Dysport 500 Units, Speywood, powder for solution for injection
Box of 1 vial of powder (CIP code: 558 105-9)

Applicant: Beaufour Ipsen
Botulinum toxin type A
List I

Medicine subject to restricted prescription: reserved for hospital use
Date of French Marketing Authorisation: 11 October 1993
Date of latest clinical amendment: 08 September 2005 (New indication for local symptomatic treatment of upper and/or lower limb spasticity (muscle hyperactivity)).

Reason for request: inclusion on the list of medicines approved for hospital use in the following extended therapeutic indications:
- symptomatic treatment of upper and/or lower limb spasticity (muscle hyperactivity),
- treatment of dynamic equinus foot deformity in children with spasticity caused by cerebral palsy.
1. CHARACTERISTICS OF THE MEDICINAL PRODUCT

1.1. Active ingredient
Botulinum toxin type A

1.2. Indications

Adults and children over 12
- blepharospasm
- hemifacial spasm
- spasmodic torticollis
- local symptomatic treatment of upper and/or lower limb spasticity (muscle hyperactivity).

Children aged 2 and over
- Treatment of dynamic equinus foot deformity in children with spasticity caused by cerebral palsy.

Drug therapy treatment should form part of wider multidisciplinary care (including a neurologist, paediatrician, physical medicine and rehabilitation specialist, and orthopaedic surgeon). Dysport 500 Units (Speywood) should be administered by specialist doctors experienced in using the toxin in these indications.

1.3. Dosage and method of administration

- Local symptomatic treatment of spasticity

The exact dosage, volume and number of injection sites should be individually tailored according to patient size, the number and position of the muscles involved, severity of spasticity, presence of local muscle weakness and patient response to prior therapy. The recommended starting dose is 1000 units per patient. The dose should never exceed 1500 units per patient per injection session. The total dose should be divided between the different muscles to be injected, which are usually: flexor digitorum profundus (deep finger flexor), flexor digitorum superficialis (superficial finger flexor), flexor carpi ulnaris (ulnar flexor muscle of wrist), flexor carpi radialis (radial flexor muscle of wrist), biceps brachii (brachial biceps), gastrocnemius, soleus, tibialis posterior (posterior tibial muscle), flexor digitorum longus (long toe flexor), adductor. See SPC for the recommended dose distribution for each muscle.

A 1 or 5 ml syringe should be used, depending on the volume to be injected (23–25 gauge needle). The injection site is determined by electromyographic guidance (especially for deep muscles) or using evoked muscle response detection. Because electromyographic guidance is a difficult technique, injections in the tibialis posterior require specialist training and competence on the part of the doctor giving the injection. Clinical improvement usually appears during the two weeks following the injection session. Injection sessions can be repeated if necessary, but should always be at least 3 months apart. At repeat injection sessions, the dose of Dysport 500 Speywood Units and the choice of muscles to be injected may need to be modified according to the intensity and type of muscle spasticity.
• Dynamic equinus foot deformity in children with spasticity caused by cerebral palsy

Two injections should be given in each medial head and lateral head of the affected gastrocnemius. The dose depends on the child’s weight. In patients with diplegia, the recommended initial dose is 20 units/kg divided between the two legs. In patients with hemiplegia, the total recommended initial dose is 10 units/kg, injected into the leg concerned. If only the gastrocnemius is injected, the recommended initial dose is 5 units/kg bodyweight per head of the gastrocnemius. If injections are to be given in the soleus and tibialis posterior (posterior tibial muscle), the total recommended amount should be divided between the different muscles injected. The amount injected into these 2 muscles should be 25–50% of the total recommended amount. A lower initial dose should be used in patients in whom the muscles to be treated are underdeveloped, or who need a concomitant injection in another muscle group. Depending on the clinical response to the initial dose, doses given in subsequent sessions should be adjusted to 10–30 units/kg divided between the two legs, without exceeding the total maximum dose of 1000 units per patient per injection session.

A 1 mL syringe should be used (23–25 gauge needle). Electromyographic guidance can be used to identify the most active muscles. However, because it is a difficult technique, injections in the tibialis posterior require specialist training and competence on the part of the doctor giving the injection. Clinical improvement usually appears during the two weeks following the injection session. Injection sessions should be repeated as necessary depending on how long the clinical effect lasts, but should always be at least 3 months apart.

## 2. SIMILAR MEDICINAL PRODUCTS

### 2.1. ATC Classification 2006:

- M : Musculo-skeletal system
- 03 : Muscle relaxants
- A : Muscle relaxants, peripherally acting agents
- X : Other muscle relaxants, peripherally acting agents
- 01 : botulinum toxin

### 2.2. Medicines in the same therapeutic category

#### 2.2.1 Comparator medicines

Botulinum toxin type A:
- Botox 50 IU, 100 IU and 200 IU, powder for solution for injection

Botulinum toxin type B:
- Neurobloc, solution for injection, 5000 IU/mL

### 2.1 Medicines with a similar therapeutic aim

Medicines indicated for certain types of spasticity:
- Dantrium (dantrolene), capsules,
- Lioresal (baclofen), tablets and solution for intrathecal injection,
- benzodiazepines (without Marketing Authorisation).
3. ANALYSIS OF AVAILABLE DATA

3.1. Efficacy

3.1.1. Local symptomatic treatment of upper and/or lower limb spasticity (muscle hyperactivity)

The applicant submitted 7 trials assessing the efficacy of Dysport in treating spasticity of the upper limbs (4 trials) and lower limbs (3 trials).

Upper limbs

- **Trials DYSP/016 and Smith 2000**

  These were dose-ranging trials and the Transparency Committee did not take their results into account.

- **Trial DYSP/049 (Bakheit 2001)**

  A trial to assess the efficacy and safety of botulinum toxin type A (BTX-A) in treating upper-limb spasticity after stroke.
  - **Design**: 16-week randomised, double-blind, placebo-controlled trial in 59 patients.
  - **Inclusion criteria**: patients with moderate to severe upper-limb spasticity (hypertonia score ≥ 2 on the MAS scale for at least 2 of 3 flexion zones (wrist, elbow and fingers) and score ≥ 1 for the third flexion zone) ≥ 3 or more months after stroke.
  - **Treatment**: BTX-A, 1000 IU (n = 27; divided into several injections: 300-400 IU in the biceps, 150-250 IU in the flexor digitorum superficialis muscles and 150 IU in the flexor digitorum profundus muscles); placebo (n = 32).
  - **Primary endpoint**: assessment of muscle tone in the wrist, elbow and fingers after 4 weeks using the MAS (modified Ashworth scale).

**Results**

Analysis by intent-to-treat.

<table>
<thead>
<tr>
<th>Change in MAS score</th>
<th>Placebo</th>
<th>BTX-A 1000 U*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 32)</td>
<td>(n = 27)</td>
</tr>
<tr>
<td>4 point decrease</td>
<td>0</td>
<td>2 (7.4%)</td>
</tr>
<tr>
<td>3 point decrease</td>
<td>4 (12.5%)</td>
<td>5 (18.5%)</td>
</tr>
<tr>
<td>2 point decrease</td>
<td>3 (9.4%)</td>
<td>7 (25.9%)</td>
</tr>
<tr>
<td>1 point decrease</td>
<td>15 (46.9%)</td>
<td>8 (29.6%)</td>
</tr>
<tr>
<td>Unchanged</td>
<td>10 (31.3%)</td>
<td>5 (18.5%)</td>
</tr>
</tbody>
</table>

*p = 0.004

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3 Ashworth scale definitions: 0 = No increase in muscle tone; 1 = Slight increase in muscle tone; 2 = More marked increase in muscle tone; 3 = Considerable increase in muscle tone; 4 = Affected part is rigid in flexion or extension.
After 4 weeks of therapy, MAS scores decreased (see table), showing a significant improvement in hypertonia in all muscles in patients given BTX-A 1000 IU compared with placebo. This improvement was maintained at 16 weeks in the wrist and fingers but not in the elbow.

- **Trial DYSP/013 (Hesse 1998)**.

A trial to assess the efficacy of botulinum toxin type A in combination with electrical stimulation, compared with treatment with botulinum toxin alone, in treating upper-limb spasticity after stroke.

- **Design**: 12-week randomised double-blind placebo-controlled trial in 24 patients.
- **Inclusion criteria**: patients with severe upper-limb spasticity (hypertonia score ≥ 3 on the MAS scale) 6–12 months after stroke.
- **Treatment**: 4 groups.
  - Group A: one injection of 1000 units + electrical stimulation (n = 6),
  - Group B: 1000 units (n = 6),
  - Group C: placebo + electrical stimulation (n = 6),
  - Group D: placebo (n = 6).
- **Endpoints**: at weeks 0, 2, 6 and 12.
  - MAS assessment of muscle tone in the wrist, elbow and fingers,
  - Assessment of limb position at rest on a 5-point scale (0 = flexed, 4 = completely extended).

**Results**

Assessment of muscle tone showed no statistically significant difference between groups A, B, C and D for the wrist, elbow and fingers, whatever the assessment timepoint. Similarly, there was no difference in limb position at rest.

**Lower limbs**

- **Trial DYSP/044 (Pittock 2003)** and **DYSP/006: (Hyman 2000)**

These were dose-ranging trials and the Transparency Committee did not take their results into account.

- **Trial Burbaud 1996**.

A trial to assess the efficacy of botulinum toxin type A in treating plantar flexor spasticity in patients with hemiparesis after stroke or head injury.

- **Design**: 3-month randomised double-blind placebo-controlled crossover trial in 23 patients.
- **Inclusion criteria**: patients with moderate to severe plantar flexor spasticity of the heel and foot for at least 3 months, not responding to usual physical and drug therapy.
- **Treatment**: BTX-A 1000 units on day 0 followed by placebo on day 90 (n = 10); placebo on day 0 followed by BTX-A on day 90 (n = 13). Rehabilitation was begun 3 months before the start of therapy and continued throughout the trial.

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- **Endpoints:**
  - subjective assessment by the patient at day 0 and day 30 (scale of 0–3),
  - video of gait,
  - assessment of gait velocity,
  - Fugl-Meyer\(^8\) scale (cumulative numerical score measuring improvement in patients’ motor function and balance),
  - assessment of heel flexor and foot invertor muscle tone using the Ashworth scale,
  - assessment of active dorsiflexion using an overall score (scale of 0–6).

**Results**

A statistically significant improvement in the subjective assessment score by the patient was seen in the BTX-A group (1.5 ± 0.8) over the placebo group (0.2 ± 0.4) (p = 0.0014), showing that patients receiving this treatment felt some clinical improvement.

<table>
<thead>
<tr>
<th>Change in mean scores before and one month after injection of BTX-A: results for the 23 patients enrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Without BTX-A</td>
</tr>
<tr>
<td>(n = 23)</td>
</tr>
<tr>
<td>After BTX-A</td>
</tr>
<tr>
<td>(n = 23)</td>
</tr>
<tr>
<td>Video (gait pattern)</td>
</tr>
<tr>
<td>3.1 ± 0.6</td>
</tr>
<tr>
<td>2.0 ± 0.6**</td>
</tr>
<tr>
<td>Gait velocity (cm/s)</td>
</tr>
<tr>
<td>25.1 ± 17.1</td>
</tr>
<tr>
<td>29.4 ± 16.4</td>
</tr>
<tr>
<td>Fugl-Meyer score</td>
</tr>
<tr>
<td>23.5 ± 4.9</td>
</tr>
<tr>
<td>25.0 ± 4.7*</td>
</tr>
<tr>
<td>Ashworth extension</td>
</tr>
<tr>
<td>3.7 ± 0.7</td>
</tr>
<tr>
<td>2.4 ± 0.9**</td>
</tr>
<tr>
<td>Ashworth inversion</td>
</tr>
<tr>
<td>2.8 ± 0.9</td>
</tr>
<tr>
<td>1.8 ± 0.9**</td>
</tr>
<tr>
<td>Ankle dorsiflexion</td>
</tr>
<tr>
<td>2.2 ± 1.5</td>
</tr>
<tr>
<td>3.3 ± 1.4**</td>
</tr>
</tbody>
</table>

*p < 0.05; **p < 0.001

**3.1.2. Dynamic equinus foot deformity in children with spasticity caused by cerebral palsy**

The applicant submitted 3 trials.

- **Trial DYSP/040 (Baker 2002\(^9\))**
  This was a dose-ranging trial and the Transparency Committee did not take its results into account.

- **Trial DYSP/038 (Ubhi 2000\(^10\))**
  A trial to assess the efficacy of BTX-A injection in improving walking in children with cerebral palsy.
  - **Design:** 3-month randomised double-blind placebo-controlled trial in 40 children.
  - **Inclusion criteria:** children (aged 2–16) with dynamic talipes equinovarus foot deformity; 28 with diplegia and 12 with hemiplegia. Children had to be able to walk with or without help but not place the heel on the ground.
  - **Treatment:** BTX-A, one injection of 250-700 units (n = 22) vs. placebo (n = 18).
  - **Primary endpoint:** walking improvement on video at weeks 2, 6 and 12.

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Results

Mean dose administered:
- children with diplegia: 485 ± 120 units
- children with hemiplegia: 336 ± 93 units.

Analysis of walking improvement seen on video: percentages calculated on the number of patients actually analysed at each stage of the study (per protocol analysis)

<table>
<thead>
<tr>
<th></th>
<th>BTX-A (n = 22)</th>
<th>Placebo (n = 18)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Week 2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number analysed:</td>
<td>n = 20</td>
<td>n = 17</td>
<td></td>
</tr>
<tr>
<td>- worsening</td>
<td>1 (5%)</td>
<td>4 (24%)</td>
<td>NS</td>
</tr>
<tr>
<td>- no change</td>
<td>12 (60%)</td>
<td>10 (59%)</td>
<td></td>
</tr>
<tr>
<td>- improvement</td>
<td>7 (35%)</td>
<td>3 (18%)</td>
<td></td>
</tr>
<tr>
<td>- data missing</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Week 6</strong></td>
<td></td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>Number analysed:</td>
<td>n = 21</td>
<td>n = 18</td>
<td></td>
</tr>
<tr>
<td>- worsening</td>
<td>1 (5%)</td>
<td>4 (22%)</td>
<td></td>
</tr>
<tr>
<td>- no change</td>
<td>10 (48%)</td>
<td>11 (61%)</td>
<td></td>
</tr>
<tr>
<td>- improvement</td>
<td>10 (48%)</td>
<td>3 (17%)</td>
<td></td>
</tr>
<tr>
<td>- data missing</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Week 12</strong></td>
<td></td>
<td></td>
<td>0.003</td>
</tr>
<tr>
<td>Number analysed:</td>
<td>n = 20</td>
<td>n = 18</td>
<td></td>
</tr>
<tr>
<td>- worsening</td>
<td>0</td>
<td>3 (17%)</td>
<td></td>
</tr>
<tr>
<td>- no change</td>
<td>10 (50%)</td>
<td>13 (72%)</td>
<td></td>
</tr>
<tr>
<td>- improvement</td>
<td>10 (50%)</td>
<td>2 (11%)</td>
<td></td>
</tr>
<tr>
<td>- data missing</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Walking improved with BTX-A compared with placebo at weeks 6 and 12. It is difficult to quantify this improvement. There was no difference between the two groups at week 2. Interpreting the results is difficult because of the weak power of the trial (70%) and the type of analysis used (per protocol).

- **Trial DYSP/046: unpublished**

A trial to assess the efficacy and safety of Dysport in treating dynamic equinus spasticity in children with cerebral palsy.

- **Design:** 16-week randomised double-blind placebo-controlled trial in 52 children.
- **Inclusion criteria:** children with diplegia (aged 2–7) able to perform 10° dorsiflexion of the ankle.
- **Treatment:** BTX-A, 30 U/kg (total dose: 300-1000 units, n = 26) vs. placebo (n = 26).
- **Primary endpoint:** improved motor function at 4 weeks (GMFM).

Results

There was no significant difference between BTX-A and placebo.

3.2. Undesirable effects

The most common undesirable effects in the trial were pain at the injection site and tiredness.

As with the efficacy data, long-term safety (beyond 16 weeks) is unknown.

Following cases of spread of botulinum toxin at a distance from the target muscle, Dysport SPC has recently been modified and all companies marketing botulinum toxin products will be asked for a European risk management plan.
3.3. Conclusion

The 7 trials had design limitations, notably the small number of patients enrolled and the multiplicity of endpoints per trial.

- **Local symptomatic treatment of upper and/or lower limb spasticity (muscle hyperactivity)**

The dossier includes 4 trials assessing the efficacy of BTX-A in treating spasticity of the lower limbs (2 trials) and upper limbs (2 trials).

Statistically significant improvement on the MAS score was seen in the groups treated with BTX-A compared with placebo in 2 of these trials, showing that there was some clinical improvement in patients given this treatment.

No other trials are available comparing BTX-A with active comparator drugs (e.g. phenol, alcohol, dantrolene or baclofen). No safety or efficacy data are available for therapy lasting more than 12 weeks.

The Transparency Committee regretted that there were few data that could be used to assess the contribution of BTX-A compared with or in combination with functional rehabilitation.

- **Dynamic equinus foot deformity in children with spasticity caused by cerebral palsy**

The dossier includes 2 placebo-controlled trials assessing the efficacy of BTX-A in treating dynamic talipes equinovarus foot deformity in children.

Statistically significant improvement in walking was seen on video in the groups treated with BTX-A compared with placebo in only one of these trials.

No other trials are available comparing BTX-A with active comparator drugs (e.g. phenol or alcohol).

No efficacy or safety data are available for therapy lasting more than 16 weeks.

The Transparency committee regretted that there were few data that could be used to assess the contribution of BTX-A compared with or in combination with functional rehabilitation.

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4. TRANSPARENCY COMMITTEE CONCLUSIONS

4.1. Actual benefit

**Local symptomatic treatment of upper and/or lower limb spasticity (muscle hyperactivity)**

- Spasticity is a disabling handicap that can impair quality of life and have serious consequences for social and family life.
- Dysport is symptomatic therapy.
- It is a first-line medical therapy that should be used in combination with physiotherapy.
- There are few alternative treatments. There is a need for therapy in this area.
• Public health benefit
  − The seriousness of spasticity lies in the functional and psychosocial handicap it creates. As the impact of spasticity varies, and in view of the lack of epidemiological data on this condition, it is not possible to quantify the burden on public health.
  − Improving handicap is a public health priority. As the results of existing treatments are not satisfactory, there remains a therapeutic need which is important in terms of public health.
  − However, the data available are not sufficient to quantify the expected impact of botulinum toxin on the quality of life of patients with spasticity, even in the short term. Furthermore, the expected impact of this therapy in the longer term cannot be predicted because of the lack of long-term studies.
  − It is not therefore expected that Dysport will benefit public health in this indication.
• The efficacy/safety ratio is moderate.

The actual benefit of Dysport in this indication is substantial.

Dynamic equinus foot deformity in children with spasticity caused by cerebral palsy
• Dynamic talipes equinovarus foot deformity is a disabling handicap that can impair quality of life and have serious consequences on social and family life.
• Dysport is symptomatic therapy.
• It is a first-line medical therapy that should be used in combination with physiotherapy.
• There are few alternative treatments. There is a need for therapy in this area.
• Public health benefit:
  − The seriousness of spasticity lies in the functional and psychosocial handicap it creates. As the impact of spasticity varies, and in view of the lack of epidemiological data on this condition, it is not possible to quantify the burden on public health.
  − Improving handicap is a public health priority. As the results of existing treatments are not satisfactory, there remains a therapeutic need which is important in terms of public health.
  − However, the data available are not sufficient to quantify the expected impact of botulinum toxin on the quality of life of patients with spasticity, even in the short term. Furthermore, the expected impact of this therapy in the longer term cannot be predicted because of the lack of long-term studies.
  − It is not therefore expected that Dysport will benefit public health in this indication.
• The efficacy/safety ratio is moderate.

The actual benefit of Dysport in this indication is substantial.

4.2. Improvement in actual benefit

It is not possible to estimate the place and benefit of Dysport in current therapy for these conditions based on the data available.

The Transparency Committee therefore considered that Dysport does not offer any improvement in actual benefit (IAB V) either in local symptomatic treatment of upper and/or lower limb spasticity, or in treating dynamic equinus foot deformity in children with spasticity caused by cerebral palsy.
4.3. Therapeutic use

Local symptomatic treatment of upper and/or lower limb spasticity (muscle hyperactivity)\textsuperscript{11}

Muscle spasticity is an increased contraction response to stretching and a pathological increase in muscle tone (hypertonia) due to overactivity of the afferent fibres. It can cause pain and spasms and result in functional impotence of the upper and lower limbs.

Spasticity is caused by vascular, traumatic, infectious or degenerative damage to the central nervous system (brain or spinal cord). Central neurological pain may appear in the same conditions, so spasticity and central neuropathic pain often occur together.

Muscle spasticity requires treatment when it causes problems. From the functional point of view, it can be a handicap or, in some patients, a means of compensating for motor deficit. The therapist must weigh up the expected benefit in terms of pain reduction and consequences for gross motor function. Management depends on the clinical picture, the treatments available, and the consequences, depending on whether the functional handicap is diffuse or local and how serious it is.

Rehabilitation techniques that encourage muscle stretching and which can be combined with the use of splints and plaster casts to position the limb should be favoured as first line of therapy.

Any drug therapy should always be combined with physiotherapy. In localised spasticity, the muscles involved should be treated locally. The different methods are:

- injection of botulinum toxin in the muscle
- nerve block (e.g. alcohol, phenol)
- intrathecal baclofen.

In all cases, the aim of treatment is to induce a localised decrease in muscle activity in order to improve motor function, and reduce the handicap and functional problems caused by spasticity.

In patients with diffuse lesions, antispastic drugs such as baclofen, dantrolene, tizanidine (Temporary Authorisation for Use) or benzodiazepines (outside the terms of the Marketing Authorisation) may be proposed. In extreme cases, central neurostimulation or destructive surgery (Dorsal Root Entry Zone (DREZ) lesion, cordotomy) could be considered.

Botulinum toxin (Dysport) should be administered by specialist doctors experienced in its use in these indications. Botulinum toxin injection is a reversible, adaptable local therapy.

Dynamic equinus foot deformity in children with spasticity caused by cerebral palsy\textsuperscript{12}

Cerebral palsy (CP) is caused by brain damage in the antenatal or perinatal period. It is a nonprogressive motor disorder secondary to abnormality in or damage to the maturing brain. The resulting motor handicap combines varying degrees of posture and movement disorder.

Management is based on improving motor function, especially walking, and helping with rehabilitation or getting used to the equipment used.

Physiotherapy is essential to maintain good range of movement in the joint and stimulate the stages of motor development (rolling over, sitting, crawling, knee walking, standing, and walking).

Equipment and technical aids can be useful to help prevent muscle shortening (maintaining posture) or facilitate movements.

\textsuperscript{11} Fletcher D, “Spasticité et douleur”, Evaluation et traitement de la douleur, SFAR 2003, p 125-133.
\textsuperscript{12} Physiotherapy and orthopaedic treatment for isolated congenital foot deformity during the first six months of life, ANAES guidelines, January 2004.
Medical treatment for local spasticity can involve injections of botulinum toxin in the muscles, or nerve blocks (alcohol or phenol).

When using botulinum toxin, the choice of muscles to be injected should not be made without a detailed assessment of the extent of spasticity and an assessment of the joints (expert opinion).

Botulinum toxin (Dysport) should be administered by specialist doctors experienced in its use in these indications. Botulinum toxin injection is a reversible, adaptable local therapy.

4.4. **Target population**

Local symptomatic treatment of upper and/or lower limb spasticity (muscle hyperactivity)

The target population is that of patients with upper and/or lower limb spasticity of diverse origin (e.g. stroke, MS, head injury, spinal damage or Parkinson’s disease).

The target population cannot be estimated on the basis of the data available.

Dynamic equinus foot deformity in children with spasticity caused by cerebral palsy

The target population is that of children born with cerebral palsy (CP) with unilateral spasticity causing dynamic talipes equinovarus foot deformity.

The estimated incidence of cerebral palsy (CP) is 2 per 1000 births\(^\text{13}\). According to INSEE data, around 760 000 births were recorded in 2004.

Around 1500 children per year are born with cerebral palsy.

Around 85% of these children have spasticity\(^\text{13}\). Dynamic talipes equinovarus foot deformity generally occurs with unilateral spasticity (35% of patients with spasticity – expert opinion), giving a figure of 450 children per year.

Treatment continues throughout the growing period lasting an estimated average of 10 years.

Based on these figures, the target population for Dysport in this indication would be around 4500 patients.

4.5. **Transparency Committee recommendations**

The Transparency Committee recommended inclusion on the list of medicines approved for use by hospitals and various public services in the new indication and at the posology in the marketing authorisation.

\(^{13}\) Cans Ch. et al. *Épidémiologie de la Paralysie Cérébrale, Motricité Cérébrale* 2005; 26:51-58