A 2026 Update on Pain in NF1: Where We Have Been and Where We Are Going

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In 2016, we were asked to write an article for NF Midwest on the topic of pain in NF1. In it, we discussed common causes of NF-related pain, such as plexiform neurofibromas, scoliosis and its treatment, chronic headaches, and gastrointestinal complications. We also talked about the impact of pain on daily life. Finally, we summarized the existing medications, including nonsteroidal anti-inflammatory drugs (NSAIDS) like ibuprofen and narcotics like oxycodone. We noted that, while drugs targeting tumor shrinkage were being investigated, none had been found to be effective in clinical trials. Psychological treatments were also mentioned, although again, no examples of effective interventions had been documented in the literature for people with NF1.

When NF Midwest reached out to request an update to this article, we reviewed the previous article and were surprised by how much has changed. The first big accomplishment was achieved when a drug treating plexiform neurofibromas (PNs) received FDA approval. A study called SPRINT (Selumetinib in Pediatric Neurofibroma Study) tested the medicine Selumetinib (Koselugo) which is a MEK-inhibitor, in 50 children with NF1 and their symptomatic PNs that could not be surgically removed safely. PNs are tumors that grow along nerves that can cause pain, changes in appearance, motor function, and other problems. The study showed that Koselugo shrank the PNs in 68% of the children, and many of them experienced less pain and PN-related problems, plus improved their quality of life. Koselugo became the first approved treatment for children with NF1 and PNs in the U.S. It is now approved for children in many countries around the world, including Canada, Europe, Australia, China, and Japan. You can read more about Koselugo and the SPRINT trial in this summary published in the 2023 PLSP. Most recently, Koselugo showed meaningful benefit to adults with symptomatic PNs, including tumor shrinkage and reduced symptoms like pain. As a result of these findings, Koselugo is now approved for adults with symptomatic PNs in the US and Europe.

In 2025, another medicine called Mirdametinib (Gomekli), which also a MEK-inhibitor was approved for children as young as two years old up through adults. Based on the ReNeu study, which included children and adults with NF1 and symptomatic PNs, the results showed that their PNs shrank in 41% of the adults and 52% of the children being treated with Mirdametinib. Both adults and children reported improvement in pain and quality of life. In addition to being approved in the U.S., Mirdametinib (Ezmekly) has also been approved in Europe for children and adults living with NF1 and symptomatic PNs.

For children who have trouble swallowing capsules, both Koselugo and Gomekli are available in forms that are easier for kids to take.

Since our previous article in 2016, there are now two FDA-approved treatment options available for families affected by NF1 with PNs. This exciting progress gives families more choices and hope in managing their NF1 PNs.

One important thing to add. Studies of Selumetinib at the NIH found that both child and adult participants did a fantastic job of taking their clinical trial medication as prescribed. This high adherence contributes to the powerful effects of the drug on shrinking tumor size. Also, a sample of 12 adults on the adult trial were interviewed as part of an adherence substudy. Factors that made it easier to follow their medication regimen included the fact that tumor pain increased when they stopped taking the drug as instructed or when their team temporarily paused the drug for medical reasons.

A lot has happened in the last decade from a psychological standpoint as well. In fact, just months after the last version of this article was published, a group at the National Cancer Institute published the first paper focused on a psychological intervention for NF1-related pain. This study enrolled adolescents and young adults ages 12-21 years and their parents to participate in a 2-day small-group workshop featuring Acceptance and Commitment Therapy, or ACT (pronounced as the word, not the letters). Three months post-intervention, patients and parents each reported a significant decline in the extent to which pain interfered with daily functioning, and patients also reported a decline in pain intensity. In 2021, building upon that study, a larger randomized controlled trial published in 2021 enrolled people with NF1 and plexiform-related pain ages 16 to 56. About half of the participants received the ACT intervention immediately, while the other half underwent an 8-week wait-list period first. The ACT group had decreased pain interference significantly more than the wait-list group. The data also showed that patients' willingness to experience pain in order to connect with what matters most to them (their values) was a key factor driving the pain interference improvements.

In 2023, researchers at Massachusetts General Hospital published a study testing the effectiveness of a mind-body intervention delivered through weekly online modules for 8 weeks among mostly adults with NF1, although a few people with NF2 and NF2-related schwannomatosis were included as well. Results showed that the intervention was helpful in increasing gratitude, coping, and mindfulness. The following year, some of those same researchers conducted another study looking at a similar mind-body intervention aimed at reducing pain in adults with NF. This study compared the intervention to a group of patients who received health education only. While there were no differences between the groups, the group that received the mind-body intervention showed a decrease in the extent to which pain interfered with daily life. Research on psychological interventions for people with NF continues to explore ways to maximize the impact of these tools to help improve quality of life in a variety of areas.

We continue to learn more about NF and the complexities of pain management. The path ahead is not always straightforward, but bends and weaves as new information emerges. Treatment trials are now exploring combination therapies - in other words, instead of testing a single medicine, scientists are studying two medicines together to see if this approach can lead to greater PN shrinkage and relief from related PN symptoms. Additionally, other trials are focusing on medicines aimed at treating cutaneous neurofibromas, which can cause cosmetic concerns as well as itchiness and discomfort. We hope that great strides in these areas will have been made in the next decade, and perhaps we will publish an update in another ten years with a lot more good news!