs) in patients with anemia concomitant with chemotherapy may thus not reflect current clinical practice.

Objective: The goal of this study was to examine the use and costs of ESAs in clinical practice in patients with anemia concomitant with chemotherapy.

Methods: Using 2 large US health care claims databases, all adults (aged ≥18 years) were identified who received ESAs in 2008 and had evidence of receipt of chemotherapy ≤42 days before initial ESA receipt (ie, the index date). Episodes of care were defined as beginning on the index date and ending on the date of the last ESA claim that was followed by a ≥42-day gap without any receipt of ESAs, to which was added an assumed duration of clinical benefit (in days) based on the ESA and corresponding dose received. DA- and EA-treated patients were matched using propensity scoring. The mean weekly dose and cost of DA and EA during episodes of care was calculated using all information from relevant claims noted during such episodes. Each database was analyzed separately.

Results: In the first database, 475 patients with DA episodes of care were matched to an equal number of patients with EA episodes; in the second database, there were 424 matched pairs. In the first database, the mean (95% CI) weekly dose was 37,444 U (35,942 U–39,001 U) during EA episodes and 110 μg (108 μg–113 μg) during DA episodes; the mean weekly EA/DA dose ratio was 340 to 1. In the second database, the mean (95% CI) weekly dose was 37,047 U (35,944 U–38,175 U) during EA episodes and 121 μg (117 μg–125 μg) during DA episodes; the mean weekly EA/DA dose ratio was 306 to 1.

Conclusions: The mean weekly EA/DA dose ratio during episodes of ESA care has declined in patients with anemia concomitant with chemotherapy, due at least in part to the availability and use of a new dose/dosing schedule for DA without similar changes for EA. (*Clin Ther*. 2012;34:1350–1363)

Key words: anemia, clinical practice patterns, darbepoetin alfa, epoetin alfa, neoplasms.

INTRODUCTION

Epoetin alfa (EA) and darbepoetin alfa (DA) (collectively, erythropoiesis-stimulating agents [ESAs]) have been approved for use in the United States to treat anemia in patients with nonmyeloid malignancies in which the anemia is due to the effect of concomitant myelosuppressive chemotherapy (anemia concomitant with chemotherapy [ACC]).[1,2] EA and DA differ with respect to their approved frequency of dosing, reflecting differences in their duration of biologic activity. In a previous analysis we conducted that focused on the use of ESAs in 1226 patients who received either EA or DA for CIA between January 1, 2005, and June 30, 2005, the estimated multivariate-adjusted mean weekly dose of EA was 39,473 U, whereas that of DA was 98 μg; the corresponding mean weekly dose ratio (EA/DA) was 403 to 1.[3] Our earlier findings therefore suggested that use of these products in clinical practice

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was consistent with their use in randomized controlled trials, in which the dose ratio was ~400 to 1.[4–12]

Since publication of our previous work,[3] a 500-μg dose of DA was approved in 2006 with a dosing schedule of once every 3 weeks (Q3W). Subsequently, after discussions with the US Food and Drug Administration, the manufacturers of both DA and EA modified the prescribing information for these agents, strengthening the warnings section and revising the dosing and administration sections.[13] At that same time, the Food and Drug Administration also approved a Risk Evaluation and Mitigation Strategies for ESAs. In addition, in 2007, the Centers for Medicare & Medicaid Services issued its national coverage determination for ESAs in cancer and related neoplastic conditions with reimbursement restrictions on these products; the national coverage determination was later modified in January 2008 and became effective in April 2008.[13] All of these factors may have changed the way that physicians use DA and EA. It is unknown whether our earlier findings are applicable to clinical practice today. We therefore undertook a new study to examine ESA use in patients with cancer who have ACC, using information from 2 health insurance claims databases.

METHODS

Data Sources

Data for this study were obtained from the Thomson Reuters MarketScan Commercial Claims and Encounters Database (ie, MarketScan database) and the IMS LifeLink® Health Plan Claims Database (formerly the PharMetrics Patient-Centric Database) (ie, IMS database). Together, the databases contain facility, professional service, and retail (ie, outpatient) pharmacy claims from ~200 US health plans providing coverage to ~30 million persons annually throughout the United States. Both databases spanned the period January 1, 2008, through December 31, 2008 (ie, the study period).

Information available in each database for each facility and professional service claim includes dates and place of service, diagnoses (in *International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] format), procedures (in ICD-9-CM [selected plans only], Current Procedural Terminology, Fourth Edition, and Healthcare Common Procedure Coding System formats), provider specialty, and charged and paid (including both insurer and patient liability) amounts. All patient identifiers in both databases are fully encrypted, and both databases are fully compliant with the Health Insurance Portability and Accountability Act of 1996. Because the databases did not contain any protected health information and our study was retrospective and did not involve any intervention or patient contact, institutional review board approval was not required.

Selection of Source Population

Within each database, all patients were identified who received either EA or DA during the study period, based on relevant Healthcare Common Procedure Coding System codes on medical claims. Patients receiving ESAs dispensed from retail pharmacies were excluded from the study sample because actual usage of these therapies cannot be reliably ascertained from these types of claims. The date of the first-noted medical claim for an ESA during the study period was designated as the index date; patients not continuously enrolled for at least 6 months before their index date (ie, the preindex period) were excluded. Among all remaining patients, only those presumed to have ACC were included. ACC was defined based on evidence of receipt of chemotherapy ≤42 days before the index date and ≥2 claims with an ICD-9-CM diagnosis code for cancer (ie, breast [174.XX-175.XX], lung [162.XX], non-Hodgkin's lymphoma [200.X, 202.X], other neoplasms [140.XX–161.XX, 163.XX-173.XX, 176.XX–199.XX, 201.XX, 203.XX–209.XX, 230.XX–234.XX]) during the preindex period. As with our previous study,[3] patients with evidence of renal insufficiency, invalid diagnostic or demographic information, and/or missing or invalid reimbursement information were excluded.

ESA Dosing

As with our prior analysis,[3] ESA dose in each database was calculated by multiplying the "billed units" value in each claim by a constant that was based on the accompanying Healthcare Common Procedure Coding System code.[14] The range of calculated doses thought to represent "valid" information for DA was expanded to 50 to 500 μg to reflect the release of the 500-μg dose in 2006; since there have been no changes in the marketed doses of EA, the corresponding range assumed to represent valid values was left unchanged, from 10,000 to 80,000 U. To account for the new dose of DA specifically, and price increases for both products since the previous study, valid claims for DA and EA were required to have reimbursed amounts be-