

# Androgenic side effects of danazol may affect its reception in the DME market

Magdalene Crabbe — Senior Healthcare Analyst, GlobalData

Diabetic macular edema (DME) is a condition where fluid accumulates within the macula, which is a small, oval-shaped part of the retina that is responsible for high acuity vision. Sight-threatening DME is characterised by the death of existing retinal blood vessels, the formation of abnormal, fragile blood vessels and the presence of cysts around the macula. DME is treated with anti-angiogenic drugs such as Roche/Genentech's Lucentis (ranibizumab) and Bayer/Regeneron's Eylea (aflibercept).

In general, ocular complications of diabetes are driven by the dysregulation of retinal vasculature. Pharmaceutical companies have therefore been investigating the efficacy of vasoprotective drugs that reduce the hyperpermeability of retinal blood vessels.

A drug that has shown promise in the prevention of the degradation of retinal blood vessels is danazol, which is an orally administered capsule and lipophilic androgen. In placebo-controlled studies involving patients with DME, danazol improved visual acuity most significantly in overweight patients. This finding was based on a prescribed dose of 0.5mg danazol twice daily for 12 weeks.

However, danazol is associated with a considerable side-effect burden and is contraindicated in patients with porphyria and clotting disorders, as well as impaired hepatic, renal, or cardiac function. Despite the development of an ultra-low-dose formulation for the potential management of DME, danazol is not recommended for pregnant or breastfeeding women. The androgenic side effects of danazol, such as acne, hoarseness and hirsutism, may preclude the drug from being well received by women with DME. This is notable as danazol may be able to address the longstanding unmet need of non-injectable, effective therapies for patients with DME.

Although the aforementioned side effects are of considerable significance for women who are diagnosed with DME, it is likely that the greatest conflict of interest arises between the association of danazol with dyslipidemia and its increased efficacy in patients who are overweight. Danazol may be effective in reducing the rate of sight loss in patients with DME. However, the consequences of untreated dyslipidemia such as atherosclerosis and peripheral vascular disease, far outweigh the benefits of slowing the progression of vision loss. Given the evidence, GlobalData considers it unlikely that danazol will be the revolutionary oral therapy that patients with DME need.