FDA Grants Accelerated Approval to Iberdomide Combination for Multiple Myeloma

The FDA's decision makes iberdomide the first approved CELMoD for patients with relapsed/refractory multiple myeloma.

The FDA granted accelerated approval to iberdomide (Zenbexus; Bristol Myers Squibb) in combination with daratumumab and hyaluronidase-fihj (Darzalex Faspro; Janssen Biotech) and dexamethasone (IberDd) for adults with relapsed/refractory multiple myeloma (RRMM) who have received at least 1 prior line of therapy containing both a proteasome inhibitor and an immunomodulatory agent.[1]

The August 13, 2026, decision establishes iberdomide, an oral cereblon E3 ligase modulator (CELMoD), as a new treatment option in earlier RRMM. The approval was based on minimal residual disease (MRD)-negative complete response (CR) findings from the ongoing phase 3 EXCALIBER-RRMM trial (NCT04975997).[1,2]

EXCALIBER-RRMM Demonstrates Higher MRD-Negative CR Rate

EXCALIBER-RRMM is a 2-stage, randomized, multicenter, open-label trial evaluating IberDd against daratumumab and hyaluronidase-fihj, bortezomib, and dexamethasone (DVd) among adults with RRMM who had received 1 or 2 prior lines of therapy. Patients with disease refractory to a previous anti-CD38 monoclonal antibody or bortezomib were excluded.[1,2]

Overall, 939 patients were randomized across the study. Stage 1 included 279 patients assigned to 1 of 3 iberdomide dose levels administered with daratumumab and dexamethasone or to DVd. Stage 2 enrolled another 660 patients and evaluated iberdomide 1 mg with daratumumab and dexamethasone against DVd.[1,2]

The primary efficacy population for accelerated approval consisted of the first 420 patients randomized to iberdomide 1 mg plus daratumumab and dexamethasone (n = 207) or DVd (n = 213) across the 2 stages.[1]

The major efficacy end point was MRD-negative CR at any time. The MRD-negative CR rate reached 41% (95% CI, 34%-48%) with IberDd compared with 21% (95% CI, 15%-27%) with DVd ($P < .0001$), representing an approximately 2-fold improvement with the iberdomide-containing regimen.[1]

Progression-free survival remains an efficacy end point under continued evaluation in EXCALIBER-RRMM.[2,3] Because the authorization was granted through the accelerated approval pathway on the basis of MRD-negative CR, continued approval may depend on verification and description of clinical benefit in ongoing studies.[1]

Iberdomide Introduces a CELMoD-Based Approach

Iberdomide is designed to bind cereblon, a component of the E3 ubiquitin ligase complex, leading to degradation of the transcription factors Ikaros and Aiolos and producing both direct antimyeloma and immune-stimulatory effects.[3,4] Earlier phase 1/2 findings demonstrated clinical activity with iberdomide plus dexamethasone in heavily pretreated RRMM, including patients with disease refractory to prior immunomodulatory agents.[4]

These findings supported subsequent development of iberdomide in combination regimens, including the daratumumab-based approach evaluated in EXCALIBER-RRMM.[2,3]

Dosing, Safety, and REMS Requirements

The recommended iberdomide dosage is 1 mg orally once daily on days 1 through 21 of each 28-day cycle, with or without food. It is administered with subcutaneous daratumumab and hyaluronidase-fihj 1800 mg and dexamethasone 20 mg or 40 mg according to the recommended schedules. Treatment continues until disease progression or unacceptable toxicity.[1]

The prescribing information carries a boxed warning for embryo-fetal toxicity and serious venous and arterial thromboembolism. Additional warnings and precautions include neutropenia, infections, and secondary primary malignancies.[1] Previous clinical experience with iberdomide has also identified hematologic toxicity and infections as important considerations during treatment.[4]

Because of embryo-fetal toxicity risk, iberdomide is available only through the restricted ZENBEXUS Risk Evaluation and Mitigation Strategy (REMS) program.[1] Pharmacists may therefore play an important role in REMS compliance, patient counseling, adherence to the 21-day oral dosing schedule, thrombosis-risk management, and monitoring for cytopenias and infection.

The application received priority review, breakthrough therapy designation, and orphan drug designation. FDA also reviewed the application through Project Orbis, collaborating with Switzerland's Swissmedic.[1]

References

1. FDA grants accelerated approval to iberdomide with daratumumab and hyaluronidase-fihj and dexamethasone for multiple myeloma. FDA. August 13, 2026. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-iberdomide-daratumumab-and-hyaluronidase-fihj-and-dexamethasone
2. A study comparing iberdomide, daratumumab and dexamethasone with daratumumab, bortezomib and dexamethasone in participants with relapsed or refractory multiple myeloma (EXCALIBER-RRMM; NCT04975997). https://clinicaltrials.gov/study/NCT04975997
3. Bristol Myers Squibb. U.S. Food and Drug Administration accepts Bristol Myers Squibb's New Drug Application for iberdomide in patients with relapsed or refractory multiple myeloma. Published February 17, 2026. https://news.bms.com/news/corporate-financial/2026/U-S--Food-and-Drug-Administration-Accepts-Bristol-Myers-Squibbs-New-Drug-Application-for-Iberdomide-in-Patients-with-Relapsed-or-Refractory-Multiple-Myeloma/default.aspx
4. Lonial S, Popat R, Hulin C, et al. Iberdomide plus dexamethasone in heavily pretreated late-line relapsed or refractory multiple myeloma (CC-220-MM-001): a multicentre, multicohort, open-label, phase 1/2 trial. *Lancet Haematol*. 2022;9(11):e822-e832. doi:10.1016/S2352-3026(22)00290-3
5. Lonial S, Dimopoulos MA, Berdeja JG, et al. EXCALIBER-RRMM: a phase III trial of iberdomide, daratumumab, and dexamethasone in relapsed/refractory multiple myeloma. *Future Oncol*. 2025;21(14):1761-1769. doi:10.1080/14796694.2025.2501920

News Source:

https://www.pharmacytimes.com/view/fda-grants-accelerated-approval-to-iberdomide-combination-for-multiple-myeloma