Date

Regarding:

Date of birth:

Insurance number:

To Whom It May Concern,

XXX was seen in the XXX Genetics Clinic on XXX at the referral of his pediatrician, XXXX, MD. On physical exam, XXX has a large tongue, umbilical hernia, hemihypertrophy, small glabellar hemangioma, and history of being large for gestational age at birth. The pregnancy was complicated by polyhydramnios. These findings are consistent with Beckwith-Wiedemann syndrome (BWS), an overgrowth syndrome that carries a 15% incidence of cancer.

The underlying genetic etiologies of BWS are complex, but important to identify, especially for recurrence risks and medical management. Cytogenetically detectable abnormalities involving 11p15 are found in only 1% of cases. Clinically available molecular genetic testing can identify several different types of 11p15 abnormalities in individuals with BWS: (1) loss of methylation at DMR2 is observed in 50% of individuals; (2) gain of methylation at DMR1 is observed in 2% to 7%; (3) paternal uniparental disomy for chromosome 11p15 is observed in 10-20%. Testing reveals mutations in the *CDKN1C* gene (previously called *p57 KIP2* ) in 40% of familial cases and 5-10% of non-familial cases.

**We are requesting preauthorization for diagnostic studies that are medically indicated**. These are high-resolution chromosome studies with FISH for 11p, methylation studies and testing for uniparental disomy.

1. **High-resolution banding chromosome study**: Chromosome analysis reveals a cytogenetically detectable translocation or inversion of a maternal chromosome 11 or a cytogenetically detectable duplication of a paternal chromosome 11 involving band 11p15 in 1% of individuals with BWS. The analysis also rules out other chromosomal rearrangements, deletions or duplications and is standard of care, required by the laboratory to perform FISH testing.

* CPT codes are 88230, 88262, 88280 and 88289

1. **FISH (fluorescence in situ hybridization) for 11p** detects small deletions of this region of 11p.
   * The CPT codes are 88273, 88271, and 88291
2. **Methylation for BWS** –Up to 60% of individuals fulfilling diagnostic criteria for BWS have detectable *KCNQ1OT1* methylation abnormalities. Between 2% and 7% of individuals fulfilling diagnostic criteria for BWS have gain of methylation at *H19*.
   * CPT codes are 83890, 83892, 83894, 83898, 83912
3. **Uniparental disomy studies:** Approximately 10-20% of individuals fulfilling diagnostic criteria for BWS have paternal UPD for the BWS critical region. Paternal UPD for 11p15 is

associated with isolated hemihyperplasia and Wilms tumor.

* CPT codes are 83891, 83894, 83898, 83912

Making a diagnosis of Beckwith-Wiedemann syndrome is important for medical management because of its potential complications. Children with BWS have an increased risk of mortality associated with neoplasia, particularly Wilms tumor and hepatoblastoma, but also neuroblastoma, adrenocortical carcinoma, and rhabdomyosarcoma. Also seen are a wide variety of other tumors, both malignant and benign. The estimated risk for tumor development in children with BWS is 7.5%. Those children who have asymmetrical overgrowth (hemihyperplasia) such as XXX seem to have a higher risk of developing tumors than those who are symmetrical. **Tumor surveillance with frequent abdominal ultrasounds (every 3 months) and serum Alpha Fetal Protein levels is indicated**. Testing is particularly important for this family as a sister has an inoperable brainstem glioma.

We hope this information is helpful. Please do not hesitate to contact us with further questions or concerns. The family is anxious to pursue this diagnostic testing.

Sincerely,