Patients Against Lymphoma

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ELECTRONICALLY: http://www.regulations.gov/

Donald M. Berwick, MD
Administrator
Centers for Medicare and Medicaid Services
Room 445-G, Hubert H. Humphrey Building,
200 Independence Avenue, S.W.
Washington, D.C. 20201

RE: [CMS–1525–P] Medicare Program: Proposed Changes to the Hospital Outpatient Prospective Payment System and CY 2012 Payment Rates

"*These products [radioimmunotherapy agents] have been underutilized because of the complexity of treatment coordination and concerns regarding reimbursement.*"
Dillion, Clin Exp Med. 2006 March

Dear Dr. Berwick:

Patients Against Lymphoma (PAL) is a non-profit organization founded in 2002. PAL operates independent of health-industry funding and takes pride in providing patient-centered perspectives on clinical research and access to approved therapeutics.

We thank you for providing the opportunity to comment on the Proposed Rule, entitled "Hospital Outpatient Prospective Payment; Ambulatory Surgical Center Payment; Hospital Value-Based Purchasing Program; Physician Self-Referral; and Provider Agreement Regulations on Patient Notification Requirements."

We are writing to express our concern that the complex classifications by Centers for Medicare and Medicaid Services (CMS) for radioimmunotherapy agents (Zevalin and Bexxar) contributes to the under-use of these vital therapeutics … for "incurable" types of lymphoma that affect many thousands of American citizens.

For example, it is our understanding that the dosimetric dose of the Bexxar regimen is coded as Diagnostic by CMS and reimbursed at a lower rate, presumably because this phase of the Bexxar therapeutic regimen is also used to image the tumors. Of concern to patients is not the classification per se, but that the lower rate of reimbursement that results from it, which is often cited as a reason for the underutilization of a highly efficacious – potentially curative - targeted drug.

This classification is challenging for patients to understand because the treatment of lymphoma already requires a prior diagnosis of a b-cell lymphoma.

As we understand it, the dosimetric dose of Bexxar has two roles, and neither is diagnostic:

1) **Dose-optimizing** – based on the clearance rate of the antibody;

2) **Therapeutic** – based on the known treatment activity of labeled and unlabeled antibodies in lymphoma

Like the first dose of the four-part Bexxar therapeutic regimen, the dosimetric antibody binds to cd20, a receptor that is present only on mature b-cells, normal and malignant.

The dosimetric dose is radio-labeled with a gamma isotope that can be imaged (similar to a PET scan). The antibody binds almost exclusively to the tumor cells, because it is given after the unlabeled antibody, which is administered first in order to clear (kill off) normal b-cells so the subsequent doses of antibody are concentrated on the malignant b-cells.

Unlike PET imaging, the images made possible by the dosimetric dose of Bexxar are captured at least twice during the same week: once for a baseline and then repeated in order to calculate how fast the antibody is cleared from the body (which can vary) so that the next part of the treatment regimen can be optimized (personalized) for patient safety and treatment efficacy.

As with the unlabeled antibody, the dosimetric antibody has a therapeutic role as well – it almost certainly contributes to the killing of normal and abnormal b-cells expressing cd20. Presumably, this is why the Food and Drug Administration (FDA) considers all parts of the Bexxar regimen to be therapeutic, and if the sponsor removed the dosimetric step from the regimen we expect that FDA would require a proof from clinical trials that the Bexxar therapy is as safe and effective without this component.

So we ask: Why has CMS classified parts of an approved FDA therapeutic as diagnostic? And what would be the side effect of such policy if not a disincentive to develop novel, personalized therapeutics that can improve safety and efficacy?

A critical aspect of this matter deserves very close attention. The Bexxar regimen is the only therapy for low grade b-cell lymphoma that we are aware of that has clinical data strongly suggesting it has curative potential – based on very long follow-up in multiple clinical trials.[1],[2],[3],[4]
(Zevalin might prove to be as efficacious, but the data is not yet mature enough to make this assertion with confidence.)

Finally, GlaxoSmithKline announced recently that it was forced to cut back on the manufacturing of Bexxar and that it will no longer provide on-demand access,[5] which we take to be a signal that a vital therapeutic is approaching extinction for non-clinical reasons.

In summary, we ask that CMS amend the reimbursement policy for radioimmunotherapy agents so that there are no unnecessary disincentives related to reimbursement for these agents (for hospitals or physicians) to prescribe them. We ask that you do this for the benefit of cancer patients, present and future – for all of us.

Thank you for your kind attention to this matter.

Sincerely,

Karl Schwartz
President, Patients Against Lymphoma

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[1] Fludarabine Plus I-131 Tositumomab as Initial Treatment for Follicular Lymphoma: Half of Patients In Remission at Over 10 Years Median Followup
http://ash.confex.com/ash/2010/webprogram/Paper34376.html

[2] CVP followed by tositumomab and iodine-131-tositumomab in patients with untreated low-grade follicular lymphoma: eight-year follow-up of a multicenter phase II study.
http://www.ncbi.nlm.nih.gov/pubmed/20458031

[3] Tositumomab and iodine-131 tositumomab produces durable complete remissions in a subset of heavily pretreated patients with low-grade and transformed non-Hodgkin's lymphomas.
http://www.ncbi.nlm.nih.gov/pubmed/16186600

[4] 131I-tositumomab therapy as initial treatment for follicular lymphoma
http://www.ncbi.nlm.nih.gov/pubmed/15689582

[5] An Open Letter to GlaxoSmithKline (GSK): Urging GlaxoSmithKline to provide timely patient access to Bexxar http://www.lymphomation.org/perspectives-gsk-bexxar.htm