MS
RESEARCH AUSTRALIA

CENTRE FOR COMMUNITY-DRIVEN RESEARCH

MS
AUSTRALIA

PBAC Secretariat
MDP 952
Department of Health and Ageing
GPO Box 9848
Canberra ACT 2601

7 October 2020

Re: Submission of eculizumab for NMOSD to PBAC meeting November 2020

This is a joint submission to the Pharmaceutical Benefits Advisory Committee (PBAC) in relation to eculizumab (Soliris) for neuromyelitis optica spectrum disorder (NMOSD) from MS Research Australia, the Centre for Community-Driven Research and MS Australia.

- MS Research Australia is the largest national not-for-profit organisation dedicated to funding MS discoveries and coordinating MS research in Australia.
- The Centre for Community-Driven Research is a non-profit organisation with expertise in gathering patient experience and expectations data.
- MS Australia is the national voice for people with multiple sclerosis. MS Australia works in advocacy and communications and collaborates with their stakeholders to benefit thousands of people affected by MS across the country.

MS Research Australia and MS Australia are writing to support the inclusion of eculizumab on the Pharmaceutical Benefits Scheme (PBS) for people with NMOSD. The Centre for Community-Driven Research is keen to inform the PBAC about the experience of people with NMOSD and their expectations of new treatments.

The NMOSD community in Australia is not represented by a national peak body and as NMOSD and MS have some similarities, we are proud to advocate on behalf of those living with NMOSD. One area we are all particularly passionate about is the provision of affordable and accessible treatments that can improve the lives of people with NMOSD.

About NMOSD

NMOSD is a recently defined inflammatory disorder of the central nervous system (CNS) that was previously either misdiagnosed as MS or identified as Devic's disease. NMOSD is associated with antibodies to aquaporin-4 (AQP4) which are thought to be pathogenic and cause damage to astrocytes through complement activation in the CNS.[1] There are many symptoms that overlap with MS. Differential diagnosis of MS from NMOSD is critically important because disease-modifying treatment for MS, such as interferon-β, fingolimod, natalizumab, and alemtuzumab, are inefficacious in or may aggravate NMOSD[2]. Given the importance of differential diagnosis for effective therapy for both diseases, MS Research Australia also funds research into NMOSD.

It is estimated that there are about 200 people with NMOSD in Australia[3,] though advice from the sponsor of this treatment has provided a higher estimate of around 350. The disease is generally more aggressive, with more frequent attacks and greater disability (both vision and mobility), when compared with MS.[4,5] NMOSD can be diagnosed and distinguished from MS reliably through the detection of antibodies to AQP4 using a commercial fixed-cell assay (Euroimmun®).[6]

Symptoms of NMOSD

The symptoms of an acute event in NMO include inflammation of the optic nerve (optic neuritis) causing eye pain, loss of clear vision; inflammation of the spinal cord (acute myelitis) causing pain in spine and limbs, bladder and bowel problems, sensory loss, limb weakness, and numbness; and prolonged hiccups, nausea, vomiting or dizziness[7]. These symptoms can cause long-term disability following an acute event[8].

Current treatment for NMOSD

Current treatment guidelines for NMOSD are based on case series and uncontrolled comparison studies[9]. Acute relapses are treated with steroids and plasma exchange. Treatment to prevent future relapses consists of immunosuppressive therapy or rituximab. Immunosuppression is achieved with steroids, azathioprine, mycophenolate, methotrexate or less commonly with cyclophosphamide. Rituximab is currently favoured to be the most effective therapy for the prevention of relapses in NMOSD[10] and is currently being funded through hospital pharmacy budgets in Australia. It is estimated that 25% of patients with NMOSD will continue to have relapses on rituximab. There is therefore a clear need to have additional treatment options for NMOSD.

Our understanding of eculizumab (Soliris)

Eculizumab is a monoclonal antibody which is an antagonist of complement component 5 and thereby inhibits the complement cascade. Eculizumab has been demonstrated to dramatically reduce the risk of relapse in a randomised, placebo-controlled clinical trial.[11] This treatment effect is of particular importance as studies show that the accrual of disability in NMOSD almost exclusively occurs as a result of relapses with a secondary progressive disease course being rare, unlike MS.[4]

There were four clinical trials sponsored by Alexion Pharmaceuticals on the use of eculizumab in an NMOSD patient population. Results of these clinical trials report that eculizumab reduces relapse, and can maintain or reduce the level of disability in patients with NMOSD [11,12]. It is generally well tolerated and has been approved for the treatment of NMOSD from the FDA and the European Medicines Agency [13]. Similar to other monoclonal antibodies, common side effects include infusion related reactions, and infection, in particular meningococcal infections [11,12]. This side effect could be mitigated with the use of meningococcal vaccinations[8].

Experience and expectations of individuals in the NMOSD community

Female, Qld, 55 – 64 age group

How do you currently manage with your NMO?

I've had bladder issues for several years, bladder urgency. I was on bladder medication, which last year I was determined to come off and experiment with. I still have the occasional accident, but I'm much, much better. I've managed to come off my immunosuppression only on 1,000 milligrams of Mycophenolate as opposed to 3,000 milligrams a day. I'm on Baclofen. Every time I try and come off the antispasmodic drug, I just get spasms. I can't really reduce that one. I take Endep for the nerve pains as needed. Generally, in the summer months when it's humid, I get burning sensations in my legs. I can get flare-ups usually…I usually have something every six months or so.

Has having NMO had an impact on your quality of life?

My kids, when I got NMO, were teenagers. They were going through, basically, teenager puberty. My marriage broke up because of NMO, the strain that it put on our relationship was enormous. It's actually quite well documented that people with chronic disease marriages, they often don't work out. That cost to me was enormous.

The children witnessing me having these massive spasm attacks, being in bed, not being able to speak or move. It's traumatic for them. I know my daughter, especially, being a little bit younger, was traumatized. I wanted to have family counselling, but that didn't happen. It was probably all too late.

When you are using a treatment, what needs to improve for you to feel as though the treatment has worked?

I think it was quite dramatic going from azathioprine to mycophenolate because I wasn't able to walk far at all, when I was contemplating life in a wheelchair just to get around to within a matter of a month later of being on mycophenolate, being able to walk 20 minutes. That was quite dramatic for me, the ability to walk.

If a treatment improved those things, what would that mean to you in your everyday life, that is, what would you be able to do that you couldn't do if the treatment wasn't doing its job?

Well, obviously, I haven't been able to work. I can't work because I don't have the stamina anymore. Even one phone conversation will exhaust me. The ability for treatment to give my life back to me. Even though I had a fantastic life now, then I've made it so that way, it would give me stamina, it would give me the ability to walk and hike for much longer.

I think, probably, just to live a more normal life. I don't think at my age, I would contemplate going back to work, but I possibly might do more volunteer work. I've shied away from doing volunteer work because of the unpredictability of the disease. If medication meant that I live to live unpredictable life, then that would also help me with my volunteer work. I could commit to things. There's a lack of commitment. You have to arrange your life around being flexible, day by day, sometimes hour by hour.

If you were having an infusion of a new treatment, what kind of information or support would you need to feel comfortable with the new treatment?

Just more the understanding of what side effects I might have and if I may need care. If I may need support from that point of view, it's more worrying about the side effects of the actual treatments.

I'd much prefer it at home. I don't want to be exposed more than I have to, to being immunosuppressed and just the convenience of having it in your own home is much, much better.

In relation to NMO, what would you most like to see from new treatments? This might be about the way they are administered, or the side effects they have or cost or things like that.

I think what would be great is to actually know what the new treatments are, and how effective they are, and what the side effects are. I think knowledge is what gives us power. If we don't have that knowledge, how can we make informed decisions.

Female, Qld, 25 - 34 age group

How do you currently manage with your NMO?

At this very moment in time I have still poor vision in my right eye and I also during the space of two days of being diagnosed with the blood test, I had a TM episode so I now have a lesion on my spine, so I walk with a walker or a stick if I've got my husband or somebody with me and it's only short. I have hand controls in my car now but fatigue and mobility and vision impairs me doing my old life, put it that way. I have a new life, which is okay.

Has having NMO had an impact on your quality of life?

Yes. Initially, it was horrendous. You can't see, you can't walk. It affects relationships. I don't go to work and I don't have that feeling of being capable and being able to…I'm the kind of person who wants to help people and it's hard when other people were helping me. By doing these kinds of things with you and stuff, it makes me feel that I'm helping people. That's good for me. Hopefully, once the COVID thing gets a bit better, I can hopefully start going and maybe working some voluntary work with some community groups and stuff like that.

Obviously, I get that I have to put myself first for a change. I have to say, "No, I can't do some things," which is hard. That's hard for me to fully accept that I can't do things. I do have a cleaner that comes in and I can't do those things, or if I do them, that means I can't do anything for two days.

When you are using a treatment, what needs to improve for you to feel as though the treatment has worked?

I suppose being able to move without pain. Being less stiff. Medication treatments only do like pain and stuff and just stop the flares. The only other treatments being the physio, then I see a positive every time I go. Just the fact of being able to do things and a bit more each time and stuff. I still have an aim of being able to walk a certain distance and then I will have another aim because I don't want to just sit and not do anything.

If a treatment improved those things, what would that mean to you in your everyday life, that is, what would you be able to do that you couldn't do if the treatment wasn't doing its job?

It would then help with the fatigue because I wouldn't be as tired and fatigued from doing the smallest simplest thing. Then I'd be able to spend more time with my grandchildren without being completely exhausted and not feeling like I'm a capable Nana and being able to look after your own grandchildren. Being able to go out with my husband without having to plan that I go out in the morning and not the afternoon because I get too tired by the afternoon.

If you were having an infusion of a new treatment, what kind of information or support would you need to feel comfortable with the new treatment?

I suppose knowing that the person's trained. I trust that the person that came out and gave me the infusion is fully trained and aware of what to do and would be aware. I'd be pretty good with knowing that that's the situation.

In relation to NMO, what would you most like to see from new treatments? This might be about the way they are administered, or the side effects they have or cost or things like that.

Equity. Not everyone is the same and not everyone seems to be able to access treatments and care in the a fair way.

Female, WA, 35 – 44 age group

How do you currently manage with your NMO?

I've never had treatment for NMO. I was treated with steroids initially because my presentation was a bit different, I was never put on any NMO suppressive medications or anything like that.

Has having NMO had an impact on your quality of life?

I didn't work so well. Then I had to change the kind of work that I did which was the hardest thing for me. I didn't want to accept that. I also didn't drive for about a year. My partner and my dad drove me wherever I needed to be. Nowadays my relationship with some of my friends changed because of the things that we used to do together, I used to be big into sport and stuff which I obviously can't do anymore. Some of those relationships have changed. I used to actively playing a sport at a high level and then not playing sport at a high level is pretty upsetting.

When you are using a treatment, what needs to improve for you to feel as though the treatment has worked?

If I'm noticing an improvement or if I'm still feeling optimistic that I might have an improvement, I would continue on with it. I'd like my bladder to work better.

If a treatment improved those things, what would that mean to you in your everyday life, that is, what would you be able to do that you couldn’t do if the treatment wasn’t doing its job?

One of the biggest issues is that I used to really enjoy going to sporting events or concerts or something and I don't now because if I have to wait in line for the toilet, I'll wet myself, but also I have to catheterize and I've had some experiences where I'm trying to catheterize in a public toilet and it's not all that great. If I have some improvement in my bladder, it would change a lot of things. I work from home because I'm embarrassed. I had an accident at work before, and it embarrassed me, so I work from home and stuff like that.

If you were having an infusion of a new treatment, what kind of information or support would you need to feel comfortable with the new treatment?

I don’t think there are any particular uncertainties that I would have.

In relation to NMO, what would you most like to see from new treatments? This might be about the way they are administered, or the side effects they have or cost or things like that.

Well, it's probably a dream, but I'd like to see the treatments at the moment are all like steroids with reduced inflammation and the immunosuppression stops further relapses in the future, what would be super cool is if something could be developed that actually remodel and fixes the nerves that can fix the damage that's already done because at the moment, that's the dream, we can't do that. Other than that, I mean, the steroids treatment is the first line and it's got such horrendous side effects. It's the worst. I'll avoid steroids as much as I can. I think they're awful.

Female, NSW, 40 – 45 age group)

How do you currently manage with your NMO?

Well, my peripheral vision has gone in both eyes. I'm legally blind in the right eye. I can't drive. Just doing standard chores around the house, like washing up, or just cooking things. I've got to sit down. I can't stand up for too long, but if I do…What's the word? If I do do things, I've just got to keep on moving, but I've got to be careful that my body temperature doesn't go up because that's when I've got to lay down because it feels like I'm just going to faint, just drop.

Hot days, very, very bad. I'll be on the lounge all day. I won't move until the temperature gets to a decent level again. If I sit still, I think, "Oh." Obviously apart from the vision. Then I could just walk a couple of meters and it's like, "Now that was ridiculous." [laughs] In the thought process because it's like the mind's willing, some days but the body just goes, that's not going to happen.

It is very, very frustrating, it really is because I used to be a very, very active person, do my boot camp just constantly on the go from the time I woke up to the time I actually went to bed. It's been very hard to throw that in reverse and not being able to do anything. It has been one of the hardest challenges mentally to really get through as well as no driving.

Has having NMO had an impact on your quality of life?

I'm very grateful I have a great husband that's very supportive, compared to a lot of people. I don't honestly think my family members really know the extent of what it can be. I think the main impact I honestly reckon that will hit my family is if I have to get in a wheelchair.

Cancelling things, where maybe just catching up for a coffee or something like that, and then all of a sudden, then that morning, you feel like crap, and you have to cancel. I think I cancelled more than I actually go out. That's the thing. It's a day by day thing. I can do things better in the morning, but after lunch, that's it for me for the day. It's just too much. It does impact in a lot of different areas, for sure.

When you are using a treatment, what needs to improve for you to feel as though the treatment has worked?

It's a hope because there is no drug really out there so far that is just designed for NMO. I'd like to reduce the chance so you don't relapse.

If a treatment improved those things, what would that mean to you in your everyday life, that is, what would you be able to do that you couldn't do if the treatment wasn't doing its job?

That I can still see or I can still walk. It's just those things. I'm grateful for that I can still see something. As well as still walk and be able to pick up things.

If you were having an infusion of a new treatment, what kind of information or support would you need to feel comfortable with the new treatment?

If there was a nurse or whatever that was there with you just to make sure you were doing it correctly. I don't know, depending on what treatment you had. If it was just tablets, just as long as you've got someone here like a husband or a family member or friend or something like that to make sure that you're not going to collapse or that kind of stuff.

In relation to NMO, what would you most like to see from new treatments? This might be about the way they are administered, or the side effects they have or cost or things like that.

With the cost, as what I'm saying, to the hospital, I haven't really had the cost of the rituximab treatment, which is great because Medicare covers it. I think if they can find a treatment that can try to make us more normal again, it would be fantastic. Especially the fatigue side of it, sometimes the nerve pain and that you can bear it, and then other times you can't, but it depends. To be able to target that chronic fatigue would be a huge thing in NMO. As well as obviously preventing transverse myelitis. All of those kinds of things, like your lungs being able to breathe and function and stuff. To be able to help the nerves as well. Especially that fatigue, because that is the thing that makes you not be able to do anything. That will be like, "Well, that'll be fantastic." It just feels like you're walking around and you're holding your breath.

Conclusion

We support affordable access to all proven treatment options to increase the opportunity for people with NMOSD and their doctors to access effective therapy. We would strongly support PBS listing for eculizumab for patients with NMOSD who have relapsed on existing therapy. Reducing disease relapses will improve quality for people with NMOSD and their loved ones, enabling their full participation in social and family life, and employment.

***

References

1. Lennon et al 2004. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. Lancet 364:2106-12.
2. Sung-Min Kim et al 2017. Differential diagnosis of neuromyelitis optica spectrum disorders, Ther Adv Neurol Disord. 2017 Jul; 10(7): 265–289.
3. Bukhari et al 2017. Incidence and prevalence of NMOSD in Australia and New Zealand. JNNP 88:632-8.
4. Bukhari et al 2020. The clinical profile of NMOSD in Australia and New Zealand. J Neurol 267:1431-43.
5. Khalilidehkordi et al 2020. Relapse patterns in NMOSD: evidence for earlier occurrence of optic neuritis and possible seasonal variation. Front Neurol 11:537.
6. Prain et al 2019. AQP4 antibody assay sensitivity comparion in the era of the 2015 diagnostic criteria for NMOSD. Front Neurol 10:1028.
7. Huda S, Whittam D, Bhojak M, Chamberlain J, Noonan C, Jacob A. Neuromyelitis optica spectrum disorders. Clin Med (Lond) 2019; 19(2): 169-76.
8. Collongues N, Ayme-Dietrich E, Monassier L, de Seze J. Pharmacotherapy for Neuromyelitis Optica Spectrum Disorders: Current Management and Future Options. Drugs 2019; 79(2): 125-42.
9. Kessler et al 2016. Treatment of neuromyelitis optica spectrum disorder: acute, preventive and symptomatic. Curr Treat Options Neurol 18(1):2.
10. Huang et al 2019. Effectiveness and tolerability of immunosuppressants and monoclonal antibodies in preventive treatment of neuromyelitis optica spectrum disorders: a systematic review and network meta-analysis. Mult Scler Rel Disord 35:246-52.
11. Pittock SJ, Lennon VA, McKeon A, et al. Eculizumab in AQP4-IgG-positive relapsing neuromyelitis optica spectrum disorders: an open-label pilot study. Lancet Neurol 2013; 12(6): 554-62.
12. Pittock SJ, Berthele A, Fujihara K, et al. Eculizumab in Aquaporin-4-Positive Neuromyelitis Optica Spectrum Disorder. N Engl J Med 2019; 381(7): 614-25.
13. Akaishi T, Nakashima I. Efficiency of antibody therapy in demyelinating diseases. Int Immunol 2017; 29(7): 327-35.