



# **National Protocol for Diagnosis and Care (PNDS)**

## **Inverted Duplication/Deletion of the Short Arm of 8p Chromosome**

Texte du PNDS  
Juillet 2022

Centre de Référence « Déficiences Intellectuelles de Causes Rares »

Coordonnateur : Dr Solveig HEIDE

Filière DéfiScience

Centre de Référence des Déficiences Intellectuelles de causes

This National Diagnosis and Treatment Protocol (NDTP) aims to enable all professionals involved in the care and follow-up of patients with an interstitial inverted duplication of the 8p chromosome associated with a distal deletion of the short arm of chromosome 8 [invdupdel(8p)] to better understand the specific needs related to this condition.

### **Definition**

1. Interstitial inverted duplication 8p associated with distal deletion of the short arm of chromosome 8 [invdupdel(8p)] is a rare chromosomal disorder. It involves a complex chromosomal rearrangement, combining a gain of an inverted fragment of the short arm of chromosome 8 and a loss of the distal end of the same chromosome's short arm.
2. This chromosomal anomaly is responsible for variable developmental abnormalities (malformative or polymalformative syndrome) associated with neurodevelopmental disorders. This syndrome is characterized by:
  - a. Predominant developmental delay in language with variable severity of intellectual disability (ID), and in some cases, multiple disabilities (polyhandicap).
  - b. Frequent occurrence of epilepsy.
  - c. Common occurrence of cardiac malformations.
  - d. Brain developmental abnormalities, often with agenesis or hypoplasia of the corpus callosum (ACC).
  - e. Orthopedic anomalies.
  - f. Feeding difficulties in the early months of life.
3. The diagnosis of invdupdel(8p) is made through cytogenetic examinations, including array comparative genomic hybridization (aCGH), karyotyping, and fluorescence in situ hybridization (FISH) analysis. This anomaly most commonly occurs sporadically (de novo), and genetic counseling for the family is reassuring, indicating that the risk of recurrence is low.

### **Multidisciplinary Care:**

1. To date, no curative treatment can be proposed for invdupdel(8p). The medical and educational management of individuals with invdupdel(8p) should be carried out within a multidisciplinary framework, spanning all stages of life (childhood, adolescence, and adulthood). It involves Reference Centers and Competence Centers for Rare Diseases that specialize in intellectual disability and/or developmental anomalies, in collaboration with pediatricians, general practitioners, and specialist physicians, depending on the patient's specific needs. The management should be comprehensive and coordinated across different healthcare professionals.
  
2. The management involves various healthcare professionals and facilities, including:
  - Pediatricians or general practitioners, in collaboration with specialist physicians (neuropediatrician, neurologist, orthopedist, cardiologist, gastroenterologist, urologist/nephrologist, ENT specialist, ophthalmologist, psychiatrist, specialist in physical medicine and rehabilitation) based on the patient's needs.
  - Paramedical professionals who provide rehabilitative care (physiotherapist, psychomotor therapist, speech therapist, occupational therapist, orthoptist, special education teacher, psychologist, etc.).
  - Care provided in multidisciplinary pediatric, adolescent, and adult healthcare facilities such as Early Medico-Social Action Centers (CAMSP), Specialized Education and Home Care Services (SESSAD), Medico-Psycho-Pedagogical Centers (CMPP), Motor Education Institutes (IEM), Medico-Educational Institutes (IME), Medico-Professional Institutes (IMPro), social support services (SAVS), medico-social support services for disabled adults (SAMSAH), Specialized Accommodation Homes (MAS), and Medically Assisted Residences (FAM). These facilities facilitate interaction among professionals.

This multidisciplinary approach ensures comprehensive care for individuals with invdupdel(8p) throughout their lifespan.

### 3. General Practitioner Role

The general practitioner plays a crucial role in:

- Initial patient referral: The symptomatology of invdupdel(8p) syndrome is often nonspecific, and the diagnosis is rarely suspected before cytogenetic analysis. The general practitioner refers patients presenting with developmental delay, intellectual disability, and/or (poly)malformative syndrome (such as cardiac abnormalities, orthopedic anomalies, etc.) to a Reference Center or Competence Center for Rare Diseases in the field of intellectual disability or AnDDI-Rares, to guide diagnostic genetic investigations. The general practitioner's primary role is to raise awareness and guide the family to specialized consultations. Once the diagnosis is established, the general practitioner ensures the child is referred for regular multidisciplinary follow-up, regardless of the patient's age, in collaboration with specialized services.
- Implementation of medical-administrative measures: It is necessary to request 100% coverage and exemption from copayments for healthcare expenses from the relevant Primary Health Insurance Fund (Caisse de Primaire d'Assurance Maladie) to which the individual is affiliated.

It is also important for the general practitioner to complete the necessary medical certificates for the establishment and renewal of the file at the Departmental House of Disabled Persons (MDPH) for applications for Parental Presence Daily Allowance (AJPP), Disabled Child Education Allowance (AEEH), Disabled Adult Allowance (AAH), or Disability Compensation Benefit (PCH), depending on the specific context.

- Implementation of initial rehabilitation and therapy: Early implementation of rehabilitation services (physiotherapy, psychomotor therapy, speech therapy, occupational therapy, etc.) is crucial. Referring the patient to a nearby care facility (CAMSP, CMP, CMPP, etc.) will be beneficial.
- Joint coordination with the Reference Center or Competence Center for Rare Diseases and in screening: The general practitioner should ensure that the patient's follow-up is carried out by a multidisciplinary team appropriate for the patient's age, in accordance with the national guidelines. They will monitor potential complications (such as epilepsy, spasticity, orthopedic abnormalities, constipation, feeding difficulties, etc.) in coordination with the referring teams.
- Routine medical follow-up of the patient: The doctor manages any intercurrent events and ensures compliance with public health prevention recommendations (vaccinations, screenings, etc.). They will pay attention to the prevention of dental abnormalities, which are essential for nutrition quality, and screen for sleep disorders, pain, and sensory impairments (auditory and visual).

In cases of acute behavior changes, the doctor should initially search for somatic causes that may be accompanied by pain (such as gastroesophageal reflux [GERD], dental pain, acute otitis media [AOM], fecal impaction, etc.). In the absence of language, pain assessment tools such as Pédiadol or San Salvadour pain scales can be useful (see Annex 4).

The frequency of follow-up visits should be adjusted based on the patient's specific conditions. It may vary among different specialties and will be determined by the specialist physician's judgment (see section 4.12 for the frequency and content of consultations).

Comprehensive patient care, aimed at coordinating healthcare services, should include consultations with a reference center or competence center at a biannual frequency during the first 2 to 3 years of life, followed by annual visits during childhood,

adolescence, and adulthood. The purpose of this follow-up is to evaluate and adjust care according to the patient's needs.

Here is a list of useful information and contacts for obtaining additional information:

- Orphanet website: <http://www.orpha.net>
- DéfiScience healthcare network website: <https://defiscience.fr/filiere/>
- AnDDI-Rares healthcare network website: <http://anddi-rares.org/>
- UNAPEI (French Federation of Associations for the Representation and Defense of the Interests of Persons with Intellectual Disabilities and their Families) website: <http://www.unapei.org/>
- Fondation Maladies Rares (Rare Diseases Foundation): 96, rue Didot 75014 Paris, Tel: 01.58.14.22.81, website: <http://www.fondation-maladiesrares.org>
- Alliance Maladies Rares (Rare Diseases Alliance): 96, rue Didot 75014 Paris, Tel: 01.56.53.53.40, website: <https://www.alliance-maladies-rares.org>
- Valentin APAC Association website: <https://www.valentin-apac.org/>
- Rare Chromosome Disorder Support Group: [www.rarechromo.org](http://www.rarechromo.org)
- Association La Maison 8p: <http://www.lamaison8p.com>
- Association for Enteral Nutrition: [www.lavieparunfil.com](http://www.lavieparunfil.com)
- International Society for Augmentative and Alternative Communication (ISAAC): [www.isaac-fr.org](http://www.isaac-fr.org)
- Pediatric Pain: [www.pediadol.org](http://www.pediadol.org)
- Orphanet's Guidebooks - Living with a Rare Disease in France - Aid and benefits for individuals with rare diseases and their families - December 2021 - Annual update: [www.orpha.net/orphacom/cahiers/docs/FR/Vivre\\_avec\\_une\\_maladie\\_rare\\_en\\_France.pdf](http://www.orpha.net/orphacom/cahiers/docs/FR/Vivre_avec_une_maladie_rare_en_France.pdf)
- The 19 Rare Disease Expertise Platforms (PEMR) and the 4 platforms in overseas territories:

[www.remarares.re/wp-content/uploads/2022/01/Annuaire-PEMR-PCOM-.pdf](http://www.remarares.re/wp-content/uploads/2022/01/Annuaire-PEMR-PCOM-.pdf)

- The 2 assistance networks:
  - PRIOR in the Pays de la Loire region: [prior-maladiesrares.fr](http://prior-maladiesrares.fr)
  - Maladies Rares en Occitanie in Occitanie region:  
[www.maladies-rares-occitanie.fr](http://www.maladies-rares-occitanie.fr)
- Competence and Outsourced Services Centers (PCPE):  
[https://handicap.gouv.fr/IMG/pdf/livret\\_pcpe-2.pdf](https://handicap.gouv.fr/IMG/pdf/livret_pcpe-2.pdf)

## Text of the PNDS

### 1.Introduction

Interstitial inverted duplication of chromosome 8p associated with distal deletion of the short arm of chromosome 8 [invdupdel(8p)] is a rare chromosomal disorder, estimated to occur in 1 out of 10,000 to 30,000 births. This complex chromosomal abnormality involves a gain of a fragment of the short arm of chromosome 8 and a loss of the distal end of the same chromosome. It is responsible for variable developmental abnormalities, combining a malformative or polymalformative syndrome with neurodevelopmental disorders or even a complex disability.

The invdupdel(8p) syndrome is clinically characterized by:

- Global developmental delay, consistently affecting language development, and variable degrees of intellectual disability (ranging from mild to severe), and may be associated with autism spectrum disorders and behavioral disorders;
- Epilepsy, reported in 30% to 50% of patients;
- Frequent brain malformations, including abnormalities of the corpus callosum development (agenesis or hypoplasia), sometimes associated with other brain malformations (particularly abnormalities of the posterior fossa);
- Congenital heart defects in 40% to 65% of patients [such as ventricular septal defect (VSD), atrial septal defect (ASD), patent ductus arteriosus (PDA), patent foramen ovale (PFO), tetralogy of Fallot, etc.];

- Frequent orthopedic abnormalities (joint contractures, scoliosis, hyperlaxity, etc.);-
- Feeding difficulties in the early months of life, which can be inconsistent and sometimes persistent;
- Renal and other organ malformations.

## **2.Objectives of the National Protocol for Diagnosis and Care**

- The objective of this National Protocol for Diagnosis and Care (PNDS) is to provide relevant healthcare professionals with current optimal diagnostic and therapeutic management guidelines and the care pathway for patients with invdupdel(8p) syndrome. Its aim is to optimize and harmonize the management and follow-up of this rare disease across the entire territory.

This PNDS can serve as a reference for the attending physician (the physician designated by the patient or their legal representatives with the Health Insurance Fund), in consultation with specialist physicians, particularly when establishing the care protocol, in conjunction with the medical advisor and the patient or their legal representatives, in the case of a request for exemption from co-payment for a non-listed condition, and for the drafting of the medical certificate to be included in the MDPH file. However, the PNDS cannot cover all specific cases, comorbidities or complications, therapeutic particularities, hospital care protocols, etc. It cannot claim to be exhaustive in terms of all possible management approaches and cannot replace the individual responsibility of the physician towards their patient. The protocol describes the reference management for a patient with invdupdel(8p). It should be updated based on validated new data.

This PNDS was developed using the "Method for developing a national protocol for the diagnosis and care of rare diseases" published by the French National Authority for Health (Haute Autorité de Santé) in 2012 (methodological guide available on the HAS website: [www.has-sante.fr](http://www.has-sante.fr)).



A more detailed document that served as the basis for the development of the PNDS and includes the analysis of identified bibliographic data (scientific rationale) is available on the websites of the DefiScience healthcare network and the French National Authority for Health.

### **3. Diagnostic and Initial Evaluation**

#### **3.1. Objectives**

The diagnosis of invdupdel(8p) syndrome is rarely considered clinically, as the symptoms are nonspecific. Therefore, the diagnosis is made through cytogenetic analysis (karyotype and chromosomal microarray analysis). Once the diagnosis of invdupdel(8p) is established, the patient should undergo additional investigations (see

#### **3.14 Initial Evaluation).**

This initial evaluation aims to:

- Identify comorbidities that may exacerbate the disability.
- Provide necessary information to the family about the need for regular multidisciplinary follow-up and organize such follow-up.
- Initiate early rehabilitation interventions such as physiotherapy, psychomotor therapy, speech therapy (including augmentative and alternative communication), and occupational therapy.
- Provide family support if needed.
- Inform the family about benefits and assistance provided by the MDPH (Maison Départementale des Personnes Handicapées, Departmental House for Disabled Persons).
- Request exemption from co-payment and inform about the possibility of coverage for travel expenses to a Reference Center for Rare Intellectual Disabilities (Centre de Référence des Déficiences Intellectuelles de causes rares - CRMR) for medical follow-up related to the syndrome.

### 3.2. Professionals involved in diagnosis and follow-up

The diagnostic evaluation is usually coordinated by a specialist in developmental disorders (clinical geneticist and/or pediatric neurologist) from a Reference Center of the DefiScience or AnDDI-Rares network, in collaboration with the pediatrician or primary care physician. In all cases, the input of a geneticist, particularly for genetic counseling, is advisable. Depending on the context and associated comorbidities, other specialists may be involved, including:

- Pediatric neurologist/neurologist, depending on the patient's age
- Pediatric cardiologist or cardiologist
- Orthopedic specialist
- Specialist in Physical Medicine and Rehabilitation (PMR)
- Gastroenterologist or pediatric gastroenterologist, depending on the age
- Dentist/Orthodontist
- Child psychiatrist or psychiatrist
- Otolaryngologist (ENT)
- Ophthalmologist
- Nephrologist and/or urologist

The majority of affected patients present with global developmental delay and intellectual disability. Various allied healthcare professionals should be involved in early intervention and rehabilitation to optimize the patient's learning and development, including:

- Physiotherapist
- Psychomotor therapist
- Speech and language therapist
- Psychologist and neuropsychologist
- Special education teacher
- Occupational therapist
- Social worker

- Dietitian

### 3.3. Clinical presentation

The diagnosis of invdupdel(8p) syndrome is made in different circumstances depending on the age of the patients. The diagnosis can be made prenatally when there are abnormalities in the development of the corpus callosum or other organ malformations identified during obstetric ultrasound. Prenatal ultrasound follow-up may also show no detectable anomalies.

After birth, the diagnosis can be made following the discovery of a congenital heart defect or feeding difficulties requiring nutritional support in an infant with psychomotor developmental delay and/or axial hypotonia.

In older children, intellectual disability, manifested as learning difficulties and/or adaptation problems at school, can lead to the diagnosis. Invdupdel(8p) is the most frequently identified chromosomal rearrangement in patients with corpus callosum abnormalities and intellectual disability (3%).

This syndrome is rarely clinically suspected since the clinical signs are nonspecific. Thus, the diagnosis is made following genetic testing: karyotype and chromosomal microarray analysis.

#### 3.3.1. Developmental Delay/Intellectual Disability (DI)

Developmental delay and intellectual disability are nearly constant features of invdupdel(8p) syndrome. The severity of intellectual disability correlates with the size of the duplication and can range from mild to severe. Cognitive impairment typically manifests as delayed psychomotor and language skills in the early years.

Oral language is particularly affected, and 40% of reported patients are non-verbal. First words are typically acquired between the ages of 2 and 6 in patients who develop oral language. However, oral language often remains limited to a few words or short phrases.

Over 70% of patients achieve walking ability, on average around 2 to 3 years of age. Motor skills may be hindered by motor coordination difficulties, with often fluctuating muscle tone (hypotonia, spasticity).

Behaviorally, individuals with invdupdel(8p) syndrome are often sociable, interactive, and enjoy sensory activities. Communication difficulties hinder learning, independence, and can lead to behavioral issues such as frustration intolerance and self or hetero-aggression.

Co-occurring autism spectrum disorders and/or attention disorders are also reported.

### 3.3.2. Neurological Disorders

#### Tone Disorders

- Moderate hypotonia in infancy is a common neurological manifestation in invdupdel(8p) syndrome. Spasticity, primarily affecting the lower limbs and occasionally accompanied by dystonia, may gradually appear in older children, potentially leading to tendon retractions and joint contractures that impede mobility.

#### Epilepsy

- Seizures are reported in approximately 30 to 50% of patients. The average age of onset for the first seizure is 4 years, with significant interindividual variability ranging from 2 months to 9 years among the patients described in the literature. Various types of seizures have been reported, with the most frequent being absence seizures, generalized tonic-clonic seizures, myoclonic seizures, focal motor seizures, and infantile spasms.

#### Sleep Disorders

- Some children experience sleep disorders such as difficulty falling asleep, nocturnal awakenings, and/or sleep apnea.

## Brain Malformations

- Brain malformations are observed in the majority of patients (between 75 and 85% according to various studies) who have undergone imaging. The most common malformation of the central nervous system is the abnormal development of the corpus callosum (complete or partial agenesis, short or dysgenetic corpus callosum). Other abnormalities that have been noted include widening of the subarachnoid spaces or cerebral ventricles, abnormalities in white matter, cerebellar or brainstem hypoplasia, cortical and subcortical atrophy, vertebral and basilar artery dysplasia, Dandy-Walker anomaly, arachnoid cysts, Blake's pouch dilatation, mega cisterna magna, and gyration anomalies.

### 3.3.3. Cardiac Malformations

Cardiac malformations are present in approximately 40 to 65% of patients with invdupdel(8p) syndrome. The most common malformations are ventricular septal defects (30%) or atrial septal defects (15%). Other malformations reported include tetralogy of Fallot, bicuspid aortic valve, and persistence of the ductus arteriosus or foramen ovale.

### 3.3.4. Osteoarticular Manifestations

Osteoarticular abnormalities are present in nearly 30% of patients and may be absent or mild at birth but can worsen during growth. The most common manifestations include ligamentous hyperlaxity, abnormal spinal alignment (scoliosis, kyphosis, or hyperlordosis), narrow chest or chest deformity. Other anomalies include delayed bone maturation, polydactyly, flat feet, and femoral anteversion.

### 3.3.5. Feeding Difficulties and Digestive Disorders

Feeding difficulties, including sucking and swallowing problems, are common in the first months or weeks of life and can be found in 30% of infants. The severity of the impairment varies and needs to be assessed based on the child's overall health and nutritional status. These difficulties may require temporary nutritional assistance through

a nasogastric tube and sometimes persist beyond the first year. In severe cases, the consideration of a gastrostomy tube placement may be discussed to promote oral feeding and reduce prolonged nasogastric tube use.

Gastroesophageal reflux can cause digestive discomfort and hinder the development of oral feeding skills. In some cases, gastroesophageal reflux can lead to esophagitis.

Constipation is common and may be exacerbated by relative lack of physical activity and low intake of food and fluids.

#### 3.3.6. Genitourinary Manifestations

Although not a frequent feature, some patients may have minor abnormalities in the genitourinary system, such as hydronephrosis, renal hypoplasia, and horseshoe kidney.

Hypospadias and/or cryptorchidism (undescended testicles) may also be present.

#### 3.3.7. Growth

Intrauterine growth retardation (IUGR) is one of the most frequently associated signs during the prenatal period in individuals with invdupdel(8p) syndrome.

After birth, oral feeding difficulties in the early months of life can impact weight gain and growth. Patients generally tend to exhibit growth retardation, with lower weight and height compared to the average for their age. However, there is limited data available for adolescents and adults.

#### 3.3.8. Sensory Disorders

Patients may experience refractive errors such as myopia (most common), hyperopia, and astigmatism.

Rare ocular malformations have been reported, including iris coloboma, microphthalmia, abnormalities in retinal and optic nerve development.

Serous otitis media (SOM) and acute otitis media (AOM) are common. Some patients may have sequelae of hearing loss.

### 3.3.9. Dental Anomalies

Many children with invdupdel(8p) syndrome exhibit bruxism, which can lead to premature enamel wear.

Some children may have hypoplastic enamel, increased susceptibility to cavities, delayed eruption and early loss of primary teeth.

Anomalies such as supernumerary teeth, large teeth, and hypertrophic gums have been reported anecdotally.

### 3.3.10. Morphological Features

Patients with invdupdel(8p) syndrome may have morphological features that are generally nonspecific. Some facial characteristics may be subtle at birth or develop during the first year of life. In adults, these traits are often less pronounced. The main morphological features may include:

- Prominent forehead with possible bumps, plagiocephaly, round or square face, and microretrognathia.
- Hypertelorism, enophthalmos, and occasionally the presence of an epicanthic fold.
- Large mouth (macrostomia) and thin upper lip.
- Macrotia (larger-than-average ears).
- Anteverted nostrils.
- Dry and curly hair with receding hairline.

### 3.3.11. Diagnostic confirmation

The diagnosis of invdupdel(8p) is confirmed through cytogenetic examinations, including array comparative genomic hybridization (aCGH), along with karyotyping and

fluorescence in situ hybridization (FISH) analysis. These tests reveal a terminal deletion of 8p, combined with an interstitial inverted duplication of 8p.

Invdupdel(8p) is typically homogeneous, meaning it is present in all cells, in the majority of cases, and rarely occurs in mosaic form, where some cells have the abnormal chromosomal formula while others have a normal chromosomal formula.

### 3.3.12. Differential diagnosis

In general, patients with invdupdel(8p) exhibit similarities with individuals who have other chromosome 8 abnormalities:

- Duplication of the short arm of chromosome 8, which generally manifests as neonatal hypotonia, developmental delay, learning difficulties, agenesis of the corpus callosum, and cardiac malformations.
- Mosaic trisomy 8: Patients present with variable intellectual disability, ranging from mild to severe, agenesis of the corpus callosum or other brain developmental abnormalities, as well as morphological features including hypertelorism and dental anomalies. Deep, padded palmar and plantar creases and skeletal malformations are also described.

Several other genetic syndromes that involve intellectual disability, morphological characteristics, with or without corpus callosum abnormalities, may be considered in patients with invdupdel(8p). These include:

- Mowat-Wilson syndrome, caused by an abnormality in the ZEB2 gene, characterized by intellectual disability, brain malformations with corpus callosum anomalies, cardiac, genitourinary, and ophthalmological malformations, but with a different dysmorphic appearance.
- Pitt-Hopkins syndrome, caused by mutations in the TCF4 gene, which combines developmental delay with intellectual disability, epilepsy, and sometimes corpus callosum anomalies.



- Vici syndrome, associated with a mutation in the EPG5 gene, characterized by intellectual disability, corpus callosum anomalies, hypotonia, and cataracts.

### 3.3.13. Search for treatment contraindications

Currently, there is no specific treatment available for invdupdel(8p). Management is symptomatic and tailored to the needs of each patient. Prior to prescribing any new treatment (particularly psychotropic and antiepileptic medications), contraindications should be carefully evaluated.

### 3.3.14. Initial assessment / Comorbidity search / Prognostic evaluation

Upon diagnosis of invdupdel(8p), the initial assessment should aim to identify common manifestations and associated complications of this syndrome. The specific components of the assessment will depend on the patient's age at the time of diagnosis, previous examinations conducted, and will help guide their medical management and follow-up.

<b>Organ or Organ System</b>	<b>Purpose of Evaluation</b>	<b>Détails de l'évaluation</b>
<b>Neurologique</b>	Evaluation of psychomotor development	Evaluation of motor skills, adaptive skills, cognitive skills, and language skills.  Evaluation in psychomotricity, speech therapy, and occupational therapy.  Neuropsychological evaluation for guidance in treatment and academic adaptation
	Search for seizure activity or convulsive episodes.	Interrogation of the patient for gathering relevant information.  Systematic cerebral MRI (Magnetic Resonance Imaging). EEG (Electroencephalogram) if there is suspicion of epilepsy.  Consultation with a neurologist or a pediatric neurologist.
	Search for spasticity.	Clinical examination.  Consultation with a Physical Medicine and Rehabilitation specialist if necessary.
	Search for sleep	Consultation at a specialized sleep center and

	disorders.	polysomnography if necessary.
<b>Cardiovascular</b>	Search for a cardiac malformation.	Auscultation during the clinical examination. Consultation with a cardiologist and systematic cardiac ultrasound.
<b>Musculoskeletal</b>	Search for joint abnormalities or scoliosis.	Clinical examination, spinal X-ray if necessary, orthopedic consultation if necessary.
<b>Digestive</b>	Evaluation of oral motor function or oral motor evaluation	Interrogation, growth chart assessment (height and weight) Evaluation by a specialized speech therapist, psychologist, or psychomotor therapist if necessary Evaluation of energy intake with a dietitian Consultation with a gastroenterologist or pediatric gastroenterologist if necessary
	Search for gastroesophageal reflux	Interview, 24-hour pH monitoring in case of suspected non-erupted reflux, consultation with a gastroenterologist or pediatric gastroenterologist if necessary.
	Search for constipation	Interview, consultation with a gastroenterologist or pediatric gastroenterologist if necessary.
	Growth and weight development.	Measurement of height, weight, head circumference. Growth charts. Evaluation of energy and nutritional intake with a dietitian.
<b>Uro-génital</b>	Search for hypospadias and/or cryptorchidism. Search for renal anomalies.	Clinical examination. Systematic abdominal and renal ultrasound.
<b>Ophtalmological examination.</b>	Recherche d'un strabisme, d'un trouble visuel, voire d'une malformation oculaire	Search for strabismus, visual impairment, or even ocular malformation.
<b>ORL</b>	Search for hearing impairment.	ENT (Ear, Nose, and Throat) consultation with systematic audiogram.
<b>Oral cavity</b>	Search for dental anomalies, malocclusion, and caries	Clinical examination Dental consultation Orthodontic consultation if necessary

### 3.3.15. Diagnosis disclosure and patient information

The diagnosis should be disclosed during a dedicated consultation, in a suitable environment, allowing sufficient time, and preferably with both parents or legal guardians of the patient present.

If the prescriber of the chromosomal analysis (karyotype/ACPA) is not an expert in chromosomal anomalies, they may collaborate with a clinical geneticist or cytogeneticist for this consultation, and depending on the circumstances, involve another team member (psychologist, genetic counselor, nurse, etc.).

The disclosure should include information about:

- The diagnosis and various biological results
- The disease, its main symptoms, and complications
- The need for regular follow-up
- The proposed management plan
- Mode of transmission and genetic counseling

The presence of a psychologist is essential, either during the disclosure consultation, immediately afterward, or as part of the ongoing care. Telemedicine consultations with the physician or psychological support should be offered.

Contact information for patient associations can be provided to the family.

If the patient does not already benefit from 100% coverage and recognition of their disability through the MDPH (Maison Départementale des Personnes Handicapées), necessary steps should be taken to obtain them. This is important because, on the one hand, expenses related to medical follow-up, additional examinations, and rehabilitation can be reimbursed by the primary health insurance fund (CPAM - Caisse Primaire

d'Assurance Maladie). On the other hand, the patient and their family may be eligible for additional benefits through the MDPH.

### 3.3.16. Genetic counseling

In the vast majority of cases, invdupdel(8p) occurs sporadically or de novo.

A polymorphic paracentric inversion may be found in a parent when specifically sought. This inversion is asymptomatic and common, present in approximately 25% and 30% of individuals of European and Japanese origin, respectively. In the rare cases of invdupdel(8p), this paracentric inversion undergoes recombination, resulting in the production of a dicentric chromosome, which subsequently undergoes secondary division, resulting in a monocentric chromosome with an invdupdel(8p).

The clinical significance of a paracentric inversion diagnosis is limited, as it does not impact genetic counseling. Therefore, there is no need to systematically search for it.

In rare cases, there have been reports of families with transmission of invdupdel(8p) across two generations, with mildly intellectually disabled individuals being carriers. Therefore, for a couple who has had a child with invdupdel(8p), parental karyotyping should be performed to verify the absence of invdupdel(8p) in a parent who may have mild symptoms. If the rearrangement occurred de novo, the risk of recurrence is very low, but prenatal diagnosis during pregnancy may be offered. Preimplantation genetic diagnosis is not currently recommended.

## **4. Therapeutic management and follow-up:**

### 4.1. Treatment and Follow-up Approach

In the absence of specific treatment for invdupdel(8p), the therapeutic objectives are as follows:

- Monitoring neurodevelopmental trajectory and early implementation of rehabilitation measures (speech therapy with the use of alternative and augmentative communication strategies if necessary, physiotherapy, psychomotricity, occupational therapy, orthoptics if needed).
- Screening and management of neurological complications (spasticity, epilepsy) and behavioral disorders, including ASD (autism spectrum disorder).
- Screening and management of known or identified cardiac, urogenital, and musculoskeletal malformations during the initial assessment.
- Screening and management of sensory deficits (visual and auditory) and dental abnormalities.
- Nutritional and growth monitoring.
- Coordination of medical follow-up and paramedical care.
- Providing the family with updated information on the advancement of knowledge.

**4.2. The professionals involved in the coordination may include:**

<b>Medical Professionals</b>	<b>Role in Healthcare Provision</b>
<b>General practitioner or pediatrician.</b>	<p>Coordination with the reference or specialized center. Implementation and renewal of medical-administrative measures, rehabilitation, and treatment.</p> <p>Screening for any anomalies that may arise during follow-up and requesting further investigations or referrals to specialized consultations.</p> <p>Prevention and provision of initial care for complications related to the condition.</p> <p>Regular medical follow-up of the patient, including monitoring psychomotor development and growth, monitoring school progress, and adherence to the vaccination schedule.</p>

<b>Clinical Geneticist</b>	Diagnosis Coordination of patient follow-up Genetic counseling Organization of prenatal diagnosis Screening of at-risk relatives if necessary Providing the family with information on the evolving understanding of the disease.
<b>Cytogeneticist</b>	Chromosomal diagnosis Genetic counseling, if necessary
<b>Neuropediatrician or neurologist.</b>	Screening and management of epilepsy, spasticity, and other possible neurological complications. Implementation and coordination of rehabilitation. Monitoring of psychomotor development and schooling.
<b>Psychiatrist or Child Psychiatrist.</b>	Management of behavioral disorders and/or autism spectrum disorders.
<b>Cardiologist</b>	Management and follow-up of cardiovascular malformations.
<b>Cardiac Surgeon.</b>	Management and follow-up of cardiac malformations, if necessary.
<b>Gastroenterologist.</b>	Management and follow-up of gastroesophageal reflux and esophagitis, oral aversion, and gastrointestinal transit disorders if necessary.
<b>Visceral surgeon</b>	Management and follow-up of gastroesophageal reflux and oral feeding difficulties, if necessary
<b>Nephrologist or urologist</b>	Management and follow-up of urinary, renal, and genital abnormalities
<b>Ophthalmologist (Ophthalmologist)</b>	Screening for visual disorders or possible ocular malformations, management and follow-up of ophthalmological abnormalities
<b>ORL</b>	Screening for possible hearing impairment, management and follow-up of serous otitis media, and monitoring of ENT superinfections
<b>Stomatologist, Dentist, Orthodontist</b>	Management and follow-up of dental anomalies. Systematic screening and management of cavities.
<b>Orthopedic surgeon</b>	Management and follow-up of musculoskeletal anomalies, scoliosis, clubfoot, and deformity prevention
<b>MPR</b>	Management of spasticity. Implementation of adaptation strategies and rehabilitation approaches based on the severity of neurological and orthopedic impairments and their functional impact

Reference Center for Rare Causes of Intellectual Disabilities DéfiScience - Health Network 'Rare Diseases of Brain

<b>Medical Professionals</b>	<b>Roles of Medical Professionals</b>
------------------------------	---------------------------------------

<b>Physical therapist</b>	Management and prevention of various orthopedic complications
<b>Psychomotricien</b>	Rehabilitation and management of postural and motor disorders as well as oral motor difficulties.
<b>Occupational Therapist</b>	Adaptation of the patient's environment, assistance with autonomy, learning of AAC/computer tools.
<b>Dietician</b>	Management of energy intake, adaptation of textures, adaptation of enteral nutrition if necessary.
<b>Speech therapist</b>	Management of oral sensory and motor disorders.  Management of language disorders, early implementation of alternative and augmentative communication methods, simultaneous work on oral language development
<b>Management of behavioral disorders</b>	Management of behavioral disorders and/or autism spectrum disorders
<b>Neuropsychologist</b>	Evaluation of the neurocognitive profile, advice on adapting support and rehabilitation
<b>Social worker</b>	Assists the patient and their family in the process of establishing or updating administrative files to obtain social benefits and recognition of rights related to the patient's disability/health (AEEH, AAH, PCH, family caregiver support, ALD...).  Provides support in accessing ongoing healthcare and medical-social services.

#### 4.3. Therapeutic Management (Pharmacological and Others)

There is no specific pharmacological treatment for invdupdel(8p). The management is symptomatic. Any necessary therapies are used according to the approved indications and conditions specified in the market authorization.

Surgical protocols for the malformations observed in invdupdel(8p) and the treatment of disease complications typically do not differ from those used for the general population.

Based on the patient's overall condition, proposed surgical interventions should undergo an ethical discussion to evaluate the expected benefits of the intervention in relation to the risks for the patient.

If the patient has multi-organ involvement or severe disability, careful preparation for the postoperative period should be anticipated.

#### 4.4. Cognitive Development, Behavior, and Neurological Disorders

Psychomotor and Behavioral Development:

- Neurodevelopmental follow-up should occur at least annually for children. During each annual consultation, the clinician will assess the need for additional neurologic examinations (electroencephalogram, brain MRI, etc.), especially considering the possibility of epilepsy onset. Identifying neurodevelopmental disorders is crucial for implementing early intervention, following the recommendations provided by the French National Authority for Health (HAS), available at:  
[https://www.has-sante.fr/jcms/p\\_3161334/fr/troubles-du-neurodeveloppement-reperage-et-orientation-des-enfants-a-risque](https://www.has-sante.fr/jcms/p_3161334/fr/troubles-du-neurodeveloppement-reperage-et-orientation-des-enfants-a-risque)

Neurodevelopmental evaluations conducted by specialized physicians and paramedical professionals will help define the appropriate rehabilitation methods and educational accommodations required for patients.

Since oral language impairment is constant, early speech therapy intervention is essential. An ENT assessment ensures the absence of exacerbating factors. The use of augmentative and alternative communication (AAC) devices should be considered early on (e.g., PECS, Makaton, French Sign Language, Partial Sign Language, etc.). AAC helps improve the child's receptive skills, leading to a beneficial impact on frustration



management and behavioral disorders. The proposed AAC approach may be multimodal (signs, pictograms, oral language), independent of speech therapy and focused on developing oral language skills.

Behavioral Disorders, Autism Spectrum Disorders (ASD):

- A child psychiatric evaluation, particularly before entering school, may be necessary to identify behavioral disorders and screen for autism spectrum disorder, if warranted, in collaboration with an Autism Resource Center.

In cases of acute behavior changes, it is important to first investigate somatic causes that may be accompanied by pain (e.g., gastroesophageal reflux, dental pain, otitis media, fecal impaction, etc.). In the absence of expressive language, pain assessment tools such as Pédiadol or San Salvadour grids can be useful for evaluating pain (see Annex 4).

Depending on the context and team recommendations, when assessing the age of onset, diagnosing behavioral disorders, or coordinating with the Early-Onset Psychiatric Expression Reference Center (CRMR) within the DéfiScience Healthcare Network, the CRMR for Neurodevelopment of the same network may be recommended. Depending on the specific disorder, behavioral, cognitive, cognitive-behavioral therapies, cognitive remediation, or techniques such as Applied Behavior Analysis (ABA) can provide assistance.

Education:

- Due to the variable degree of psychomotor delay or intellectual disability, the education of each child should be tailored to their individual needs and abilities, assessed in part through psychometric testing. Inclusion in mainstream schools is possible for some children, depending on the

severity of their condition and the adaptability of the school environment. The use of a human aide, such as an Accompanying Worker for Students with Disabilities (AESH), is often beneficial, and the request for such support should be made in advance to the Maison Départementale des Personnes Handicapées (MDPH). A meeting involving the future educational team, the school doctor or nurse, the designated teacher, and the parents is useful for determining the child's needs.

Depending on the child's cognitive abilities, the educational path may be adapted as follows:

- Continuation of mainstream schooling with the support of an AESH, with necessary adjustments to the timetable and school supplies, within the framework of an Individualized Education Plan (Plan Personnalisé de Scolarisation, PPS).
- Placement in a specialized unit for inclusive education (Unité Localisée pour l'Inclusion Scolaire, ULIS), with the support of an AESH and a PPS if necessary.
- Placement in a medico-educational institute (Institut Médico-Éducatif, IME), which is the case for the majority of children with invdupdel(8p).
- Placement in an external educational unit (Unité d'Enseignement Externalisée, UEE), such as an EEAP (establishment for children and adolescents with multiple disabilities).

Regarding follow-up and care, there are various local structures depending on the child's age. In CAMSP (Medical-Psycho-Pedagogical Center), care can be continued until the age of 6, after which it should be transferred to a SESSAD (Specialized Home Care and Support Service), CMP (Medico-Psycho-Pedagogical Center), or equivalent

structure. The request for orientation towards such a structure should be anticipated and made through the MDPH. If placement in an IME is being considered, rehabilitative care can be provided there.

Regular reassessment of rehabilitation needs and educational accommodations throughout childhood, adolescence, and adulthood is necessary to facilitate progress in learning.

Epilepsy:

- The occurrence of epilepsy is frequent in invdupdel(8p) and should be investigated in a specialized setting, such as a pediatric neurology department. Treatment and follow-up should be implemented according to the recommendations of specialists, based on the observed seizure type and the results of complementary investigations conducted during the initial assessment. There is no specific medical treatment for epilepsy in invdupdel(8p) when it occurs.

In cases of worsening epilepsy that was initially stable under treatment, triggering factors should be investigated, such as pain (constipation, orthopedic pain, dental pain, gastroesophageal reflux), infection (urinary tract infection, otitis media, etc.), sleep disorders, changes in bowel movements, recent weight gain, or poor treatment adherence.

A seizure should be considered in patients experiencing regression of motor skills, cognitive abilities, or the onset of behavioral changes, even in those who have never had a seizure before.

Spasticity and Joint Stiffness:

Spasticity and joint stiffness frequently occur in patients with invdupdel(8p) syndrome. They can cause pain, difficulties in positioning the patient, and a loss of motor skills. Preventive management and intervention to address these complications should be implemented, including physiotherapy and the use of orthoses. The use of muscle relaxants or localized injection of botulinum toxin may be necessary.

- A consultation with a Physical Medicine and Rehabilitation (PMR) physician or an orthopedic specialist should be scheduled. The input of an occupational therapist is also important to adapt the patient's daily environment for activities of daily living.

#### Sleep Disorders:

Sleep disorders should be systematically assessed and screened through medical interviews and caregiver questionnaires. In cases of sleep disorders such as delayed sleep onset or nocturnal awakenings, treatment with extended-release melatonin may be useful.

- The interview should also screen for sleep apnea, and if indicated, referral to a specialized sleep center should be considered. In cases of confirmed and severe sleep apnea, the specialist physician may prescribe nocturnal positive pressure ventilation.

#### Congenital Heart Defects:

If a congenital heart defect is present, the management (surgical or medical) does not differ from the protocols typically used for the same condition in the general population.

- Surgical and cardiological follow-up should be determined by specialized practitioners. If the patient did not have a congenital heart defect during the diagnostic assessment, systematic follow-up is not necessary in the absence of symptoms.

#### 4.6. Orthopedic/Musculoskeletal Issues:

Spinal alignment should be examined at each medical visit to screen for scoliosis.

Treatment does not differ from that of the general population, taking into account the patient's reduced mobility.

To prevent the risk of fractures, the patient's calcium intake should be regular and sufficient. Vitamin D supplementation is indicated, as it is for all children.

Regular and adapted physical activity should be practiced to ensure adequate bone density.

#### 4.7. Digestive Problems:

##### Gastroesophageal Reflux:

No further diagnostic tests are necessary in cases of externalized gastroesophageal reflux (GER) and particularly vomiting. However, for non-externalized GER, diagnosis should involve a 24-hour pH monitoring before confirming it and initiating medication.

The management of GER is not specific to the syndrome and relies on simple measures (thickening of feedings, proper positioning during meals and postprandial periods) and usual symptomatic medical treatments (mainly proton pump inhibitors).

- If the patient has complicated and uncontrolled GER (esophagitis, aspiration pneumonia) despite standard measures, the possibility of Nissen fundoplication surgery can be considered.

##### Oral Feeding Disorders:

Specialized speech therapy rehabilitation should be implemented in cases of feeding and/or oral motor disorders.

- Temporary enteral nutrition through a nasogastric tube may be necessary if it affects growth. In cases of prolonged feeding difficulties (> 6 months), gastrostomy tube feeding may be required to avoid prolonged use of a

nasogastric tube, which negatively impacts oral feeding. The indication for this type of device should be discussed with the patient's healthcare team (gastroenterologist, cardiologist, pediatric neurologist, etc.). It is not specific and depends on the severity of feeding difficulties, the patient's dependence on nasogastric tube feeding, and the risk of aspiration during oral feeding.

En cases of oral motor disorders associated with severe and uncontrolled gastroesophageal reflux, the consideration of performing a Nissen fundoplication during the same surgical procedure as the gastrostomy tube placement can be discussed.

Chronic Constipation:

- The management of constipation primarily involves simple hygienic and dietary measures (increased fiber intake, hydration). In cases of persistent constipation, the use of medical treatments such as laxatives (macrogol, PEG) is necessary due to the negative impact of constipation on food intake. The treatment should be continued for an extended period (at least 1 month) to prevent recurrence and discomfort. The use of enemas or suppositories should be exceptional. Special attention should be given to medications that have the side effect of slowing down bowel transit (psychotropic drugs, etc.).

4.8. Genitourinary Problems:

Some patients may have minor abnormalities such as hydronephrosis, renal hypoplasia, or horseshoe kidney. It is important to diagnose these conditions, although simple monitoring is usually sufficient, and their treatment is not specific. In the case of genital malformations (hypospadias, etc.), surgical consultation is essential.

#### 4.9. Growth Disorders:

Oral motor disorders in the early months of life can negatively impact growth and require careful monitoring. Patients often have lower weight and height compared to the average for their age. Generally, growth in terms of height and weight should be regularly monitored (at least every 3 months before the age of one, then every 6 months). Weight, height, and head circumference should be plotted on growth charts in the health record. If there is a slowdown or deviation from the growth curve, a diagnostic evaluation is necessary to identify the cause and provide appropriate treatment. Dietary assessment to optimize calorie and nutritional intake should be conducted systematically in cases of abnormal growth.

#### 4.10. Sensory Disorders:

The diagnosis and management of associated sensory disorders are particularly important in the context of developmental delay. Treatment is symptomatic, and the follow-up frequency is determined by the specialist physician.

An annual screening ophthalmological consultation is recommended. Due to the frequency of refractive errors and strabismus, an examination, including atropine, by a pediatric ophthalmologist, should be performed at least once and as early as possible.

Hearing tests should be conducted during the initial assessment and may be repeated during follow-up if there is suspicion of hearing loss.

#### 4.11. Dental care and follow-up

Just like for all children, tooth brushing should be started as soon as the first teeth erupt.

Regular oral and dental follow-up should be implemented to identify dental abnormalities (crowding, poor tooth alignment) and the development of cavities. Preventive measures, tailored to each individual's context, can be taken (application of fluoride varnish).

This can be done in a standard dental office. For some patients, seeking professionals experienced in welcoming and treating patients with disabilities, and the possibility of conscious sedation using MEOPA, may require dental care in a hospital setting, an accredited dental office, or within one of the Handidents networks at [www.soss.fr/les-reseaux-en-france](http://www.soss.fr/les-reseaux-en-france) (examples include Handident Hauts de France, Handident PACA, RhapsolleDeFrance).

Profesionals	0-2 Years	During Childhood	Adult
<p><b>General Practitioner or Pediatrician</b></p>	<p><b>Systematic clinical examination (monthly until 6 months, then at 9, 12, 18, and 24 months)</b></p> <ul style="list-style-type: none"> <li>- Monitoring growth and screening for oral issues</li> <li>- Growth charts</li> <li>- Monitoring of bowel movements, feeding, and sleep</li> <li>- Screening for orthopedic abnormalities</li> <li>- Vaccination program</li> <li>- Evaluation of psychomotor development</li> <li>- Screening for epilepsy</li> </ul>	<p><b>Annual systematic clinical examination</b></p> <ul style="list-style-type: none"> <li>- Growth charts</li> <li>- Screening for scoliosis</li> <li>- Monitoring of bowel movements, feeding, and sleep</li> <li>- Vaccination program</li> <li>- Evaluation of psychomotor development and schooling</li> <li>- Screening for epilepsy</li> </ul>	<p><b>Annual systematic clinical examination</b></p> <ul style="list-style-type: none"> <li>- Monitoring of weight</li> <li>- Monitoring of bowel movements, feeding, sleep</li> <li>- Vaccination program</li> <li>- Screening for epilepsy</li> </ul>



<p><b>Geneticist</b></p>	<p><b>Annual follow-up consultation</b>  <b>Comprehensive clinical examination</b>  Search for specific complications related to the condition  Prescription of additional tests to complete the initial assessment if necessary  Identification of key contacts  Informing the family about the possible evolution of knowledge  Genetic counseling</p>	<p>Annual follow-up consultation  Comprehensive clinical examination  Search for specific complications related to the condition  Prescription of additional tests to complete the initial assessment if necessary  Identification of key contacts  Informing the family about the possible evolution of knowledge  Genetic counseling</p>	<p>Annual follow-up consultation  Comprehensive clinical examination  Screening for specific complications related to the condition  Prescription of additional tests to complete the initial assessment if necessary  Identification of key contacts  Providing the family with information about the potential evolution of knowledge  Genetic counseling</p>
<p><b>Nuerologist</b></p>	<p>Annual follow-up consultation, to be adjusted based on symptoms</p> <ul style="list-style-type: none"> <li>- Monitoring of psychomotor development</li> <li>- Prescription and adjustment of rehabilitation</li> <li>- Screening and treatment of epilepsy</li> </ul>	<p>Annual follow-up consultation</p> <ul style="list-style-type: none"> <li>- Monitoring of psychomotor development and schooling</li> <li>- Prescription and adjustment of rehabilitation</li> <li>- Screening and treatment of epilepsy</li> </ul>	<p>Transition to adult care (geneticist/neurologist)  Follow-up consultation every 2 to 3 years, to be adapted based on individual needs</p> <ul style="list-style-type: none"> <li>- Monitoring of weight</li> <li>- Monitoring of bowel movements, nutrition, sleep</li> <li>- Vaccination program</li> <li>- Screening for epilepsy</li> </ul>
<p><b>Cardiologist</b></p>	<p>If there is a cardiac condition, the follow-up care should be adapted based on the symptoms.</p>	<p>If there is a cardiac condition, the follow-up care should be adapted based on the symptoms.</p>	<p>If there is a cardiac condition, the follow-up care should be adapted based on the symptoms.</p>
<p><b>Orthopedic Surgeon</b></p>	<p>If there is an orthopedic anomaly, the follow-up care should be adapted accordingly.</p>	<p>If there is an orthopedic anomaly, the follow-up care should be adapted accordingly.</p>	<p>If there is an orthopedic anomaly, the follow-up care should be adapted accordingly.</p>
<p><b>MPR</b></p>	<p>If necessary, the follow-up care should be adjusted accordingly.</p>	<p>If necessary, the follow-up care should be adjusted accordingly.</p>	<p>If necessary, the follow-up care should be adjusted accordingly.</p>
<p><b>Gastroentolog ist and Dietician</b></p>	<p>If there are difficulties with feeding, oral aversion, growth deceleration or faltering, constipation, or gastroesophageal reflux, appropriate measures should be taken.</p>	<p>If there are difficulties with feeding, oral aversion, growth deceleration or faltering, constipation, or gastroesophageal reflux, appropriate measures should be taken.</p>	<p>If there is weight loss, gastroesophageal reflux, or constipation, it is important to assess the underlying causes and provide appropriate management.</p>

<b>Ophthalmologist</b>	<b>During the neonatal period and at 9 months,</b> several systematic examinations are typically conducted to assess the health and development of the child.	<b>At 2 and a half years and 6 years of age,</b> systematic examinations are typically conducted to evaluate the child's health and development.	If necessary, the follow-up care should be adjusted accordingly.
<b>ORL</b>	After the initial diagnosis, systematic examinations may be conducted as needed, including the screening and treatment of ear infections (otitis) and audiograms.		If necessary, the follow-up care should be adjusted accordingly.
<b>Dentist</b>	During regular dental check-ups, systematic dental examinations are conducted to monitor the eruption of teeth and ensure proper dental development.	<b>Annual Dental Exam</b>	<b>Annual Dental Exam</b>
<b>Psychiatrist or child psychiatrist, Nephrologist, Endocrinologist, others</b>	If necessary, the follow-up care should be adjusted accordingly.	If necessary, the follow-up care should be adjusted accordingly.	If necessary, the follow-up care should be adjusted accordingly.

4.13. Therapeutic education and lifestyle modifications (on a case-by-case basis)

Therapeutic education aims to help patients and their families acquire or maintain the skills they need to manage their lives with a chronic illness.

In invdupdel(8p) syndrome, there are no specific aspects compared to other developmental disorders involving intellectual disability, orthopedic risks, feeding difficulties, etc. (see "Intellectual Disabilities, Synthesis and Recommendations," Expertise Collective, Les éditions Inserm, 2016).

The objectives of therapeutic education are to help patients and their families:

- Understand the disease.
- Understand the treatments, their potential side effects, and precautions to be taken.

- Know how to act and react on a daily basis in specific situations, including managing epilepsy seizures and discomfort.
- Prevent certain complications.
- Master technical skills (such as enteral nutrition through a tube or gastrostomy, managing epilepsy seizures, dental hygiene, etc.) related to the management of the disease.

These therapeutic education actions require the involvement of various healthcare professionals, who can provide individual care to the patient/family or engage in group education.

#### 4.14. Involvement of patient associations

Patient associations and family support groups on social networks are essential partners of Rare Disease Reference or Competence Centers. They play a crucial role in supporting families by providing information, assistance, and support.

They also serve as a source of information and allow patients and their families to feel less alone by providing opportunities to connect with others in similar situations and offer practical advice to help individuals in their daily lives.

They contribute to strengthening and supporting patient care in collaboration with reference and competence centers, with the support of the DéfiScience network. They participate in research projects and, if necessary, provide funding for projects that are of significant interest to patients. The contact information of these associations is systematically provided to families, but the decision to engage with an association remains the choice of the family or the patient.

## Appendix 1. List of participants

This work was coordinated by Dr. Solveig HEIDE, Clinical Genetics Department, CRMR "Rare Causes of Intellectual Disabilities," APHP. Sorbonne University, Pitié-Salpêtrière site, Assistance Publique Hôpitaux de Paris, Paris.

Contact: solveig.heide@aphp.fr

This work was supported by the Défiscience network.

Contributors to the development of the PNDS:

Writers:

- Dr. Solveig HEIDE, Department of Genetics, APHP Sorbonne
- Dr. Anna GERASIMENKO, Department of Genetics, APHP Sorbonne
- Dr. Béatrice DUBERN, Pediatric Gastroenterology, APHP Sorbonne
- Dr. Stéphanie VALENCE, Pediatric Neurology, APHP Sorbonne
- Dr. Jean-Pierre SIFFROI, Cytogenetics, APHP Sorbonne
- Mrs. Isabelle MARCHETTI-WATERNAUX, VALENTIN-APAC association
- Mrs. Jennifer M REYES, "la maison 8p" association

Review group (in alphabetical order):

- Dr. Yline CAPRI, Department of Genetics, APHP Nord-Hôpital Robert Debré
- Mrs. Barbara CHIARONI, Neuropsychologist, Department of Genetics, APHP Sorbonne
- Dr. Jamal GHOU MID, Clinical Genetics, CHR de Lille
- Mrs. Lauryne KOBLY, Social Worker, Department of Genetics, APHP Sorbonne
- Dr. Cyril MIGNOT, Clinical Genetics, Department of Genetics, APHP Sorbonne
- Dr. Pauline PARISOT, Pediatric Cardiology, APHP Sorbonne
- Dr. Laurent PASQUIER, Clinical Genetics, CRDI Rennes
- Dr. Damien SANLAVILLE, Department of Genetics, Lyon University Hospital

Bibliographic references (see Rationale):

A more detailed document that served as the basis for the development of this PNDS and included the analysis of identified bibliographic data (scientific rationale) is available on the website of the network.

Center for Reference on Rare Causes of Intellectual Disabilities

DéfiScience - Rare Diseases Health Network "Rare Brain Development Disorders and Intellectual Disability"

Conflict of Interest Declarations:

All participants involved in the development of the PNDS have submitted conflict of interest declarations. These declarations of interest are available online and can be consulted on the website of the reference center(s).

## **Appendix 2. List of Reference Centers**

Reference Centers for Rare Causes of Intellectual Disabilities

### **Centers of Reference for Rare Intellectual Disabilities**

CR constitutif APHP Pitié-Salpêtrière,  
PARIS  
Dr Delphine HERON

CR constitutif Hospices Civils de LYON  
Pr Vincent DES PORTES

CR constitutif APHM de Marseille Pr  
Mathieu MILH

CR constitutif APHP Trousseau,  
PARIS Dr Stéphanie VALENCE

CR constitutif APHP Necker, PARIS Pr  
Nadia Bahi Buisson

CR constitutif CHU de DIJON Pr  
Christel THAUVIN-ROBINET

CR constitutif APHP Necker, PARIS Dr  
Marlène RIO

CR constitutif APHP Robert Debré,  
PARIS Dr David GERMANAUD

CR constitutif CHRU de BREST Dr  
Sylviane PEUDENIER

CR constitutif CHU de RENNES Dr  
Laurent PASQUIER

CR constitutif CHU de STRASBOURG  
Dr Salima EL CHEHADEH

### **Centers of Expertise for Rare Intellectual Disabilities**

Centre Compétence CHU TOURS Pr  
Annick TOUTAIN

Centre Compétence APHP Kremlin  
Bicêtre, PARIS Dr Anya  
ROTHENBUHLER PEN

Centre Compétence CHU LILLE Dr  
Audrey RIQUET

Centre Compétence CHU AMIENS Pr  
Patrick BERQUIN

Centre Compétence CHU de BESANCON  
Dr Elise BRISCHOUX-BOUCHER

Centre Compétence CHU NANCY Dr  
Laetitia LAMBERT

Centre Compétence CHU NANTES Dr  
Bertrand Isidor

Centre Compétence CHU NICE Dr  
Fabienne GIULIANO

Centre Compétence CHU POINTE A  
PITRE  
Dr Marilyn LACKMY PORT LIS

Centre Compétence CHU REIMS Pr  
Nathalie BEDNAREK

Centre Compétence CHU TOULOUSE  
Dr Caroline KARSENTY

Centre Compétence CHU de  
BORDEAUX Pr Cyril GOIZET

Centre Compétence CHU  
MONTPELLIER Dr Philippe MEYER

DéfiScience - Filière de santé maladies  
rares du développement cérébral et  
déficience intellectuelle -  
<http://www.defiscience.fr>

### **Appendix 3. Socio-Administrative Assessment**

Financial Assistance - MDPH (Departmental House of People with Disabilities) - CAF  
(Family Allowance Fund)

The preparation of a file for financial assistance must be anticipated due to the time required to gather all the necessary documents. Requests should be renewed 6 months in advance to avoid any interruption of rights, or in case of worsening or change in rehabilitation situation. In case of refusal, a gracious or contentious appeal, or even conciliation, is possible.

The medical certificate issued by the referring physician of a Reference Center for Rare Causes of Intellectual Disabilities (or by the treating physician, or both) is essential for granting rights in terms of paramedical, medico-social, educational, vocational, residential care, or even legal protection for adults. This certificate accompanies the application files.

### **Before the age of 20**

Parents are responsible for applying for the Disabled Child Education Allowance (AEEH), the Disability Compensation Benefit (PCH) from the MDPH, or the Daily Parental Presence Allowance (AJPP) from the Family Allowance Fund (CAF).

- There are three types of Mobility Inclusion Cards (CMI) issued by the MDPH: priority and parking from 50% disability rate, and disability card from 80%.
- There is a specific benefit called "AEEH supplement." This benefit is not automatic but can be received by patients and families for specific expenses or impacts on professional life (urinary protection, reduced working hours). The AEEH with supplement and the PCH cannot be combined, and the family must choose between the AEEH with supplement and the PCH. Regardless of this choice, they can request assistance for housing and vehicle modifications, as well as additional costs related to transportation. Requests for educational guidance and medico-social structures can also be included. The assistance of a social worker is crucial in asserting one's rights.
- The AJPP can be combined with the basic AEEH, but not with the AEEH supplement.
- From the age of 18, it is necessary to discuss with the family the need to establish guardianship or legal protection measures for vulnerable adults (guardianship, trusteeship, or family authorization). These measures can be exercised by the family or a professional third party (judicial protection administrator for adults). These procedures are carried out with the guardianship judge at the district court.

### **From the age of 20**

Planning ahead is recommended 9 to 12 months before the transition to adulthood, which is set at 20 years old for the MDPH. Parents, guardians, or curators are responsible for applying for the Adult Disability Allowance (AAH), PCH, and CMI. Note:

If the young person was receiving AEEH, the eligibility criteria for AAH are different. A disability recognition of 80% or higher or a recognition of a lasting restriction for employment access is required.

There are services that support independent living: Medico-Social Accompaniment Service for Disabled Adults (SAMSAH) or Social Life Accompaniment Service (SAVS). The MDPH will assess vocational orientation towards mainstream or adapted environments: Work Assistance and Support Centers (ESAT) or Adapted Enterprises (EA) or mainstream employment. The recognition as a disabled worker (RQTH) may need to be requested before the age of 20 in the case of internships, apprenticeships, etc. If no diploma has been obtained or if it does not correspond to the person's disability, an evaluation at a Vocational Rehabilitation Center (CRP) may be conducted. Registration with Pôle Emploi, CAP emploi, and Supported Employment (MDPH notification) assist individuals with disabilities in finding employment or qualifying training.

In case of incapacity for work, the person will be directed to a residential care facility, occupational care facility, medical care facility (FAM), or specialized accommodation facility (MAS). The medical certificate issued by the attending physician or referring physician accompanies the application documents.

A social worker is essential to assist with the applications, as well as the "rare disability relay teams" if necessary. The National Solidarity Fund for Autonomy (CNSA) has published a booklet for MDPH on "Chromosomal Anomalies: Support document for determining the disability rate for individuals with chromosomal anomalies."

**Other resources:**

- Orphanet's "Cahiers d'Orphanet - Living with a Rare Disease in France - Support and Benefits for Individuals with Rare Diseases and their Families" - December 2021, updated annually:



[www.orpha.net/orphacom/cahiers/docs/EN/Living\\_with\\_a\\_rare\\_disease\\_in\\_France.pdf](http://www.orpha.net/orphacom/cahiers/docs/EN/Living_with_a_rare_disease_in_France.pdf)

- ERHR (Rare Diseases Reference Centers): [www.gnchr.fr/](http://www.gnchr.fr/)
- 360 Communities: [www.cnsa.fr/grands-chantiers/communautes-360](http://www.cnsa.fr/grands-chantiers/communautes-360)
- The 19 Rare Diseases Expertise Platforms (PEMR) and the 4 in overseas territories:  
[www.remarares.re/wp-content/uploads/2022/01/Annuaire-PEMR-PCOM-pdf](http://www.remarares.re/wp-content/uploads/2022/01/Annuaire-PEMR-PCOM-pdf)
- The 2 support networks:
  - PRIOR in the Pays de la Loire region: [prior-maladiesrares.fr](http://prior-maladiesrares.fr)
  - Rare Diseases in Occitanie: [www.maladies-rares-occitanie.fr](http://www.maladies-rares-occitanie.fr)
  - Poles of Competence and Outsourced Services (PCPE):  
[https://handicap.gouv.fr/IMG/pdf/livret\\_pcpe-2.pdf](https://handicap.gouv.fr/IMG/pdf/livret_pcpe-2.pdf)

#### **Annex 4. Pain Assessment**

Pain assessment allows:

- Objectifying a subjective phenomenon for which there are no specific markers.
- Determining the presence or absence of pain, assessing its intensity, location, and type.
- Evaluating the effectiveness of analgesic treatment and adjusting it as needed.

Pain assessment is an integral part of the clinical evaluation of a patient. Any healthcare professional (physicians, paramedics, as well as educational staff in facilities for individuals with disabilities) can assess pain. There are no specific scales for patients with a microdeletion invdupdel(8p). Pain should be assessed using a validated scale that is appropriate for the patient's age, cognitive abilities, and context. Self-assessment (evaluation by the patient themselves) is preferred when possible. Hetero-assessment (evaluation by one or more observers) is performed when the patient is unable to

self-assess (e.g., young children under 4 years old, patients with multiple disabilities or non-communicative).

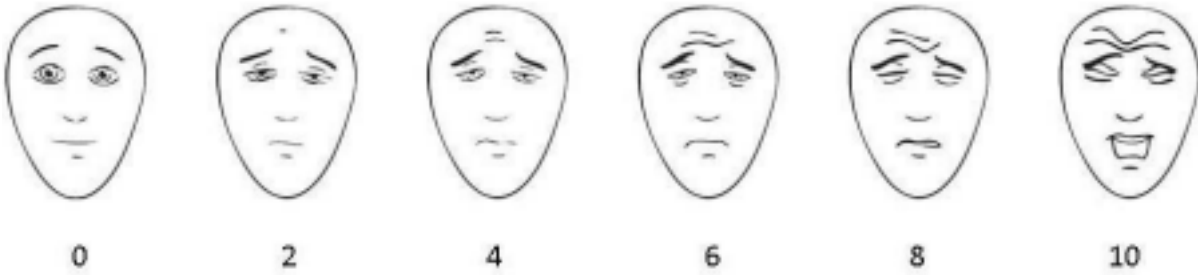
The scale used for the initial assessment serves as a reference for subsequent evaluations unless it is deemed inappropriate.

Self-assessment scales:

- The choice of scale depends on the patient's age, cognitive development, and preferences. It is essential to use a tool that the patient understands. Between 4 and 6 years old (and sometimes in older children or adults with intellectual disabilities), two self-assessment tools can be used together to test their evaluation abilities. From the age of 4, the following scale can be used:
  - Faces Pain Scale - Revised (FPS-R): Six Faces Scale.

Please note that this translation is based on the assumption that the abbreviations and terms used in the original text have their commonly understood meanings in the context of pain assessment and evaluation.

This scale can also be used by certain non-communicative patients (children, adolescents, or adults) or in cases of autism spectrum disorders. The therapeutic threshold is 4/10. Instructions given: "These faces show how much pain someone can have. This face (point to the one on the left) shows someone who has no pain at all. These faces (point to them one by one from left to right) show someone who is experiencing increasing pain, up to this one (point to the one on the right), which shows someone who is in very, very much pain. Show me the face that shows how much pain you are currently feeling."



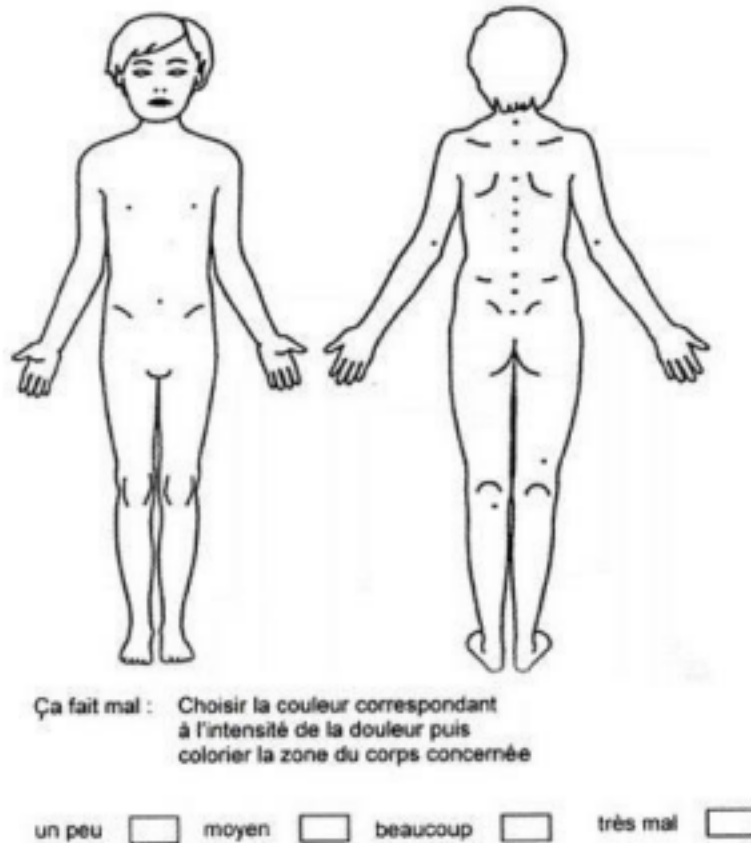
The scores range from left to right: 0, 2, 4, 6, 8, 10. Therefore, 0 corresponds to "no pain at all," and 10 corresponds to "very, very much pain." Clearly express the extreme limits: "no pain at all" and "very, very much pain." Do not use the words "sad" or "happy." Clearly specify that it refers to their internal sensation, not the displayed expression on their face.

#### Token Scale (Poker Chips)

- This scale can be used from the age of 4, but it is not widely used in France. The child is given a set of poker chips representing different levels of pain, and they are asked to select the chip that corresponds to their current level of pain.

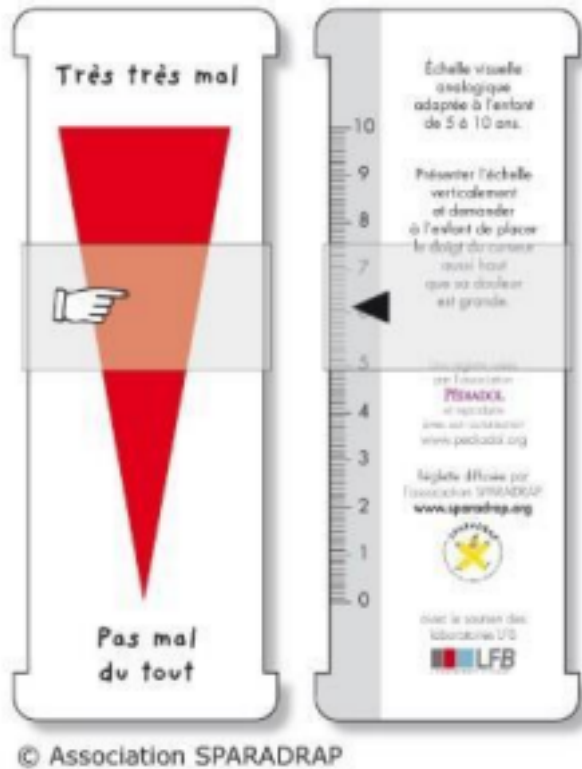
#### Visual Analog Scale (VAS)

- The VAS is presented vertically, and the child is asked to indicate their pain level by placing a mark along the scale. The low end of the scale represents "no pain" or "not at all," and the high end represents "very strong pain" or "very, very bad." It's important to ensure that the child understands how to position their pain on the scale by providing clear instructions.



There is no consensus on how to explain the VAS to children, and it's important to adapt the explanation to each child without referencing past experiences or imagination. One way to present the scale is by saying, "Place your finger as high as your pain is." Before measuring pain intensity, it's important to verify that the child understands the principle of the scale. Some children may tend to place their pain at the extreme ends (0 or 10) of the VAS. In such cases, it can be helpful to use other pain assessment scales, particularly a facial expression scale. If the results still appear contradictory to the child's behavior, a hetero-evaluation scale can be used.

For adolescents, it may be preferable to use a horizontal VAS similar to the one used for adults or a simple numerical scale. The treatment threshold is set at 3/10, indicating that pain management interventions are typically initiated when the pain level reaches or exceeds this threshold.



From the age of 10 (middle school level):

#### Numerical Rating Scale (NRS)

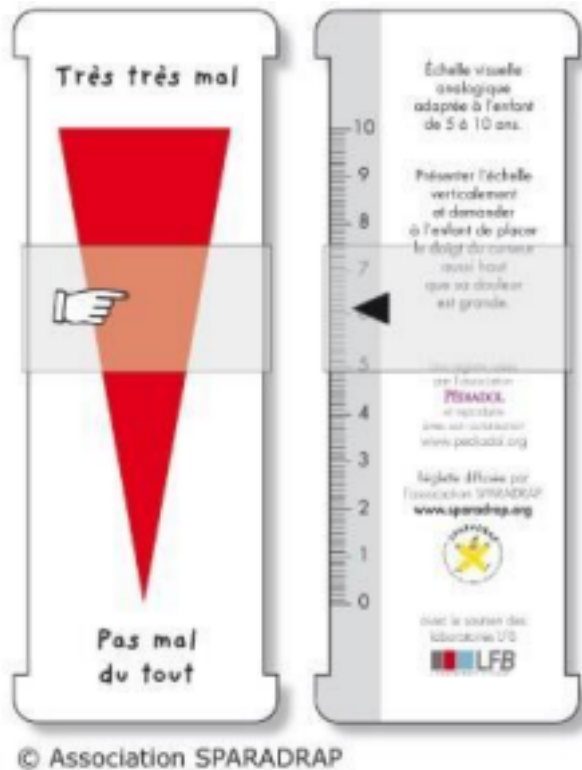
- "Give a number to your pain between 0 and 10." It is necessary to define the meaning of the endpoints, where "0" represents no pain at all, and "10" represents very intense pain. This scale requires the ability to mentally represent quantities and compare them. It involves a complex mental operation beyond basic counting skills. The treatment threshold is set at 3/10, indicating that pain management interventions are typically initiated when the pain level reaches or exceeds this threshold.

#### Hetero-evaluation Scales

- Different scales exist depending on the context: acute pain (post-operative, medical condition, pain caused by a procedure, etc.), prolonged pain, pain in intensive care (for intubated and sedated individuals), pain in individuals with disabilities, pain in newborns, pre-hospital or emergency department pain assessment, among others. These specific situations are not discussed in this text. Other scales can be

consulted on the websites of Pédiadol ([www.pediadol.org](http://www.pediadol.org)) or the Centre National Ressources de lutte contre la Douleur (CNRD - [www.cnrdr.fr](http://www.cnrdr.fr)).

2.



L'hetero-evaluation requires referring to the usual behavior of a child of the same age or the usual behavior of the person being assessed (particularly in individuals with disabilities). Any modification in their usual behavior should raise the possibility of pain and prompt an evaluation. These modifications can manifest in various ways in individuals with multiple disabilities or autism spectrum disorders. In addition to the typical signs of pain (crying, facial expressions of pain, whimpering, defensive reaction to a painful area), the following observations can be made:


- Atonia or psychomotor regression (decreased interest in the environment, reduced interaction abilities)
- Self or hetero-aggression
- Paradoxical laughter
- Increased abnormal movements or spasticity

Several hetero-evaluation scales that are most suitable for the patients covered by this PNDS are presented below.

EVENDOL (Évaluation ENfant DOuLeur):

- Initially validated for children from birth to 7 years old for acute and prolonged pain in emergency settings, it has since been validated for use in pediatric wards (medical conditions), post-operative pain, and pre-hospital settings.

**Evaluation  
Enfant  
Douleur**



Echelle validée  
de la naissance à 7 ans.  
Score de 0 à 15,  
seuil de traitement 4/15.

Notez tout ce que vous observez... même si vous pensez que les signes ne sont pas dus à la douleur, mais à la peur, à l'inconfort, à la fatigue ou à la gravité de la maladie.

Non	Signe absent	Signe faible ou passager	Signe moyen ou environ la moitié du temps	Signe fort ou quasi permanent	Analgésique		Evaluations suivantes					
					Evaluation à l'arrivée		Evaluations après analgésique <sup>1</sup>					
					ou repos <sup>2</sup> ou calme (R)	à l'examen <sup>2</sup> ou la mobilisation (M)	R	M	R	M	R	M
Expression vocale ou verbale <i>pleure et/ou cris et/ou gémis et/ou dit qu'il a mal</i>	0	1	2	3								
Mimique <i>à la front plissé et/ou les sourcils froncés et/ou la bouche crispée</i>	0	1	2	3								
Mouvements <i>s'agite et/ou se raidit et/ou se crispe</i>	0	1	2	3								
Positions <i>à une attitude inhabituelle et/ou analgésique et/ou se protège et/ou reste immobile</i>	0	1	2	3								
Relation avec l'environnement <i>peut être consolé et/ou s'adresse aux yeux et/ou communique avec l'entourage</i>	normale 0	diminuée 1	très diminuée 2	absente 3								
Remarques	Score total /15											
	Date et heure											
	Initiales évaluateur											

<sup>1</sup>Au repos ou calme (R) : observez l'enfant avant tout soin ou examen, dans les meilleures conditions possibles de confort et de confiance, par exemple à distance, avec ses parents, quand il joue...  
<sup>2</sup>À l'examen ou la mobilisation (M) : il s'agit de l'examen dirigé ou de la mobilisation ou position de la zone douloureuse par l'observateur ou le médecin.  
<sup>3</sup>Retarder régulièrement un particulier après analgésique, au moment du pic d'action : après 30 à 45 minutes si oral ou rectal, 5 à 30 minutes si IV. Préciser la situation, ou repos (R) ou à la mobilisation (M).  
 Echelle validée pour mesurer la douleur (intense ou prolongée) chez l'enfant, de 0 à 7 ans, en ambulatoire, aux urgences, en SAMU, en salle de soins, en postopératoire - Référence bibliographique - Archives de Pédiatrie 2006, 13, 922, F129-F130. Archives de Pédiatrie 2012, 19, 922, P43-44. Journaux Français Pédiatrie 2009 - 2005,376. Juin 2012, 153 - 157/1582. Contact : albert@k.lucas@chcmucl.fr © 2011 - Groupe EVENDOL

FLACC (Face Legs Activity Cry Consolability - usable from 2 months to 7 years of age) and Modified FLACC (usable from birth to 18 years of age in individuals with disabilities)

This scale is validated for post-operative pain assessment and for evaluating pain related to medical procedures. It does not require knowledge of the child's usual behavior, making it particularly useful in healthcare settings, especially pediatric surgery.

However, it does not take into account signs of psychomotor regression in cases of prolonged pain. The therapeutic threshold is 3/10.

### ÉCHELLE FLACC : Face Legs Activity Cry Consolability

Élaborée pour mesurer la douleur de la personne handicapée de 0 à 18 ans – *[Items modifiés écrits en italique entre crochets]*

Chaque item est coté de 0 à 2

Score de 0 à 10

		Date					
		Heure					
<b>VISAGE</b>	<p>0 Pas d'expression particulière ou sourire</p> <p>1 Grimace ou froncement occasionnel des sourcils, retrait, désintéressé <i>[semble triste ou inquiet]</i></p> <p>2 Froncements fréquents à permanents des sourcils, mâchoires serrées, tremblement du menton <i>[visage effrayé : expression d'effroi ou de panique]</i></p>						
<b>JAMBES</b>	<p>0 Position habituelle ou détendue</p> <p>1 Gêné, agité, tendu <i>[térébrations occasionnelles]</i></p> <p>2 Coups de pieds ou jambes recroquevillées <i>[agitation marquée de la quatuorité, térébrations ou sursauts permanents]</i></p>						
<b>ACTIVITÉ</b>	<p>0 Allongé calmement, en position habituelle, bouge facilement</p> <p>1 Se tortille, se balance d'avant en arrière, est tendu <i>[mouvement agité (ex. : bouge sa tête d'avant en arrière, agressif) : respiration superficielle, saccadée, soupirs intermittents]</i></p> <p>2 Arc-bouté, figé, ou sursaute <i>[agitation sévère, se cogne la tête, tremblement (sans rigidité) : retient sa respiration, halète ou bouge profondément : respiration saccadée importante]</i></p>						
<b>CRIS</b>	<p>0 Pas de cris (éveillé ou endormi)</p> <p>1 Gémissements ou pleurs, plainte occasionnelle <i>[explosion verbale ou gémissement occasionnel]</i></p> <p>2 Pleurs ou cris constants, huchements ou sanglots, plaintes fréquentes <i>[explosion verbale répétée ou gémissement constant]</i></p>						
<b>CONSOLABILITÉ</b>	<p>0 Content, détendu</p> <p>1 Rassuré occasionnellement par le toucher, l'étreinte ou la parole. Peut être distrait</p> <p>2 Difficile à consoler ou à réconforter <i>[repushse le soignant, s'oppose aux soins ou aux tentes de confort]</i></p>						
<b>SCORE TOTAL</b>							
<b>OBSERVATIONS</b>							

© 2006, Université de Michigan, Système de santé. Droits réservés.  
 Traduction par l'équipe de l'Unité d'évaluation et de traitement de la douleur, Centre hospitalier universitaire Robert Debré, Paris, France.  
 Contre-traduction par le Dr Marie-Claude Gergonne, FWH Health Centre, Dalhousie University, Halifax, Canada et par le Dr Peter Jones, Centre hospitalier universitaire Robert Debré, Paris, France.



### Instructions

**Patients éveillés** : Observer pendant au moins 2 à 5 minutes. Observer les jambes et le corps découverts. Repositionner le patient ou observer sa motricité, évaluer la rigidité et le tonus. Consoler le patient si nécessaire.

**Patients endormis** : Observer pendant au moins 5 minutes ou plus. Observer les jambes et le corps découverts. Si possible repositionner le patient. Toucher le corps et évaluer sa rigidité et son tonus.

### Visage

**Cotez 0** si le patient a un visage détendu, un contact visuel et s'il manifeste de l'intérêt pour son environnement.

**Cotez 1** si le patient a une expression du visage anxieuse, les sourcils froncés, les yeux mi-clos, les pommettes surélevées, la bouche pincée.

**Cotez 2** si le patient a des plis marqués sur le front (le front très crispé) et les yeux fermés, les mâchoires serrées ou la bouche ouverte et des sillons naso-labiaux accentués.

### Jambes

**Cotez 0** si le patient a une motricité et un tonus habituels au niveau des membres (jambes et bras).

**Cotez 1** si le patient a un tonus augmenté, une rigidité, une tension, des mouvements de flexion-extension intermittents des membres.

**Cotez 2** si le patient a une hypermotricité, les jambes raides, des mouvements de flexion-extension des membres exagérés, des trémulations.

### Activité

**Cotez 0** si le patient se mobilise facilement et librement, s'il a une activité motrice habituelle.

**Cotez 1** si le patient change fréquemment de position ou au contraire hésite à bouger, si le torse est raide, si une partie du corps est tendue.

**Cotez 2** si le patient est figé ou au contraire se balance, bouge sa tête de part et d'autre, frotte une partie de son corps.

### Cris

**Cotez 0** si le patient n'émet aucun cri ou gémissement, qu'il soit éveillé ou endormi.

**Cotez 1** si le patient gémit, crie, pleure ou soupire de temps en temps.

**Cotez 2** si le patient gémit, crie ou pleure fréquemment ou continuellement.

### Consolabilité

**Cotez 0** si le patient est calme et n'a pas besoin d'être consolé.

**Cotez 1** si le patient est réconforté par le toucher ou la parole en 30 à 60 secondes.

**Cotez 2** si le patient a besoin d'être réconforté en permanence ou ne peut être consolé.

À chaque fois qu'il est possible, l'évaluation comportementale de la douleur doit être associée à une autoévaluation. Quand celle-ci est impossible, l'interprétation des manifestations comportementales de la douleur et la prise de décision thérapeutique nécessitent une analyse attentive du contexte dans lequel les manifestations de douleur ont été observées.

Chaque item est coté de 0 à 2, ce qui donne un score total entre 0 et 10 :

0 = détendu et confortable

1-3 = léger inconfort

4-6 = douleur modérée

7-10 = douleur sévère ou inconfort majeur

© 2006, Université de Michigan, Système de santé. Droits réservés.

Traduction par l'équipe de l'Unité d'évaluation et de traitement de la douleur, Centre hospitalier universitaire Robert Debré, Paris, France.

Contre-translation par le Dr Marie-Claude Gatzert, DHK Health Center, Dalhousie University, Halifax, Canada et par le Dr Peter Jones, Centre hospitalier universitaire Robert Debré, Paris, France.

## GED-DI (Grille d'Évaluation de la Douleur - Déficience Intellectuelle)

- This scale is used for individuals aged 3 years and above who are unable to self-assess or verbally communicate due to cognitive disabilities, particularly in the context of multiple disabilities (polyhandicap). It does not require knowledge of the patient's usual behavior and is validated for post-operative pain assessment. However, it is a bit lengthy to complete (30 items) and is not widely used in France. The therapeutic threshold is set at 6/90 (or 6/81 in the post-operative setting, where 3 evaluation items are removed). Detailed information about this scale can be found on the Pédiadol website ([www.pediadol.org](http://www.pediadol.org)).

## DESS (Douleur Enfant San Salvador)

- This scale allows the assessment of pain in polyhandicapped patients. The rating is done retrospectively over an 8-hour period. The scale is

coupled with a baseline record describing the patient's usual behavior, obtained from the person regularly caring for the child. Pain is considered certain when the score reaches 6/40 or higher. This scale is particularly useful in long-term care settings for polyhandicapped patients (rehabilitation centers, IMEs, MAS, etc.) where the usual behaviors of the individuals being assessed are well-known. Detailed information about the scale can be found on the Pédiadol website ([www.pediadol.org](http://www.pediadol.org)).

#### PPP (Pediatric Pain Profile)

- This scale is used for individuals aged 1 to 18 years with severe neurological disabilities or polyhandicap. It is primarily intended for those who usually provide care, especially parents. A baseline score, when the child is well, is a prerequisite. The prescription threshold is set at 14/60. The complete documentation (baseline record and scale) can be found on the Pédiadol website ([www.pediadol.org](http://www.pediadol.org)).

#### EDAAP (Évaluation de l'expression de la Douleur chez l'Adolescent et l'Adulte Polyhandicapé)

- This assessment measures the difference between the person's usual expression (baseline state) and the disturbed expression hypothesized to be indicative of pain. The presence of pain is affirmed for any score equal to or higher than 7, and it is confirmed by a gradual return to the person's usual expression after care or the implementation of effective treatment. This scale is particularly suitable for long-term care facilities for adult polyhandicapped patients (especially MAS). The scale can be found on the CNRD website ([https://www.cnrdr.fr/documents/documentation/fichiers/2018/12/A1544025616SD\\_grille%20edaap.pdf](https://www.cnrdr.fr/documents/documentation/fichiers/2018/12/A1544025616SD_grille%20edaap.pdf)).

A modified version of this scale exists (EDD: Évaluation de l'expression de la Douleur chez les personnes dys-communicantes) and can be found on the website of the

Association Nationale pour la Promotion des Soins Somatiques en Santé Mentale  
<https://www.anp3sm.com/actus/rndsm>).

- ESDDA (Échelle Simplifiée d'évaluation de la Douleur chez les personnes Dyscommunicantes avec troubles du spectre de l'Autisme)
- This specific scale has been recently developed for individuals with autism spectrum disorders who are unable to self-assess their pain. Pain is suspected when the score reaches a threshold of 2/6. The ESDDA scale aims to provide a simplified and adapted assessment tool for individuals with communication difficulties related to autism spectrum disorders.



Mode d'emploi: Répondre à chaque item par OUI ou NON, un TOTAL > 2 OUI fait suspecter une douleur.

# ESDDA

Echelle Simplifiée d'évaluation de la Douleur  
chez les personnes Dyscommunicantes  
avec troubles du spectre de l'Autisme

IDENTIFICATION DE LA PERSONNE ÉVALUÉE

Nom :  
Prénom :  
Date de naissance :

Date de l'évaluation	.../.../...		.../.../...		.../.../...		.../.../...		.../.../...		.../.../...		.../.../...	
Heure	...h...		...h...		...h...		...h...		...h...		...h...		...h...	
	OUI	NON	OUI	NON	OUI	NON	OUI	NON	OUI	NON	OUI	NON	OUI	NON
1. Comportement <i>modifié par rapport à l'habitude?</i>														
2. Mimiques et expressions du visage <i>modifié par rapport à l'habitude?</i>														
3. Plaintes (cris, gémissements...) <i>modifié par rapport à l'habitude?</i>														
4. Sommeil <i>modifié par rapport à l'habitude?</i>														
5. Opposition lors de soins														
6. Zone douloureuse identifiée à l'examen														
<b>TOTAL DE OUI</b>	/6		/6		/6		/6		/6		/6		/6	
Complétée par														

Centre régional douleur et soins somatiques en santé mentale et autisme - Document réalisé par le Dr Isabelle MYTICH et le Dr Julie RENAUD-MIERZEJEWSKI - version du 31/01/2017

Avant 18 ans 0-7 ans	Douleur aiguë	
----------------------	---------------	--

Hetero-Evaluation	
0-7 Years of Age	FLACC EVENDOL
Emergencies or Emergency Care	EVENDOL
Poly-handicap (0-18 Years of Age)	FLACC modifiée (post-opérateur/soins) GED-DI DESS EDAAP (adolescents) ESDDA (troubles du spectre de l'autisme) PPP
Intensive Care (0-18 Years of Age)	COMFORT B
Auto-évaluation	
Starting from Age 4	Echelle des 6 visages EVS Schéma du bonhomme
Starting from Age 6	EVA
Age 8-10	EN

Translation:

Bibliographic references:

1. AFSSAPS 2009 Recommendations - Management of acute and chronic pain in children.
2. Professional Practice Guidelines: Management of post-operative pain; HAS June 2005.
3. Evaluation and management strategies for acute pain in outpatient settings in children aged 1 month to 15 years; ANAES 2000.

Websites:

