

Neurofibromatosis Diagnosis Criteria

Patient name: _____ Date of birth: _____

Healthcare provider name: _____ Assessment date: _____

Type	Criteria
Neurofibromatosis type 1 (NF1)	<p>If the patient has a parent diagnosed with NF1 and meets at least 1 of the criteria below, the diagnosis of NF1 is made.</p> <p>If the patient does not have a parent diagnosed with NF1, ≥ 2 of the following must be present:</p> <ul style="list-style-type: none"> • ≥ 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 or 1 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)	<p>1 of the following:</p> <ul style="list-style-type: none"> • Bilateral vestibular schwannomas • An identical NF2 pathogenic variant in at least 2 anatomically distinct NF2-related tumors (schwannoma, meningioma, and/or ependymoma) OR <p>Major criteria (2 of the following):</p> <ul style="list-style-type: none"> • Unilateral vestibular schwannoma • First-degree relative (other than a sibling) with NF2 • ≥ 2 meningiomas • NF2 pathogenic variant in an unaffected tissue (eg, blood) OR <p>One major criterion and 2 of the following minor criteria:</p> <ul style="list-style-type: none"> • 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)	<p>SMARCB1- and LZTR1-related schwannomatosis (1 of the following):</p> <ul style="list-style-type: none"> • ≥ 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 <p>22q-related schwannomatosis (all of the following):</p> <ul style="list-style-type: none"> • 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 <p>Schwannomatosis not otherwise specified (both of the following, no genetic testing done):</p> <ul style="list-style-type: none"> • ≥ 2 imaging-confirmed nonintra-dermal schwannomas • ≥ 1 pathologically confirmed schwannoma or hybrid sheath tumor
<p>* These criteria can be counted twice (ie, 2 distinct schwannomas count as 2 minor criteria).</p>	
<p>Additional notes</p>	

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>
- Plotkin, S. R., Messiaen, L., Legius, E., Pancza, P., Avery, R. A., Blakeley, J. O., Babovic-Vuksanovic, D., Ferner, R., Fisher, M. J., Friedman, J. M., Giovannini, M., Gutmann, D. H., Hanemann, C. O., Kalamarides, M., Kehrer-Sawatzki, H., Korf, B. R., Mautner, V., MacCollin, M., Papi, L., . . . Evans, D. G. (2022). Updated diagnostic criteria and nomenclature for neurofibromatosis type 2 and schwannomatosis: An international consensus recommendation. *Genetics in Medicine*, 24(9), 1967–1977. <https://doi.org/10.1016/j.gim.2022.05.007>