GUIDELINE STATEMENT
This guideline outlines the management of patients with neurofibromatosis as required by the Children’s Rehabilitative Services Program, Arizona Health Care Cost Containment System, State of Arizona. Clinical guidelines are not used within UnitedHealthcare to decide benefit coverage. Benefit coverage decisions are based upon language in the consumer-specific benefit document.

PURPOSE
Clinical Practice Guidelines represent the minimum requirements for providing care for individuals with neurofibromatosis. Care and treatment should be provided in a manner that includes adherence to and consistency with the following Guideline.

DEFINITIONS:

Children’s Rehabilitative Services (CRS): An AHCCCS program for children with certain diagnoses which provides services using an integrated family-centered, culturally competent, multi-specialty, interdisciplinary approach.

Multi Specialty Interdisciplinary Clinic (MSIC): The Specialty Medical Home for the members with diagnoses as designated by the Arizona Administrative Code (AAC) R9-7-202 (R9-22-1303, 10-1-2013).
I. PROCEDURAL GUIDELINES for POLICY COMPLIANCE

A. CRS Enrollment:
Children diagnosed with neurofibromatosis must be enrolled in a NF Multispecialty Interdisciplinary Clinics (MSIC). The patient may be seen at other clinics as appropriate as determined by the Interdisciplinary Team. All treatment must be consistent with the goals set in the Neurofibromatosis Clinic and records from other clinics must be sent to the NF MSIC site.

B. Interdisciplinary Team Membership:
It may not be necessary for each team member to see the patient at each visit. One team member can fill more than one role if properly trained:

- Child Psychologist
- Child Psychiatrist
- CRS member / Caregiver
- Geneticist/Genetic Counselor
- Pediatrician/PNP
- Pediatric Neurologist
- Primary Care Physician (Invited)¹
- Registered Nurse Coordinator
- Social Worker
- Vocational Rehabilitation for teenagers²

C. Available Personnel:
The following personnel must be available to the member at the neurofibromatosis clinic:

- Advocate
- Audiologist
- Child Life Specialist
- Translator

D. Consultative Personnel:
The MSIC site must have access for consultation to specialists including, but not limited to the following:

- Cardiologist
- Neurosurgeon
- Nephrologist
- Occupational Therapist
- Oncologist
- Otolaryngologist
- Ophthalmologist
- Orthopedist
- Pediatric Surgeon
- Physical Therapist
- Plastic Surgeon
- Speech Therapist
The Primary Care Physician will be invited to all Team meetings; however, it is understood that PCP will not always be able to attend. Coordination of records must occur for best integrated care for the member.

Vocational Rehabilitation Services representatives are to be invited to the Clinic.

E. Outreach Clinics:
Outreach clinics are designed to provide a limited specific set of services including evaluation, monitoring and treatment in settings closer to the family than a MSIC site. Major treatment plan changes must be communicated to the MSIC.

Members with neurofibromatosis may attend neurology, genetics, or orthopedic outreach clinics as determined by the Interdisciplinary Team.

F. Facilities and Services:
1. Age-appropriate setting for all patients
2. Access to the pharmacy
3. Defined age-appropriate services (i.e., Pediatrics, Adolescent Medicine and/or Internal Medicine)
4. Identified clinic area for NF outpatient services
5. Pediatric and Adult Intensive Care Units
6. Social Work Department

G. Team/Staff Meetings:
Team and staff meetings will be held based on the age of the patient and their diagnosis. At a minimum the following will occur:
1. Interdisciplinary Team Meetings / review and planning meetings (patient specific meetings) are to be held at least once every two years for planning and review.
2. Staff meetings annually to focus on issues of MSIC patient Care and MSIC administration.
3. Education meetings annually to focus on new information regarding the care and treatment for persons with neurofibromatosis. These may be off site meetings.
4. Member and family must have ability to participate with the interdisciplinary team meeting to have their goals, strengths, cultural needs, barriers to care and concerns addressed, as well as be active, educated participants in choice of treatments

H. Lead Physician Specialists:
Qualifications: The lead physician for patients with neurofibromatosis should be a geneticist, pediatrician or a Pediatric Neurologist with knowledge and experience in the evaluation, care, and treatment of patients with neurofibromatosis.

II. GUIDELINES FOR PATIENT SERVICES, EVALUATION, AND MONITORING FOR NEUROFIBROMATOSIS

The purpose of these guidelines is to promote a uniform level of care at CRS MSIC for members and adults with neurofibromatosis, and to provide a general framework for good patient care. Their relevance to specific situations will depend on individual variations in clinical course and professional judgment. In addition, this document should serve as a tool to assess programs, secure resources needed to enhance patient care and education, and guide the future growth and develop treatment of neurofibromatosis.
A. Diagnosis:

Goal: To provide accurate and timely diagnosis of neurofibromatosis.

Diagnosis Criteria NF1: As developed by the NIH Consensus Development Conference and subsequent changes, specified that 2 or more of the following be present1 3

1. Six or more cafe-au-lait macules more than 5 mm in greatest diameter in prepubertal individuals and more than 15 mm in greatest diameter after puberty
2. Two or more neurofibromas of any type or 1 plexiform neurofibroma
3. Freckling in the axillary or inguinal regions (Crowe sign)
4. Optic pathway tumor
5. Two or more Lisch nodules (iris hamartomas)
6. Distinctive, osseous lesion, such as sphenoid wing dysplasia or thinning of the cortex of the long bones (with or without pseudoarthrosis)
7. First-degree relative (parent, sibling, or offspring) with NF1 that met criteria 1-6 above

The diagnosis of NF1 cannot be made on the presence of cafe-au-lait spots alone; however, the family should be told that NF1 is by far the most likely diagnosis, since familial cafe-au-lait spots are an exceedingly rare condition. Additional criteria are almost always met by the age of 10 years.

Confirmation of the diagnosis for NF1 must be established prior to entry into the CRS program. Follow up within CRS requires the following activities:

- Member History
  Focus on symptoms associated with NF1, such as cognitive or psychomotor deficits, pain, visual complaints, progressive neurologic deficits, changes in bowel and bladder function, weakness, seizures, headaches, and childhood development history. 1
- Family History
  Should include grandparents, great aunts and uncles and their descendants. When possible, an effort should be made to locate medical records of affected 1st and 2nd degree relatives. 1 Parents and siblings should be referred (this is not a covered CRS service) for examination for signs and symptoms of NF13
- Physical Examination
  Should give particular attention to possible manifestations of the disorder such as hypertension, scoliosis and other skeletal anomalies, Macrocephaly, focal neurological deficits (impaired vision, ptosis, optic atrophy), developmental disabilities, proptosis, Lisch nodules, short stature, signs of precocious puberty or hypogonadism, cafe-au-lait macules, and neurofibromatosis
- Tests
  Should be dictated by findings on clinical evaluation. Laboratory tests in asymptomatic patients are unlikely to be of value, particularly computerized tomography (CT), magnetic resonance imaging (MRI), electroencephalography (EEG), and evoked potentials. As an option, DNA testing may be provided at the Discretion of the NF Team.
- Counseling
  Must be provided for all patients and their families and should include: 1
  1. Family members
  2. Follow-up
  3. Genetics
  4. Prognosis
  5. Psychological and Social Adjustment
  6. Resources

  Modified counseling is indicated for preadolescents who are likely to have NF1. 3
- Written Report
  Should summarize clinical findings, test results, and information conveyed through counseling1

Diagnostic Criteria for NF2 per the Manchester Conference:
Individuals with the following clinical features have confirmed (definite) NF2:
1. Bilateral vestibular schwannomas (VS) or First degree relative with NF2 and either
2. Unilateral VS < 30yrs or two of the following:
   a. Meningioma
   b. Glioma
   c. Schwannoma
   d. Juvenile posterior subcapsular lenticular opacity

Individuals with the following clinical feature should be evaluated for NF2:
1. Unilateral vestibular schwannomas < 30 yrs and
2. At least one of the following:
   a. Meningioma
   b. Glioma
   c. Schwannoma
   d. Juvenile posterior subcapsular lenticular opacities/juvenile cortical cataract
   e. Multiple meningiomas (2 or more) and
   f. Unilateral vestibular schwannomas <30yrs or
   g. One of the following:
      i. Glioma
      ii. Schwannoma
      iii. Juvenile posterior subcapsular lenticular opacities/Juvenile cortical cataract

Diagnostic Activities for NF2 (unless otherwise indicated): Evaluation for NF2 should never represent a single point in time but should include long term follow up. Screening can be relaxed if there are no further tumors developing during a 5 to 10 year period or if NF2 molecular testing becomes more reliable for exclusion. MR should be performed to rule out bilateral vestibular schwannomas definitely. Persons with retinal hamartomas or cortical wedge opacities should be evaluated by a trained neuro-ophthalmologist

- Member History
  Focus on symptoms possibly associated with hearing loss, tinnitus, dizziness, loss of balance, pain, headache and seizures
- Family History
  Include grandparents, great aunts and uncles and their descendants
  Should locate medical records for affected 1st and 2nd degree relatives
- Physical Examination
  Should give particular attention to possible manifestations such as cafe-au-lait macules and neurofibromas
  Neurological assessment should emphasize cranial nerves, balance and coordination
- Tests
  1. Must include audiogram and brain stem auditory evoked responses (BAER)
  2. High resolution MRI with gadolinium should be used in patients with evidence of hearing impairments or abnormal BAER
  3. Tests of vestibular function may be useful adjuncts to BAER
  4. If no MRI has been performed by puberty, it should be obtained
  5. Other tests as indicated
- Counseling
  Must be provided for all patients and their families and should include:
  1. Family members
  2. Follow-up
  3. Genetics
  4. Prognosis
  5. Psychological and Social Adjustment
  6. Resources

Written Report
Should summarize clinical findings, test results and information conveyed through counseling—

Goal: to provide accurate assessment of physical, emotional, and behavioral issues and
educational/vocational needs, and to begin patient and family education.

B. Education of Parents and Diagnosed Patients:

NF 1:
Families and patients may require support in the following areas (but not limited to these areas). Services should be provided if they are included in the CRS policy regarding covered services.

1. Adjustment to the diagnosis
2. Attention problems or ADHD (CRS will refer patients requiring Medication Management to Behavioral Health Systems)
3. Coping with medical sequelae and medical procedures
4. Educational difficulties including learning disabilities and fine motor deficits
5. Increased risk for psychological disorders/adjustment problems such as depression, low self-esteem, etc.
6. Linkage to community services such as DOD, Behavioral Health, AzEIP, ALTCS, SSI, housing, food, and transportation.

C. Ongoing Patient Evaluation and Monitoring

Goal: To anticipate and treat physical and psychosocial problems and complications of the disease.

NF1 Follow-up Examination Guidelines:
Should be performed annually for NF1 patients and counseling should parallel assessment described above.

1. Infancy
   Presence of tibial bowing should prompt referral to orthopedic surgeon familiar with management of NF1-related orthopedic problems
   Prevention of fracture is of paramount importance in individuals with tibial bowing.

2. Childhood
   a. Annual vision evaluation by an experienced ophthalmologist during first decade of life.
   b. Cranial MR imaging should be used when there is any evidence of optic nerve dysfunction. There should be special attention to the orbits and appropriate management determined by a multidisciplinary clinical team.
   c. The role of surgery in the management of optic pathway tumors is limited and treatment usually involves chemotherapy and, less commonly, radiation therapy.
   d. All members should be evaluated for psychosocial issues with an emphasis on those members suspected of having learning disabilities. Some members manifest attention deficit disorder and may benefit from treatment with stimulant medication. Medication Management of ADHD will be referred to the Behavioral Health System.
   e. Monitor for blood pressure evaluations associated with renal artery stenosis or, rarely, pheochromocytomas.
   f. Decisions about surgical treatment and frequency of follow up on plexiform neurofibromas must be made judiciously and individualized for each patient. The Interdisciplinary Team should be consulted.
   g. Members with headache or abdominal pain should have a careful physical and neurologic examination to exclude other underlying causes.

3. Lifelong (CRS Members to age 21)
   a. Specific lesions which are symptomatic/function-limiting may be removed as they occur by experienced surgeons. The long term benefit of removal of large numbers of neurofibromatosas by surgical excision or carbon dioxide laser is untested.
   b. Persons with persistent hypertension or classical signs of pheochromocytoma should be evaluated further.
   c. Rapid growth of a plexiform neurofibromas or the development of de novo pain should
prompt an immediate evaluation for bleeding or malignant transformation

4. NF2 Follow-up Examination Guidelines:
   a. The criterion Guideline for the identification of vestibular schwannomas is MR imaging of
      the head with 3-mm cuts through the internal auditory canals with and without gadolinium
      enhancement.
   b. All patients with a new diagnosis of NF2 should undergo full spinal MR imaging with or
      without gadolinium enhancements to aid in prognostication.
   c. Patients with intramedullary tumors should receive an annual follow up MR image
   d. If tumors are found, follow up MR imaging should be performed every 6 to 12 months.
   e. Part of the evaluation of a person suspected to having NF2 should include review of
      pathology reports and review of original tumor sections when possible.
   f. In families with early onset NF2, the screening protocol should begin in early childhood.
   g. Individuals with NF2 should have an annual neurologic evaluation with cranial MRI as
      well as audiometry and brainstem auditory evoked responses for those with functional
      hearing.
   h. Follow up ophthalmologic evaluations and spinal imaging is recommended for persons
      with problems in these areas.
   i. Surgical treatment should be limited to specialty tertiary care centers with experienced
      otolaryngologists and neurosurgeons
   j. The Interdisciplinary Team should work together to coordinate care and follow up
   k. Surgical planning should be done by Neurosurgeon and/or Otolaryngologist. Referral by NF
      team can be based on MRI changes or clinical symptoms.
   l. Radiation therapy should be considered carefully
   m. Treatment of vestibular tumors should include counseling of the problems with balance.
      Drowning and near drowning caused by underwater disorientation is especially important
   n. Hearing and speech augmentation is an important part of management of NF2. Lip reading
      and hearing aids may be useful
   o. Review social adjustment development and appropriateness of school/vocational placement.

D. Treatment:

   Goal: To anticipate and treat progression and complications of the disease.

Management Options for NF1 patients:

1. Management Options for Optic Glioma:
   a. Annual ophthalmologic examination using MR and CT imaging to document size, shape,
      and extension
   b. Appropriate consultation will be made if special circumstances such as disfiguring
      orbital mass or large tumors compressing adjacent structures.

2. Management Options for Other Neural Tumors:
   a. Manage these tumors in same manner as in general population

3. Management Options for Orthopedic Problems:
   a. Kyphoscoliosis and tibial bowing benefit from early intervention and should be managed
      by an orthopedist familiar with complications

4. Management Options for Vascular Problems:
   a. Thorough evaluation of hypertension
   b. Other vascular disorders must be handled on an individual basis in the same manner as
      they would be in the general population

E. Psychosocial Issues:

   Goal: to anticipate and treat social and emotional problems of patients and their families.

Patients and families should have available interdisciplinary multi-specialty care as well as follow up
services including community support research and referral services, education advocacy and placement
assistance, psychological and neuropsychological evaluations, and developmentally-appropriate support
and education to the member. This would include the services of a social worker, psychologist, child life specialist and special educator.

1. Patient advocacy through education of personnel in schools, insurers, health care services, regional and national health organizations and welfare services.
2. In-service education of health professionals and health sciences students, social sciences students and others.
3. Assist in linking adults to Vocational Rehabilitation and Vocational education and training.

References:


2. Committee on Genetics, "Health Supervision for Children with Neurofibromatosis", Pediatrics; Vol. 121, No. 3; March 2008.

3. Gutmann David H., Arthur Alysworth, Carey, John C., Kerf, Bruce, Marks, Joan, Reed E., Rubenstein, Allan, Viskochi, David l; "The Diagnostic Evaluation and Multidisciplinary Management of Neurofibromatosis 1 and Neurofibromatosis 2; JAMA; July 2, 1997.