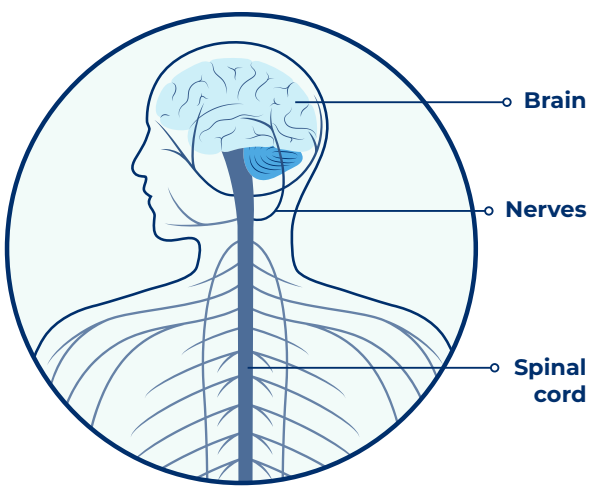
Neurofibromatosis Type 1 (NF1) Plexiform Neurofibromas (PN)

ALEXION
AstraZeneca Rare Disease

WHAT IS NEUROFIBROMATOSIS TYPE 1?

Neurofibromatosis (NF) is a rare genetic disorder that involves the development of tumors that may affect the brain, spinal cord, and nerves. The most common type of **NF is neurofibromatosis type 1 (NF1)**.[1]

NF1 is also one of the most common inherited disorders and is caused by a mutation or flaw in the NF1 gene. **Half** of all people with NF1 are estimated to **inherit the mutation** from a parent while the other half **have no family history**.[2,3]

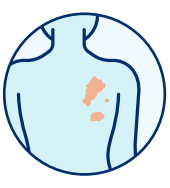


NF1 affects about
1 in 3,000
people worldwide.[4]

NF1 is **commonly recognized in early childhood** and is a lifelong, progressive condition that affects all types of people, **regardless of gender or ethnicity**.[4,5,6]

The severity of NF1 can vary significantly and people with the disease may not develop every symptom.[5]

Initial signs of NF1 may include:[2]



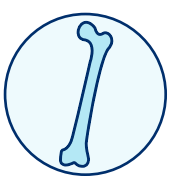
Flat, light brown spots on the skin
(called 'café au lait' spots)

Soft lumps on and under the skin
(neurofibromas)

Patients with NF1 may also experience:[2,3]

freckling in unusual places
(such as the armpits or groin area)

tiny bumps on the iris of the eye
(called 'lisch nodules')



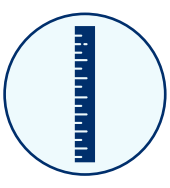
bone issues

scoliosis
(back bone deformities)

cognitive differences

irregular head size

delayed or early puberty



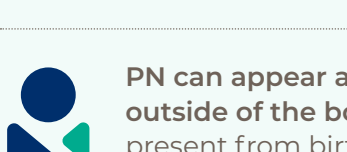
small stature

optic gliomas
(tumor that develops in the cells surrounding the optic nerve)

cosmetic concerns

hypertension
(high blood pressure)

WHAT IS NF1 PN?



Up to
50%
of children
with NF1 may develop **non-malignant (non-cancerous) tumors called plexiform neurofibromas (PN)**, also called plexiform tumors, which grow along nerves.[3,4]

PN can appear anywhere inside or outside of the body and are typically present from birth with varying degrees of severity.

However, they may not appear or become noticeable until months or years later. PN can grow fast and become large, which can progressively interfere with normal physical functions.[4]

While PN often do not cause any symptoms, complications can arise including:[2,7-10]

- **Itching**
- **Physical deformities**
- **Organ dysfunction, which may lead to:**
  - » Trouble breathing
  - » Bladder/bowel problems
  - » Pain
  - » Weakness
  - » Numbness or tingling
  - » Visual impairment, depending on the location

Although PN may start as non-malignant, **a small proportion (~10%) will later become malignant (cancer)**.[11]

HOW IS NF1 PN DIAGNOSED AND MONITORED?

Initial diagnosis of NF1 can be complex and may involve visits to multiple specialists that can evaluate signs, symptoms and family history as well as perform genetic testing.[3,12] Upon diagnosis, **a physical examination can be conducted to understand the involvement of PN**.[4,5]

Next, **an MRI (magnetic resonance imaging) of the affected body part can help determine the size and extent of the PN** on the outside and inside of the body. **Other radiology procedures may be necessary** if there is concern for the presence or development of a malignancy surrounding the nerves, including a PET (positron emission tomography) scan.[4]

HOW HAS NF1 PN TREATMENT EVOLVED?

In certain cases, surgery may be done to remove some PN, but **PN are often considered inoperable**, meaning they cannot be totally removed by surgery, or the surgery poses a high risk.[5] Previously, PN treatment options were limited to medication to help manage pain and/or physical therapy to address complications of PN, such as lack of mobility and reduced range of motion, but **research has led to more options**.[2,3,5]

Clinical studies have shown that key proteins (enzymes) are overactive in NF1 PN and can cause uncontrolled growth of tumor cells. Treatment that works by blocking these proteins has proven to **halt progression, reduce the size of tumors** and **improve symptoms** in pediatric patients with NF1 PN.[13]

HOW IS ALEXION CONTINUING TO INNOVATE FOR NF1 PATIENTS?

In addition to our therapy that is the **first and only medicine approved for pediatric patients with NF1 who have symptomatic and inoperable PN,** we continue to advance research. Alexion's ongoing clinical trials in the disease include a **Phase 3 study in adults** with NF1 PN as well as research for **new treatment options** to help more people living with this devastating disease.

Alexion continues to **innovate for patients with NF1 PN** and accelerate the **development of life-changing therapies**.

References:

1. Tamura R. Current Understanding of Neurofibromatosis Type 1, 2, and Schwannomatosis. *Int J Mol Sci.* 2021.22.5850.
2. Boyd K, et al. Neurofibromatosis type 1. *J Am Acad Dermatol.* 2009 July; 61(1): 1–16.
3. Jett K, et al. Clinical and genetic aspects of neurofibromatosis 1. *Genetics in Medicine.* 2010 Jan;12(1):1-11.
4. Ly K, Blakeley JO. The diagnosis and management of neurofibromatosis type 1. *Med Clin North Am.* 2019 Nov;103(6):1035-054. https://pubmed.ncbi.nlm.nih.gov/31582003/
5. Tonsgard, JH. Clinical Manifestations and Management of Neurofibromatosis Type 1. *Semin Pediatr Neurol.* 2006;13(1):2-7.
6. Hersh J, et al. Health Supervision for Children With Neurofibromatosis. *American Academy of Pediatrics.* 2008: Volume 121, Number 3
7. Curatolo P and Riva D. (2006) Neurocutaneous Syndrome in Development Age. Novel therapeutic approaches for plexiform neurofibromas in neurofibromatosis type 1. *John Libbey Eurotext.* Chpt 17; Pgs 207-209
8. O'Brien D, et al. Assessment of pain and itch behavior in a mouse model of Neurofibromatosis type 1. *J Pain.* 2013 June; 14(6): 628–637
9. Guiraud M, et al. Cutaneous neurofibromas: patients' medical burden, current management and therapeutic expectations: results from an online European patient community survey. *Orphanet Journal of Rare Diseases.* 2019.14:286
10. Avery A. R, et al. Orbital/Periorbital Plexiform Neurofibromas in Children with Neurofibromatosis Type 1. *American Academy Of Ophthalmology.* 2017;124:123-132
11. Evans M E Baser, et al. Malignant peripheral nerve sheath tumours in neurofibromatosis 1. *J Med Genet.* 2002; 39:311-314
12. Legius E. et al. Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: an international consensus recommendation. *Genetics in Medicine.* 2021. 23:1506–1513
13. Gross A, et al. Selumetinib in Children with Inoperable Plexiform Neurofibromas. *N Engl J Med* 2020;382:1430-42

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