

20-Feb-08 16:00 **Celgene's oral apremilast less potent than biologics for psoriasis but lower cost could propel it to first line use, physicians say**

Story Celgene's apremilast is positioned to become a first line therapy for psoriasis - even if it's less potent than the current class of biologics - because of cost considerations, dermatologists and an investigator say. The Phase II compound may be the first small molecule to treat psoriasis, if successful. Patients with mild to moderate psoriasis are often treated with phototherapy and topical ointments, both of which will still have a place in treatment, physicians note. But a small molecule drug could extend the time before patients with a more severe condition require a costly biologic such as Johnson & Johnson's Remicade, Genentech's Raptiva, Amgen's Enbrel, or Abbott's Humira. About one-third of psoriasis patients are treated with biologics, according to Dr Alan Menter, a psoriasis researcher who practices at Texas Dermatology Associates. "Cost is a dramatic problem," he said. "We struggle to get reimbursement for psoriasis. It would be wonderful to be able to use a small molecule." Payers, too, might one day require patients to try an oral drug before reimbursing a more expensive treatment, according to apremilast investigator Dr Kim Papp, a dermatologist at Probit Medical Research in Ontario. Papp noted that apremilast had a response rate of 20-30% in a Phase II trial with a twice daily dose of 20mg over 12 weeks - results he described as "not perfect but not bad". He added that Celgene may test a 30mg dose in future trials in the hopes of getting a greater response rate. "The real issue is tolerability," he said, adding that about 5% of patients had gastrointestinal problems, namely nausea. "We expect as we go to higher doses that'll be the limiting factor." There was no liver or kidney toxicity in the trial, he noted. "In an ideal world, one would like a drug that is perfectly effective, safe and cheap," Papp said. With apremilast, "the big saving grace is cost. It has the potential for first line use." Menter too noted that efficacy data on the Psoriasis Area Severity Index is "not quite as good" as the injectables. "We have not yet proven that small molecules equal greater efficacy," he said, but added that the safety profile is "excellent". He cautioned, however, that there are only 12 weeks of data available on apremilast, when at least 36 weeks are necessary. Small molecules might take longer to work than biologics, he noted, and more data could help Celgene's application. Long-term data will also determine whether the drug might have the same side effects as the current crop of biologics, which can cause serious infections like tuberculosis and have been linked to lymphoma. Menter noted that it's still unclear, however, whether psoriasis patients are more prone to lymphoma or whether the treatments themselves increase the risk of cancer. Biologics are more targeted than apremilast, which works at the cellular level and inhibits not only TNF-alpha but also PDE-4. "You shutdown the machinery of the cell," Papp said. "It's the first of its class that has shown effect and is tolerated." Dr Charles Crutchfield III, medical director at Crutchfield Dermatology, noted that he hasn't faced many reimbursement hurdles with the current biologics, but noted that some patients might find a pill to be more convenient than an injection. "An oral agent would be much welcomed," he said. "It would probably replace injectables." He added, however, that he does not expect it to be as potent as a biologic. "I treat the disease - I don't treat the cost," he said. "Different patients will respond differently to different treatments." Celgene has a market cap of USD 21.2bn.

by Beth Herskovits

Source [Pharmawire](#)

21-Feb-08 13:27 **Celgene's apremilast could face competition in 'race' to be first oral psoriasis drug to market**

Story Celgene is angling to be the first company to bring a small molecule psoriasis drug to market - but its Phase II apremilast could face competition, physicians note. Dr Kim Papp, a dermatologist at Probit Medical Research in Ontario, noted that "there's a bit of a race" between Celgene and Canadian company Isotechnika, which is also developing an oral psoriasis drug, ISA247, already in Phase III. Papp was an investigator on the Phase II trials with apremilast. ISA247 is an immunosuppressive agent that works "quite well," Papp said, but might have the "historical baggage" of cyclosporine, an earlier agent used in psoriasis that had a number of drug-drug interactions. In addition, newer, easier to use biologics are also in development. Dr Alan Menter, a psoriasis researcher who practices at Texas Dermatology Associates, noted that Centocor recently filed for FDA approval for an injection that can be given as infrequently as every three months. The current biologics - Johnson & Johnson's Remicade, Genentech's Raptiva, Amgen's Enbrel, and Abbott's Humira - must be given weekly or every other week.

The drug - CNT01275 or ustekinumab - has a novel mechanism of action, inhibiting interleukin 12 and 23. Menter noted that, while the drug is likely to be approved, a high price tag could limit its adoption. Surveys have suggested that patients choose their psoriasis treatments based on safety and cost considerations, he added.

A small molecule drug would be a fraction of the cost of a biologic, Papp said.

Further down the pike, Johnson & Johnson, Pfizer and Novartis are also in the early stages of testing oral drugs for the condition. "The new versions are arguably much more precise," Papp said.

Dr Charles Crutchfield III, medical director at Crutchfield Dermatology, noted that small molecule drugs could replace injectables in many cases - but he questioned whether they would be as potent. Biologics are often used in cases where patients have debilitating psoriasis on their hands and feet, or when the condition covers a large surface area of skin. Yet he noted that patients often continue on their current therapy without being counselled about the latest treatment options. "The vast majority of patients with psoriasis are unhappy with their treatment," he said.

A study last year from the National Psoriasis Foundation found that 57% of patients with severe psoriasis and 73% with moderate psoriasis are being treated only with topical drugs.

Menter noted that companies are entering the psoriasis market because the disease is relatively easy to study and many of these drugs can crossover to treat rheumatoid arthritis and Crohn's disease. Moreover, practitioners are realizing that psoriasis is more than just a skin condition; patients, for instance, have a higher risk of cardiovascular disease, he added.

"It is very exciting," Papp said. "It's paving the way to showing there is an unmet need."

Celgene has a market cap of USD 21.06bn. J&J, which owns Centocor, has a market cap of USD 181.06bn.

by Beth Herskovits

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