

Questcor's Acthar gel has no data in steroid failures Rheumatologists unsure of use

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- **Firm not planning to conduct studies in patients who have failed on steroids**
- **Acthar benefit in MS would be in patients who can't use IV steroids, investigators said**
- **Questcor has spoken to five rheumatologists so far, but physicians don't see market for this**

Questcor Pharmaceuticals' (NASDAQ:QCOR) product H.P. Acthar Gel (repository corticotropin injection) does not have any data supporting the drug's use in steroid failures, according to physicians.

The company recently announced plans to start marketing the drug in rheumatology-related indications already on its label, but rheumatologists are unaware of this product.

Commenting on steroid failure, Questcor CEO Don Bailey said, "There are patients who take steroids, who often don't do very well. Those are the patients that doctors use Acthar in."

Yet, he also noted that, with regard to multiple sclerosis (MS), the current data really isn't to position Acthar as a second-line therapy for patients who fail on steroid use.

The product website, however, notes that as a treatment for MS, Acthar may be the right choice if a patient is unable to cope with the side effects of corticosteroids, has been treated with a corticosteroid and it did not work, and has trouble receiving medication through his/her veins.

In relation to rheumatology, Bailey noted the company has only just begun to build up a marketing and sales force to talk to rheumatologists. "Frankly, we've only talked to 10 doctors, five of who are rheumatologists," he said in response to why rheumatologists have never heard of Acthar.

Steroid failures

Acthar is an injection that contains the hormone adrenocorticotropin (ACTH). It works by helping the body produce natural steroid hormones to reduce inflammation. The recommended dose is daily intramuscular or subcutaneous doses of 80-120 units for two-to-three weeks for acute exacerbations.

FDA first approved Acthar in 1952. The drug is indicated for use in infantile spasms, and exacerbations of multiple sclerosis and may be used for rheumatic, collagen, dermatologic, allergic, ophthalmic, respiratory, and edematous disorders, according to its label.

"I think there's no demonstrated advantage of Acthar gel over IV or high dose methylprednisolone," said Dr Aaron Miller, chief medical officer for the National Multiple Sclerosis Society, and director of the MS Center at Mount Sinai, New York. Methylprednisolone is a synthetic glucocorticoid or corticosteroid drug. It is marketed in the USA and Canada under the brand names Medrol and Solu-Medrol.

Whether the drug has other advantages, hasn't been clearly demonstrated, Miller added.

"We don't know yet if patients who failed on steroids would respond to Acthar gel. That's not adequately investigated at this point," Miller concluded. "I don't think there's currently much indication to use that, given its greater cost compared to high-dose steroids."

There's really no need to show that Acthar works when steroids don't, Bailey said.

Multiple Sclerosis

At this point, Miller believes Acthar gel would seldom be used as a first-line treatment for MS relapses. "There might be extenuating circumstances, and it's not a rare occurrence for patients to fail on generic steroids," he added.

Doctors in the major MS centers and academic centers are very difficult to see in order to educate them about Acthar use, Bailey noted. It takes time for doctors to understand the drug's positioning, he added. "That's why you're going to run into doctors, who say 'I would like to see some data,'" he added.

There are many more active ingredients than ACTH in Acthar, according to Bailey. With Acthar, the mechanism of action might be related to something else, he noted. Acthar is not well understood because money has not been spent on the science, Bailey added. "Over the next five years, we should gain a better understanding of the drug's mechanism of action."

Dr Daniel Kantor, medical director at Neurologique, and president of the Florida Society of Neurology, noted, "Questcor's pipeline drug is H.P. Acthar Gel. Since it already has so many legacy FDA approvals, the pipeline is driven by corporate decisions and the need for a niche product in patients with a multitude of inflammatory diseases who sub-respond to or can't tolerate less expensive medications."

Decisions about which specialties to market to are fueled by board room projections and investigator-initiated studies, Kantor said.

In 2009, Kantor was the lead investigator on a study comparing intramuscular Acthar and IV Solu-Medrol for the treatment of MS relapse (exacerbation) after sub-response to an initial three-day course of IV Solu-Medrol. The study has since been terminated, according to [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT00947895). [NCT00947895]

"That wasn't a company-sponsored trial," said Bailey.

He added Kantor left the institution he was originally with, when that study was running. "The trial wasn't enrolling very well anyway. It isn't something we're particularly interested in," Bailey said, adding that defining patients for that type of study is very difficult.

Dr David Snyder, a neurologist based in New York, said he has used a similar type of ACTH for injection, decades ago. "I guess it has its place, in [patients] who have difficulty with

standard Solu-Medrol. We do give a number of patients IV steroids, during the course of the year. We've just not had an opportunity to use Acthar yet," said Snyder.

"I talked to the drug reps. They tell me there are neurologists that use a fair amount of Acthar. It's difficult for me to figure out why. Essentially, it's just another way of ensuring an increased level of steroids," said Snyder. For some reason, it became very popular amongst neurologists to use IV in large doses.

Snyder noted that he rarely admits patients for IV steroids now, and cases are mostly at-home infusions. "We can also do an outpatient infusion center. I think frankly, Questcor sees a future in Acthar in other areas and not in MS. There's no benefit, unless patients have a problem with IV steroids. The insurance company wouldn't be thrilled, because it's much more expensive."

Expansion into rheumatology

Dr Nan-Hsien Kuo, a rheumatologist, New York Hospital Queens, said he has no knowledge of Acthar and there are no studies. "Corticotropin is part of a hormone injection, and it's not something we do routinely." Steroid injections are given more frequently and work further downstream compared to Acthar, he said. "[Steroids] we give have been around for years and are economically feasible," he said.

"As far as I can see, I don't see a market for this [in rheumatology]," said Kuo.

Dr Nathan Wei, a rheumatologist and CEO at Arthritis Treatment Center, and Dr J.W.J. Bijlsma, chair of the department of rheumatology and clinical immunology, University Medical Center Utrecht, both said they had not heard of Acthar. Bijlsma recently published a review called 'Disease control with glucocorticoid therapy in RA.' [Rheumatology (Oxford). 2012 Jun;51 Suppl 4:iv9-iv13.]

Wei noted he would not use the drug based on the chemical, adding there may be potential side effects due to its effect on the adrenal glands. "I would be concerned about using it, with the price point, since there is prednisone," said Wei.

"It's not common for RA patients to need to go from prednisone to another steroid," Wei noted. Usually prednisone, which is now a generic drug, is used as a bridge from NSAID to DMARD therapy, as effects take time to be felt. There is minimal use of steroids, but they are good and cheap, said Wei.

Dr Theodore Pincus, a rheumatologist and clinical professor, NYU Hospital for Joint Diseases, said pricing for 3mg prednisone a day is much cheaper and the drug is at least as effective as Acthar.

Questcor has increased the price for Acthar three times in 2011. It charges CuraScript SD, its third-party specialty distributor for Acthar, USD 27,064 per vial.

The company reported USD 218.2m in total net sales for the year ended 31 December, 2011, compared to USD 115.1m in the prior year. All sales were from Acthar, according to a recent 10-K filing. The drug is no longer subject to patent protection.

Questcor has a market cap of USD 3.32bn.

by Kimberly Ha and Casey McDonald in New York

