Neurofibromatosis Diagnosis Criteria

Patient name: xxxxxxxxxxxxx **Date of birth:** January 1, 2015

Healthcare provider name: xxxxxxxxx **Assessment date:** January 1, 2024

Type	Criteria
Neurofibromatosis type 1 (NF1)	If the patient has a parent diagnosed with NF1 and meets at least 1 of the criteria below, the diagnosis of NF1 is made. If the patient does not have a parent diagnosed with NF1, ≥ 2 of the following must be present: • ≥ 6 café-au-lait macules > 5 mm in greatest diameter in prepubertal patients and > 15 mm in greatest diameter in postpubertal patients • Freckling in the axillary or inguinal region • ≥ 2 neurofibromas of any type or1 plexiform neurofibroma • Optic pathway glioma • ≥ 2 Lisch nodules (iris hamartomas) identified by slit-lamp examination or ≥ 2 choroidal abnormalities • A distinctive osseous lesion (eg, sphenoid dysplasia, anterolateral bowing of the tibia, pseudarthrosis of a long bone) • A heterozygous pathogenic NF1 variant with a 50% variant allele fraction in apparently normal tissue (eg, white blood cells)
NF2-related schwannomatosis (NF2)	1 of the following: • Bilateral vestibular schwannomas • An identical NF2 pathogenic variant in at least 2 anatomically distinct NF2-related tumors (schwannoma, meningioma, and/or ependymoma) OR Major criteria (2 of the following): • Unilateral vestibular schwannoma • First-degree relative (other than a sibling) with NF2 • ≥ 2 meningiomas • NF2 pathogenic variant in an unaffected tissue (eg, blood) OR One major criterion and 2 of the following minor criteria: • Can be counted twice*: Ependymoma, meningioma†, nonvestibular schwannoma • Can be counted only once‡: Juvenile subcapsular or cortical cataract, retinal hamartoma, epiretinal membrane in a person < 40 years old, single meningioma • Pattern of genetic changes in unaffected tissue and in tumor tissue in NF2

Type	Criteria
Non-NF2 schwannomatosis (schwannomatosis)	SMARCB1- and LZTR1-related schwannomatosis (1 of the following): • ≥ 1 pathologically confirmed schwannoma or hybrid nerve sheath tumor and an SMARCB1 or LZTR1 pathogenic variant in an unaffected tissue (eg, blood) • A shared SMARCB1 or LZTR1 pathogenic variant in 2 schwannomas or hybrid nerve sheath tumors 22q-related schwannomatosis (all of the following): • Patient does not meet criteria for NF2-, SMARCB1-, or LZTR1-related schwannomatosis and does not have a germline DGCR8 pathogenic variant • Loss of heterozygosity of the same chromosome 22q markers in 2 anatomically distinct schwannomas or hybrid nerve sheath tumors • A different NF2 pathogenic variant in each tumor, which cannot be detected in unaffected tissue Schwannomatosis not otherwise specified (both of the following, no genetic testing done): • ≥ 2 imaging-confirmed nonintradermal schwannomas • ≥ 1 pathologically confirmed schwannoma or hybrid sheath tumor
* These criteria can be counted twice (ie, 2 distinct schwannomas count as 2 minor criteria).	
Additional notes	
Patient exhibits symptoms of NF1. Reviewed patient's personal and family medical history. Patient will undergo imaging tests and possibly, genetic testing, to confirm diagnosis.	

References

Legius, E., Messiaen, L., Wolkenstein, P., Pancza, P., Avery, R. A., Berman, Y., Blakeley, J., Babovic-Vuksanovic, D., Cunha, K. S., Ferner, R., Fisher, M. J., Friedman, J. M., Gutmann, D. H., Kehrer-Sawatzki, H., Korf, B. R., Mautner, V., Peltonen, S., Rauen, K. A., Riccardi, V., . . . Plotkin, S. R. (2021). Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: an international consensus recommendation. *Genetics in Medicine*, *23*(8), 1506–1513. https://doi.org/10.1038/s41436-021-01170-5

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