# PROPOSAL FOR THE ADDITION OF BACLOFEN TO THE WHO MODEL LIST OF ESSENTIAL MEDICINES AND TO THE WHO MODEL LIST OF ESSENTIAL MEDICINES FOR CHILDREN FOR THE TREATMENT OF SPASTICITY IN CHILDREN AND ADULTS WITH CEREBRAL PALSY

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None of the contributors have conflicts of interests to declare.

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# – Section 1: Summary statement of the proposal

This submission proposes the addition of baclofen as an individual medicine to the core list of the EML and EMLc for the treatment of spasticity in adults and children with cerebral palsy. Treating spasticity is urgent to reduce contractures, deformities and pain; and to improve posture, mobility and overall physical function. This application focuses primarily on cerebral palsy (CP), however, the benefits of baclofen can be applied to other conditions causing spasticity given a common pathophysiology.

Currently there are no medications listed in the EML and EMLc with the indication to treat spasticity. The few alternatives to baclofen have significant disadvantages: for example, in terms of surgical interventions, selective dorsal rhizotomy has uncertain but irreversible consequences; and in terms of oral medication, diazepam (which is on the list but not for spasticity) is heavily sedating. The addition of baclofen would provide a treatment option for patients who require tone reduction to help them move, rest, eat and perform other basic functions.

Baclofen is a well-established medication that is listed as a first-line treatment for spasticity in multiple clinical guidelines, including in Brazil, France, Italy, UK and USA. Evidence for the efficacy of intrathecal baclofen is stronger than for oral baclofen due to a lack of high-quality studies for the latter. However, intrathecal pump therapy, which requires a surgical intervention to place a subcutaneous device as well as maintenance and eventual replacement, is unavailable or uncommon in most low- and middle-income countries. Oral baclofen offers a useful, safe and inexpensive alternative.

Baclofen would prove a vital and useful therapy on the EML and EMLc providing a first line pharmacological treatment for spasticity.

# – Section 2: Consultation with WHO technical departments

During the preparation of this application there have been multiple meetings with Dr Chiara Servili and Dr Rodrigo Cataldi of the Brain Health Unit, Department of Mental Health, Brain Health & Substance Use, World Health Organization (WHO). They have provided guidance and suggestions, and critically assessed drafts of this application.

# – Section 3: Other organizations(s) consulted and/or supporting the submission

The following organizations were consulted on this submission, contributed data and support the addition of baclofen to the WHO EML and EMLc:

Argentina - Alegría Asociación Civil
Argentina - A.P.PA.CE.T
Argentina - Fundación Obligado*
Argentina - Red Argentina de Parálisis Cerebral
Australia - Cerebral Palsy Alliance*
Brazil - Instituto Nossa Casa*
France - Fondation Paralysie Cérébrale*
Ireland - Enable Ireland*
Italy - FighttheStroke Foundation*
Jordan - Our Lady Of Peace Center for Persons with Disabilities*
Kenya - Aga Khan University Hospital
Kenya - Green Shade Kenya Disabled Organization*
Lebanon - SESOBEL*
Luxembourg - cerebra.lu Paralysie Cérébrale Luxembourg*
Mauritius - CP Family*
Nepal - Self-Help Group for Cerebral Palsy*
Nigeria - Cerebral Palsy Center*
Pakistan - Angel's Home Welfare Organization*
People's Republic of China - University of Hong Kong, Shenzhen Hospital
Portugal - Associação do Porto de Paralisia Cerebral*
South Africa - Southern African Academy of Childhood Disability
Spain - Fundació Aspace Catalunya*
Switzerland - Vereinigung Cerebral Schweiz*
UK - Scope*
USA - Cerebral Palsy Foundation*
USA - Gillette Children's Specialty Healthcare*
USA - Shirley Ryan AbilityLab
USA - United Cerebral Palsy*
Yemen - Abs Development Organization for Woman and Child*

The organizations marked with an asterisk (*) are members of the International Cerebral Palsy Society.

Letters of support are provided as an annex.

## – Section 4: Key information summary table for the proposed medicine(s)

| | | | |
|---|---|---|---|
| **INN** | Baclofen | | |
| **ATC code** | M03BX01 | | |
| **Indication** | Treatment of spasticity in adults and children with cerebral palsy | | |
| **ICD-11 codes** | 8D20 Spastic cerebral palsy | | |
| **Dosage form** | **Strength** | **EML** | **EMLc** |
| Tablet | 10mg | Yes | Yes |
| Liquid | 10mg/5mL | Yes | Yes |
| Intrathecal pump | 500 mcg/mL | Yes | Yes |

Baclofen was first synthesized in 1962 and approved for use in Europe as Lioresal a decade later, followed by approval in the United States in 1977. Since that time it has been a first-line agent in the treatment of spasticity[1].

Baclofen is a generic medication and is produced under different brand names, including Beklo, Baclodol, Flexibac, Gablofen, Kemstro, Liofen, Lioresal, Lyflex, Clofen, Muslofen, Bacloren, Baklofen, Sclerofen, Pacifen, Ozobax, Fleqsuvy and Lyvispah.

## – Section 5: Listing as an individual medicine or as representative of a pharmacological class or therapeutic group (‘square box’ listing)

This submission relates to the individual listing of baclofen under Section 5, Medicines for diseases of the nervous system.

## – Section 6: Information supporting the public health relevance

Cerebral palsy is a condition of public health importance. It is estimated that 50 million people around the world have CP[2]. There is no cure for CP, but early diagnosis and intervention, coupled with regular treatment, can have a meaningful impact on an individual’s overall function and quality of life.

Individuals with CP may have varying degrees of neurologic impairments such as weakness, sensory deficits, cognitive impairments, loss of selective motor control,

incoordination and hypertonia including spasticity, dystonia and choreoathetosis[3]. These deficits can impair motor function and interfere with care, comfort and positioning[3]. Hypertonia, or spasticity, can also lead to the following issues: a) hip subluxation; b) torsional deformities; c) gait abnormalities; d) contractures[4]; e) higher energy expenditure[5]; f) pain[6].

The treatments that are currently available for hypertonia are able to minimize the long term impact of some of the neurologic impairments and improve function though unable to eliminate all of the associated problems[7]. The goal of hypertonia or spasticity management is to improve function and not merely to reduce muscle tone. Optimum and early management of spasticity can help achieve the following: a) developmental milestones; b) improve function; c) prevent contractures; d) increase tolerance of braces; e) help with care, comfort, and positioning; f) improve weight gain velocity[8].

Various modalities have been used in the treatment of spasticity. These modalities include range of motion exercises[9-11], casting and bracing[12], rehabilitation therapies[13], oral medications[14, 15], neurolytic blocks[16, 17], neurotoxin injections[18, 19], intrathecal baclofen pumps (ITB)[20, 21], rhizotomies[22, 23], and orthopedic surgeries[7, 24]. Baclofen is an important tool for treatment depending on the individual's needs and goals.

Given issues with access to more surgical interventions including intrathecal baclofen around the globe due to health system capabilities or lack of medical resources, access to oral medications could help provide more equity in the management of spasticity.

Currently, diazepam is the only alternative medicine on the WHO's EML and EMLc that has been used for spasticity. Spasticity, however, is not given as an indication although it is one of the oldest oral medications used to treat spasticity in children. There is level B evidence for its use in children[25]. Diazepam improves spasticity by potentiating the effects of gamma-aminobutyric acid (GABA) in the central nervous system. Diazepam, however, is very sedating and causes impaired memory/cognition and respiratory depression with higher doses[14]. People can also have paradoxical reactions to the medication and acute withdrawal from diazepam can be severe[14, 15].

## – Section 7: Treatment details

Baclofen acts at the spinal cord level to neuro-inhibit the monosynaptic reflex arc and is commonly used to treat spasticity in children[14]. Oral baclofen does not cross the blood brain barrier easily; therefore, relatively higher doses are needed for it to be effective[26]. Baclofen can also be sedating, but the sedating effects generally improve over several days to weeks[27]. Oral baclofen dosing is roughly based on body weight, and a typical starting dose is 2.5–5 mg/day, titrated up every few days to a maximum of 20-60 mg/day[28, 29].

Early investigators hypothesized that intrathecally infusing baclofen directly onto the spinal cord via pump would more effectively reduce spasticity than oral baclofen. The first report of treating spasticity in children with an intrathecal baclofen (ITB) pump was in 1985[30], and the United States Food and Drug Administration (FDA) approved ITB pumps for spasticity of cerebral origin in 1996. The intrathecal dose to reduce hypertonia is often only 1/1,000 of the oral dose since the intrathecal route bypasses the blood-brain barrier[31].

ITB can be used to treat children with hypertonia who are ambulatory or non-ambulatory and can treat both spasticity and dystonia. Typical treatment goals are facilitating care, decreasing discomfort, and improving function[32].

The ITB pump is a computerized pump with a reservoir for baclofen which is implanted subcutaneously, usually in the right lower quadrant of the abdomen. A catheter is passed subdermally from the pump to a lumbar vertebral interspace and then into the intrathecal space between the lower thoracic and upper cervical levels. Usually, a child weighing 15kg is big enough to accommodate a pump. The pump can infuse baclofen in different modes from a simple continuous constant dose to variable intermittent doses. The total daily doses can vary between 50 and 1,500 mcg/day depending on hypertonia severity, treatment efficacy, and baclofen tolerance. The dose is easily modified by changing the pump's dosing pattern using a radio frequency programmer which transmits information from a handheld computer to the implanted pump. A common initial infusion program is a total daily dose of 50-100 mcg at a simple continuous rate with baclofen concentration of 500 mcg/ml[20, 33]. The ITB dose and infusion mode are periodically adjusted as clinically appropriate. The onset of action of simple continuous infusion is 6-8 hours with peak effect at 24-48 hours, and onset of a large bolus dose is ½ to 1 hour with peak effect at 4 hours[31]. The ITB half-life is 3-5 hours[27]. The concentration of ITB can also vary, most commonly between 500 and 2,000mcg/ml[34].

The pump needs to be refilled every few months, with the frequency of refills dependent on dose[20]. Refills are done by inserting a needle through the skin into the pump reservoir. The pump’s battery life lasts typically 5 to 8 years, and the entire pump is exchanged when the battery is depleted.

# – Section 8: Review of evidence for benefits and harms

A review of the evidence for the benefits and potential harms of baclofen as a treatment for spasticity is overall supportive of its addition to the EML and EMLc. There is support for the use of intrathecal baclofen, and though there has been limited research on the use of oral baclofen, it has been reported to reduce spasticity and improve physical function and quality of life. As with many interventions for cerebral palsy, more conclusive evidence is limited by the small scale of clinical trials. Investigators often comment on the inherent difficulties in conducting large controlled trials in this population.

Despite being the preferred clinical intervention for spasticity, access to intrathecal baclofen is limited, given the costs associated with placement and maintenance of a baclofen pump. Though there is less evidence to support the efficacy of oral baclofen, it should nonetheless be included on the EML and EMLc as it has the potential to improve quality of life with limited risk of negative impact, especially in communities in which surgical interventions are inaccessible.

**Evidence of baclofen for treatment of spasticity due to cerebral palsy**

Eight different systematic reviews and meta-analyses have investigated the use of baclofen for management of spasticity in people with cerebral palsy. The summary of these studies is presented in Table 1.

*Intrathecal baclofen vs placebo*

The most recent systematic review and meta-analysis has been published in 2024. Masrour et al. [35] utilized the Cochrane Risk of Bias tool, the Risk of Bias in Non-randomized Studies - of Interventions (ROBINS-I) to assess the risk of bias in the studies included. The studies have been divided based on outcome measures, where eight of the 19 studies reported Modified Ashworth Scale (MAS) scores, while the remaining studies reported Ashworth Scale scores.

Overall, the study included 343 patients with CP diagnosis with a male-to-female ratio of 55.56%. The intervention assessed was the administration of intrathecal baclofen. In both sub-groups combined, a significant reduction in spasticity levels was observed (pooled SMD of -1.7000 (95% CI [-2.1546; -1.2454], p-value < 0.0001). Indeed, the measure of the pre-intervention score for spasticity (SD) was 3.2, compared to 1.91 post-intervention; a reduction of 40%. There were no significant differences observed when the sub-groups were analyzed separately. The pre-intervention average score (SD) for the MAS subgroup (eight studies and 157 participants) was 2.93 (0.78), and the post-intervention average MAS score (SD) was 1.82 (0.74), showing a 37.95% reduction. The pre-intervention average score (SD) for the Ashworth Scale subgroup (eleven studies and 186 participants) was 3.41 (0.79), and the post-intervention average Ashworth Scale (SD) was 1.98 (0.71), showing a 41.90% reduction. The SMD for the MAS subgroup was – 1.7845 (95% CI [-2.8704; -0.6986], I2 = 85.9%), and the SMD for the Ashworth Scale subgroup was – 1.4837 (95% CI [-1.8585; -1.1088], I2 = 19.2%). The findings of the review support the use of intrathecal baclofen for treatment of spasticity in cerebral palsy; however, authors also highlight that the findings have revealed significant evidence of publication bias among the included studies (severity of spasticity p-value = 0.000596 and motor function p-value = 0.0336).

Another key evidence in favor of intrathecal baclofen stems from a Cochrane Review published in 2015 [36]. The study included six RCTs that examined the efficacy of intrathecal baclofen and explored different outcome measures. While some RCTs compared the efficacy against placebo, other trials did not include a control group but included different outcome measures for the same intervention. The data obtained were unsuitable for the conduct of a meta-analysis, so the authors completed a qualitative summary instead. In total, 76 children with quadriplegic distribution, 15 with diplegia and four described as paraplegic in distribution were included. The age range of the participants in the included studies ranged from 4 to 27 years. The method of classification of the severity of cerebral palsy varied between studies and included modes of classification based on degree of spasticity and gross motor function. The trials included children with spasticity due to cerebral palsy and children with spasticity due to other disorders. Five included studies involved paired baclofen and placebo bolus intrathecal injection in the same individuals. Escalating doses of baclofen were given versus placebo in four studies. The dose range used was 10 to 100 Pg. One study trialed 50 Pg intrathecal injections of baclofen against placebo in a double-blind fashion. The study blind was broken after the completion of this step. If no positive response had occurred, subsequent higher doses of baclofen (75 Pg, 100 Pg) were given as open-label injections. The clinical measures of spasticity included were the Ashworth scale scores (pre and post intrathecal baclofen and placebo) in some of the studies, and Ashworth scores (at baseline and after treatment with intrathecal baclofen and placebo). The authors also noted that given the non-continuous variable of Ashworth scale, the included studies could not be combined into a single summary statistic. Another study has also utilized electrophysiological measures of spasticity (H-reflex and flexor reflex) as outcome measures. Two out of the

six studies have also included the PEDI caregiver assistance scale of the self-care domain as a primary outcome and the PEDI functional skills scale as a secondary outcome. The gross motor function GMFM-66 was used as a secondary outcome in two of the six studies included. All six studies included in this Cochrane review suggest intrathecal baclofen is effective for reducing spasticity in children with cerebral palsy. The outcomes include a) significant differences ($p<0.05$) in tone in the lower extremities between the placebo values and each of the baclofen dose values; b) statistically significant differences in mean Ashworth score in the lower limbs between treatment and control groups at four hours following injection of 50 Pg baclofen or placebo; c) a small but statistically significant alteration in Ashworth score in the upper limbs at each time point (two, four, six and eight hour post injection); d) Ashworth scores assessed at two, four and six hours after the effective intrathecal baclofen dose significantly decreased in comparison with baseline for all muscle groups except for the left hip flexors two hours after intrathecal baclofen administration; e) a statistically significant reduction in spasticity in four of the 22 muscle groups assessed in the treatment group compared to the control group at six months from baseline; f) positive difference in gross motor function (GMFM-66) in favor of the treatment group (improvement of mean 1.2 points (SD 2.3) versus worsening of mean -1.3 points (SD 3.0) in the control group, $p=0.028$) after six months of treatment. The evidence considered by this Cochrane review has shown that intrathecal baclofen is effective for reducing spasticity in children with cerebral palsy in the short-term and, despite being less clear, some of the studies considered have also shown efficacy to treat spasticity in the longer term (i.e., 6 months). The review highlights that these findings are limited by small sample sizes and methodological issues, including high or unclear risk of bias, in the studies in this review.

*Intrathecal baclofen vs other therapies*

Our searches have found only one systematic review that investigated the use of intrathecal baclofen in comparison with two approaches, selective dorsal rhizotomy and extracorporeal shockwave. Kudva et. al. [37], concluded that intrathecal baclofen is preferred due to its reversibility and customizable nature. Pumps can be easily removed or altered and doses of baclofen can be adjusted, which is not possible with the other treatment options. Intrathecal baclofen has shown the greatest efficacy on patients ranked IV and V through the gross motor function classification system (GMFCS) and evidence is also available for its efficacy in patients with GMFCS I-III. Indeed, participants included in the studies that met the inclusion criteria experienced statistically significant improvements in their MAS scores after intrathecal baclofen therapy, including those with severe spasticity (MAS > 3). Intrathecal baclofen therapy has been efficacious in reducing upper-limb spasticity; however, it may be notably more effective at reducing lower-limb spasticity. The authors conclude that intrathecal baclofen therapy can be considered for all patients with problematic, uncontrolled spasticity that interferes with daily life functions.

This study did not include a meta-analysis, thus direct comparison between the other treatments could not be made. However, the authors highlight that both dorsal rhizotomy and extracorporeal shockwave may also provide benefits and quality of life improvement. There are, though, several limitations with these procedures, which explains the fact that intrathecal baclofen is the most common and preferred choice of treatment. Dorsal rhizotomy is a permanent neurosurgery that, despite its efficacy, is a relatively unfamiliar surgical technique and its implementation is limited by the fact that only a few centers globally are able to perform it. This, together with chances of infection rate and high costs, limits its implementation, especially in low- and middle-income countries. Extracorporeal shockwave therapy is a relatively new procedure that has been demonstrated to reduce

spasticity in children and improve GMFM scores. However, most evidence is based on outcomes of studies in children and more trials are needed to assess its efficacy in adults. All in all, given the wider availability and proven efficacy, intrathecal baclofen is still the preferred choice to treat spasticity due to cerebral palsy.

*Efficacy of oral baclofen to treat spasticity*

Oral baclofen is commonly used to predict/assess responsiveness to intrathecal baclofen therapy in individuals with spasticity due to cerebral palsy. This approach is often taken because intrathecal baclofen therapy requires an invasive surgical procedure, so assessing a patient's tolerance and responsiveness to baclofen can help clinicians gauge whether the patient may benefit from the intrathecal route. As such, the availability and affordability of oral baclofen is of great importance.

Despite being available for decades, research on the efficacy of oral baclofen for treatment of spasticity is limited. Nevertheless, a systematic review designed to inform the development of a set of evidence-based interventions selected from clinical practice guidelines for Universal Health Coverage as part of the WHO Rehabilitation 2030 initiative (Damiano et al. [39]) recommended that oral baclofen be considered for adults with cerebral palsy, and oral or intrathecal baclofen for children with cerebral palsy (GMFCS levels IV or V).

A previous systematic review explored the effectiveness of oral baclofen in the treatment of spasticity in children and adolescents with cerebral palsy [38]. Six studies that included a total of 130 patients met the eligibility criteria. These have shown a great variability in the type of motor classification used, dosage of baclofen, and outcome measures, which creates barriers for a conclusive assessment. Consequently, there is conflicting evidence on the effectiveness of oral baclofen in reducing muscle tone or improving motor function or the level of activity. The main limitations of the studies relate to serious risk of bias, inconsistency of results, unpowered sample size, and publication bias. Authors have concluded that with the evidence available, it is not possible to support or refute the use of oral baclofen for reducing spasticity or improving motor function in children and adolescents with spastic cerebral palsy.

Nevertheless, in a systematic review designed to develop a set of evidence-based interventions selected from clinical practice guidelines for Universal Health Coverage as part of the WHO Rehabilitation 2030 initiative, Damiano et al. [39] recommended that oral baclofen be considered for adults with cerebral palsy, and oral or intrathecal baclofen for children with cerebral palsy (GMFCS levels IV or V).

In addition to systematic reviews, smaller studies have demonstrated baclofen’s benefit. Scheinberg, et al, conducted a double-blind, placebo controlled, randomized, crossover study looking at the effects of oral baclofen in 15 children with cerebral palsy. The authors reported a significant improvement in the modified Tardieu Scale in the patients receiving baclofen. They also found a significant improvement in their PEDI mobility scores and overall motor function.[40]

Lopez, et al, conducted a crossover trial with oral baclofen versus placebo in 20 children with cerebral palsy. The authors reported a significant improvement in the Ashworth Scale in children receiving baclofen. Ten children receiving oral baclofen had a marked improvement in their spasticity, whereas only 1 child receiving placebo had an improvement in their spasticity. They also reported more children who received oral

baclofen had an improvement in their activities of daily living (9 of 20 children) than children who received placebo (3 of 20 children). They did not see a difference in their Gross Motor Function Measure, but this measure may not have been sensitive enough to detect change during the study period. [41]

Calta, et al, conducted a double-blind, randomized, placebo controlled, crossover trial in 24 children with CP looking spasticity reduction and reported a 30% reduction in spasticity in the baclofen group. [42]

McKinlay, et al, conducted a double-blind, randomized, placebo controlled, crossover trial in 20 children with CP looking spasticity reduction and reported more improvement in spasticity in the baclofen group versus the placebo group, but the difference did not reach significance (p=0.125). They also reported no significant difference in manual dexterity and interstep distance.[43]

Milla, et al, conducted a double-blind, randomized, placebo controlled, crossover trial in 20 children with CP looking spasticity reduction and reported significant reduction in the Ashworth Scale in the baclofen group versus the placebo group. They also reported improvements in walking, scissoring, and passive range of motion in the baclofen group. [44]

The limited number of studies that explore the use of oral baclofen for treatment of spasticity due to cerebral palsy is contradictory with its wide use in clinical practice. We have, therefore, explored evidence on the use of oral baclofen for treatment of spasticity due to multiple causes. Studies using oral baclofen have reported significant improvement in flexion of the quadriceps in patients with multiple sclerosis when compared to a placebo (using the Ashworth scale) and subjective improvements in general function[45, 46]. Furthermore, one study showed the protective effects of oral baclofen on the deterioration in body musculature and metabolic profile that normally accompany spastic individuals with spinal cord injury [47]. In a more recent systematic review (2022), Dietz et. al. [48] investigated the efficacy of oral and intrathecal baclofen for treatment of spasticity in adults with spinal cord injury. Authors concluded that baclofen (oral and intrathecal) effectively improved spasticity outcome measures, though increased efficacy is observed through intrathecal administration.

All in all, oral baclofen has been widely used for treatment of spasticity and has been recommended by different clinical guidelines. It is commonly used to predict the response to intrathecal therapy before an invasive procedure is conducted. Given the higher cost associated with the intrathecal therapy (see section 10), oral baclofen presents a viable, if not the only alternative to those who cannot access the intrathecal administration.

The scarcity of data associated with oral baclofen warrants increased efforts to generate more robust data to further substantiate its wide use in clinical practice. Until such data is available to provide an absolute clear direction, we rely on clinical expertise and experience with the medication to determine which patients can derive benefit. The lack of data should not preclude the use of a medication that has had extensive use already and presents patients and their providers another treatment modality to improve their physical function and quality of life.

*Oral baclofen vs other therapies*

Alternative oral therapies to baclofen include diazepam (which is the only alternative medicine on the WHO's EML and EMLc that has been used for spasticity though this is not given as an indication) and tizanidine. The few studies comparing them suggest that baclofen is more efficacious than tizanidine and has fewer adverse side-effects than both alternatives. The studies are small and mostly conducted in the more immediate years after the approval of baclofen by the FDA. In addition most of these studies focused on patients with multiple sclerosis with very little difference between oral therapies.

Nevertheless, differences do exist. In a comparison of patients treated with oral baclofen versus diazepam, the efficacy was found to be similar in reducing spasticity, however, excessive daytime somnolence and tolerance were noted with diazepam [49]. In a study comparing tizanidine to oral baclofen in 1988, baclofen appeared to have greater efficacy. The side-effects of somnolence and xerostomia affected more patients using tizanidine and muscle weakness affected more patients treated with baclofen [50]. More recently a small study comparing diazepam and oral baclofen in children with CP found no difference in efficacy with only a slightly increased percentage of drowsiness for those treated with diazepam [51]. Other studies have underlined that diazepam is very sedating and causes impaired memory/cognition and respiratory depression with higher doses[14]. People can also have paradoxical reactions to the medication and acute withdrawal from diazepam can be severe[14, 15].

**Adverse effects, tolerance and safety**

The use of baclofen should be managed carefully to optimize its benefits and minimize adverse effects. One of the considerations with baclofen involves the potential for adverse reactions with sudden discontinuation, which may include symptoms like hallucinations, seizures, increased muscle tone, or, in rare cases, more severe complications. To avoid this, it is generally recommended to gradually taper the dosage, unless a clinical situation requires a faster approach.

In pregnant patients who use baclofen regularly, neonates may experience mild withdrawal symptoms after birth, such as increased muscle tone or jitteriness. In these cases, a gradual dose reduction before delivery is often advised when feasible. If tapering is not possible, caregivers should monitor the newborn for any signs of withdrawal.

Baclofen may also cause drowsiness or sedation in some patients, particularly when starting treatment or adjusting the dose. As with many medications that act on the central nervous system, combining baclofen with alcohol or other sedatives can enhance these effects, so patients are typically advised to avoid such combinations.

Some individuals with certain pre-existing conditions may need closer monitoring when using baclofen. For instance, patients with a history of stroke may not experience significant improvement in spasticity and may have reduced tolerance for the drug, while those with psychiatric conditions, such as psychotic disorders or schizophrenia, may experience a temporary increase in symptoms and benefit from closer supervision. In patients prone to autonomic dysreflexia, the presence of specific stimuli or sudden withdrawal of baclofen could potentially trigger an episode, while individuals with epilepsy may experience some variability in seizure control, highlighting the importance of individualized care [52].

In terms of musculoskeletal effects, baclofen may affect patients who rely on muscle spasticity to maintain posture or mobility. In such cases, dose adjustments can help balance therapeutic benefits with maintaining functional stability. Additionally, some women using baclofen long-term have reported the development of ovarian cysts, though these typically resolve without intervention.

Intrathecal baclofen pump therapy also carries risks associated with the surgical procedure required to place the pump, as well as the injections required to refill the pump later.

Baclofen's varied effects emphasize the importance of tailored dosing and monitoring, allowing patients to achieve relief from spasticity while managing any potential side effects. For many patients, the therapeutic benefits of baclofen are meaningful, and with individualized management, it remains a valuable option for improving comfort and function.

Finally, the lack of alternative evidence-based treatment options for this marginalized population in other areas should also be taken into consideration. According to a systematic review by Novak et al. (2020) [53], in the context of all interventions for cerebral palsy, intrathecal baclofen is considered effective as a treatment for spasticity and graded "do it" (green light, in the top 14% of 398 intervention outcomes), whereas oral baclofen is considered probably effective for the same treatment and graded "probably do it" (yellow light, weak positive). This study also recommended the use of ITB to improve pain and gross motor and walking skills in children with CP.

**Overview of systematic reviews**

Table 1. Systematic reviews of baclofen as a treatment for spasticity

| **Study** | **Type of study** | **Number of participants** | **Objectives** | **Main findings** |
|---|---|---|---|---|
| Masrour et al., 2024 | Systematic review and meta-analysis | 343 | To investigate the impact of intrathecal baclofen therapy on severe spasticity and motor function in patients with cerebral palsy. | Despite the risk of complications, intrathecal baclofen has a significant impact on the reduction of spasticity. A small but statistically significant improvement in motor function was also noted in a group of patients. |
| Dietz et al., 2022 | Systematic review and meta-analysis | 591 | Evaluate efficacy in spasticity reduction, functional changes, dosing and side effects of intrathecal and oral baclofen in adults with spinal cord injury | Baclofen effectively improved spasticity outcome measures (both oral and intrathecal), with increased efficacy through intrathecal administration. |

| Study | Type of study | Number of participants | Objectives | Main findings |
|---|---|---|---|---|
| Damiano et al., 2021 | Systematic review | n/a | To develop a set of evidence-based interventions selected from clinical practice guidelines for Universal Health Coverage as part of the WHO Rehabilitation 2030 initiative | Recommendations:<br>● Consider oral baclofen for adults with cerebral palsy;<br>● Consider oral or intrathecal baclofen for children with cerebral palsy (GMFCS levels IV or V). |
| Kudva et al., 2021 | Systematic review | 312 | To update the current neuromodulation procedures for the treatment of spasticity associated with CP in all age groups. | Intrathecal baclofen, selective dorsal rhizotomy and extracorporeal shockwave therapy were each found to have improvement of spasticity at a rate that achieved statistical significance. ITB pump therapy is an all-encompassing method of treating spasticity in children from CP, as it allows for a less invasive treatment that can be titrated to individual patient needs; however, its disadvantages include its long-term maintenance requirements. |
| Novak I et al., 2020 | Systematic review | n/a | To summarize the best available evidence interventions for preventing and managing cerebral palsy in 2019 | In the context of all interventions for cerebral palsy, intrathecal baclofen is considered effective as a treatment for spasticity and graded “do it” (green light, in the top 14% of 398 intervention outcomes). Oral baclofen is considered probably effective for the same treatment and graded “probably do it” (yellow light, weak positive). |

| Study | Type of study | Number of participants | Objectives | Main findings |
|---|---|---|---|---|
| Ferrer Pastor, M. et al, 2019 [54] | Systematic review | n/a | To review various interventions for treating spasticity in adults with acquired brain damage | Intrathecal baclofen therapy is an effective option for managing severe spasticity. |
| Buizer A et al., 2018 [55] | Systematic review | 469 | To investigate the effects of continuous intrathecal baclofen (ITB) therapy in children with cerebral palsy (CP) and other neurological conditions. | Continuous ITB may be effective in reducing spasticity and dystonia in CP, as well as other neurological conditions, and may improve the ease of care and quality of life of children with CP, but the level of evidence is low due to the low scientific quality of primary studies. |
| Navarrete-Opazo A et al., 2016 | Systematic review | 130 | To systematically review the effectiveness of oral baclofen versus placebo or other antispastic oral medications in terms of body function, level of activity, and quality of life in children and adolescents with spastic cerebral palsy who are younger than 18 years. | There are insufficient data to support or refute the use of oral baclofen for reducing spasticity or improving motor function in children and adolescents with spastic cerebral palsy due to the overall methodological quality of the studies conducted on this topic being low. |
| Hasnat MJ et. al., 2015 | Cochrane review | 95 | To determine whether intrathecal baclofen is an effective treatment for spasticity in children with cerebral palsy | Limited short-term evidence that intrathecal baclofen is an effective therapy for reducing spasticity in children with cerebral palsy. However, validity of the evidence is constrained by small sample sizes and methodological issues in some studies. |

# – Section 9: Summary of recommendations in current clinical guidelines

### Recommendations in existing WHO guidelines

Package of interventions for rehabilitation (Module 3: Neurological conditions), World Health Organization, 2023 (ISBN: 9789240071155)

> *5.4 Evidence tables for cerebral palsy*
>
> *Consider oral baclofen if spasticity is contributing to one or more of the following: discomfort or pain; muscle spasms (for example, night-time muscle spasms); functional disability. Baclofen is particularly useful if a sustained long-term effect is desired (for example, to relieve continuous discomfort or to improve motor function).*
>
> *If oral diazepam is initially used because of its rapid onset of action, consider changing to oral baclofen if long-term treatment is indicated.*

### Recommendations in other current clinical guidelines

Table 2. Recommendations in current clinical guidelines

| Guideline | Year | Reference | Recommendations |
|---|---|---|---|
| Brazil: Brazilian Medical Association, “Spasticity - Treatment with Baclofen” | 2016 | https://amb.org.br/files/_DIRETRIZES/Espasticidade%20-%20tratamento%20com%20Baclofeno_autores_Marta/files/assets/common/downloads/publication.pdf | Intrathecal baclofen using an implantable infusion pump in children with spastic cerebral palsy improves function and quality of life in up to 6 months. |
| France: French Agency for Health Product Safety, “Medicamental Treatments of Spasticity - Good Practice Recommendations ” | 2009 | https://ansm.sante.fr/uploads/2021/03/11/9771c86bf98d7af854c30b202846ab35.pdf | 3. Intrathecal baclofen is an effective treatment of spasticity. (...) |

| Guideline | Year | Reference | Recommendations |
|---|---|---|---|
| Italy: Italian Society of Physical and Rehabilitative Medicine & Italian Society of Neuropsychiatry of Childhood and Adolescence, “Rehabilitation of Children with Cerebral Palsy - Care Pathways” | 2022 | https://simfer.it/care-pathways-della-paralisi-cerebrale-infantile/ | Recommendation 14: For the treatment of pain caused by spasticity and dystonia in children with CP (2-18 years), a conditional recommendation is expressed in favor of:<br>● intrathecal baclofen;<br>● (...)<br><br>Recommendation 18: It is recommended to try baclofen and/or botulinum toxin to reduce spasms and pain in an attempt to improve sleep behavior. |
| UK: NICE, Guideline CG145 (Spasticity in under 19s: management) | 2016 (last update) | https://www.nice.org.uk/guidance/cg145 | 1.4.2. Consider oral baclofen if spasticity is contributing to one or more of the following:<br>● discomfort or pain<br>● muscle spasms (for example, night-time muscle spasms)<br>● functional disability.<br>Baclofen is particularly useful if a sustained long-term effect is desired (for example, to relieve continuous discomfort or to improve motor function).<br><br>1.6.1. Consider treatment with continuous pump-administered intrathecal baclofen in children and young people with spasticity if, despite the use of non-invasive treatments, spasticity or dystonia are causing difficulties with any of the following:<br>● pain or muscle spasms<br>● posture or function<br>● self-care (or ease of care by parents or carers). |
| UK: NICE, Guideline NG119 (Cerebral palsy in adults) | 2024 (last update) | https://www.nice.org.uk/guidance/ng119 | 1.3.6. Consider enteral baclofen (N.B. off-label use) as the first-line drug treatment for adults with cerebral palsy and generalised spasticity causing:<br>● functional impairment or<br>● pain or<br>● spasms. |

| Guideline | Year | Reference | Recommendations |
|---|---|---|---|
| USA: American Academy for Cerebral Palsy and Developmental Medicine: Pharmacological and neurosurgical management of cerebral palsy and dystonia: Clinical practice guideline update | 2024 | https://doi.org/10.1111/dmcn.15921 | Oral/enteral baclofen can be viewed as a first-line consideration. Baclofen may be particularly useful in individuals with both dystonia and spasticity. Baclofen may be particularly useful in individuals with both dystonia and spasticity. In individuals with CP and generalized dystonia causing interference, we suggest the use of oral/enteral baclofen (conditional recommendation, very low-certainty evidence). A trial is reasonable for individuals with CP and generalized dystonia causing interference, who value the potential for relief of dystonia symptoms over avoiding the risk of adverse effects (e.g. central nervous system [CNS] drowsiness, dizziness, confusion). |
| USA: American Academy of Physical Medicine and Rehabilitation 2024 consensus guidelines on spasticity assessment and management | 2024 | https://onlinelibrary.wiley.com/doi/10.1002/pmrj.13211 | SUR-1: The AAPM&R Spasticity TEP recommends use of intrathecal baclofen pump therapy (ITB) as an effective treatment of spinal or cerebral origin spasticity in appropriately identified patients. |

# – Section 10: Summary of available data on comparative cost and cost-effectiveness

### Intrathecal baclofen

Several studies have been conducted on cost-effectiveness for intrathecal baclofen [56, 57, 58, 59]. Current economic literature supports the use of ITB therapy at least in the short-term. ITB is effective but invasive, making it an important option for patients with severe spasticity in cerebral palsy who do not benefit from oral therapies.

In addition to the cost of the medicine, intrathecal baclofen requires a surgical procedure to install the pump and regular interventions to refill and maintain the pump, as well as further surgical procedures to replace the pump every five to eight years. One study [59] found that, on average, intrathecal baclofen therapy increased the 5-year cost of treatment by $49 000 relative to alternative treatment. However, this was accompanied by an average gain of 1.2 quality-adjusted life-years. The net result was an incremental cost-effectiveness ratio of $42 000 per quality-adjusted life-year, a figure well within the $50 000 to $100 000 range that is widely accepted as offering good value for the money. However, the additional cost and the need for surgical expertise mean that intrathecal baclofen is not available in many low- and middle-income countries.

### Oral baclofen

Oral baclofen is widely available in both high- and low- and middle-income countries, and a comparative overview of its cost is presented in Table 3. It is a generic medication and there are no recent studies on its cost-effectiveness compared to other treatments.

Table 3. Summary of available data on comparative cost and cost-effectiveness

| **Baclofen Oral 10mg** | | | | | |
|---|---|---|---|---|---|
| | **Quantity** | **Price (local currency)** | **Price in USD*** | **Price per tablet (USD)** | **Average monthly price for maintenance dose** (USD)** |
| **Argentina** | 60 tablets | 23,470.00 | 23.71 | 0.40 | 36.00 |
| **Australia** | 100 tablets | 28.34 | 18.56 | 0.19 | 17.10 |
| **Bangladesh** | 10 tablets | 70.39 | 0.59 | 0.05 | 4.50 |
| **Brazil** | 20 tablets | 13.99 | 2.48 | 0.12 | 10.80 |
| **France** | 30 tablets | 3.30 | 3.51 | 0.11 | 9.90 |
| **Greece** | 50 tablets | 4.20 | 4.56 | 0.09 | 8.10 |
| **India** | 10 tablets | 124.48 | 1.48 | 0.14 | 12.60 |
| **Italy** | 50 tablets | 17.90 | 19.43 | 0.39 | 35.10 |
| **Jordan** | 50 tablets | 5.52 | 7.78 | 0.16 | 14.40 |
| **Kenya** | 84 tablets | 1,050.00 | 8.17 | 0.09 | 8.10 |
| **Lebanon** | 50 tablets | 589,947.00 | 6.59 | 0.13 | 11.86 |
| **Mauritius** | 28 tablets | 261.80 | 5.68 | 0.20 | 18.00 |
| **Nepal** | 10 tablets | 160.42 | 1.19 | 0.11 | 9.90 |
| **Nigeria** | 84 tablets | 10,000.00 | 6.09 | 0.07 | 6.30 |
| **PR China** | 30 tablets | 75.80 | 10.65 | 0.35 | 31.50 |
| **Portugal** | 20 tablets | 3.53 | 3.83 | 0.19 | 17.10 |
| **Switzerland** | 200 tablets | 47.80 | 55.24 | 0.28 | 25.20 |
| **Tunisia** | 10 tablets | 6,200.00 | 2.03 | 0.20 | 18.00 |
| **USA** | 30 tablets | 12.00 | 12.00 | 0.40 | 36.00 |

* Prices converted to USD using the UN conversion rates
** Maintenance dose considered: 10mg three times daily

# – Section 11: Regulatory status, market availability and pharmacopeial standards

Oral baclofen was first approved by the United States of America Food and Drug Administration (U.S. FDA) for use in spasticity in 1977; baclofen in its intrathecal formulation was subsequently approved in 1984. Baclofen is also approved by other regulatory agencies including the European Medicines Agency (EMA), Swissmedic, and Japanese Health Authority PMDA.

According to the WHO Global Essential Medicines Dashboard and WHO's National Essential Medicines Lists Repository, baclofen is currently included in the national EML of at least 46 countries. Though this number is encouraging, many countries are yet to include baclofen in their national lists. This is of concern, especially given the high impact of spasticity caused by the different disorders and the fact that baclofen is the first-line therapy for treatment of spasticity.

The inclusion of baclofen on the WHO EML and EMLc will contribute to increased prioritization of the medicines within health systems, consequently leading to actions to improve its access.

Pharmacopeial standards:

United States: https://pubchem.ncbi.nlm.nih.gov/compound/4-_4-Chlorophenyl_-2-pyrrolidinone#section=Chemical-Co-Occurrences-in-Literature

European pharmacopeia: https://sds.edqm.eu/pdf/SDS/EDQM_202100168_1.0_SDS_EN.pdf?ref=1730320458

British pharmacopeia: https://www.pharmacopoeia.co.uk/content/file/products/leaflets/BPCRS-Leaflet_Cat-028_BPCRS3793_1.pdf

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Tuesday 29 October 2024

**Dear Members of the Expert Committee,**

We, the undersigned, write in support of the addition of the medication baclofen to the World Health Organization's (WHO) Model Essential Medicines List (EML) and Model Essential Medicines List for Children (EMLc). Collectively, we have witnessed the profound impact that baclofen can have on the lives of individuals living with spasticity due to neuromuscular disorders, stroke, spinal cord injuries, traumatic brain injuries, and cerebral palsy. This medication can improve quality of life and functional outcomes for patients with these conditions.

Spasticity is a common and debilitating symptom characterized by muscle stiffness, pain, and impaired movement, making basic activities of daily living challenging. Baclofen reduces spasticity, helping individuals move more easily, and experience less pain. These benefits not only improve quality of life, improve sleep, but also enhance the efficacy of rehabilitation therapies, contributing to long-term improvements in patient outcomes.

Cerebral Palsy Alliance (CPA) is one of the largest non-profit disability service providers in Australia, with an 80-year history of innovation and research. CPA supports more than 5,000 Australians with cerebral palsy and similar complex physical conditions, many of whom benefit from baclofen to treat spasticity.

In Australia, baclofen in the form of oral 10mg tablets is widely available as a prescription drug, subsidised through the Federal Government's Pharmaceutical Benefits Scheme (PBS) as of September 2024. Baclofen is an approved and licensed medicine assessed by the Therapeutic Goods Administration (TGA) for quality, safety and efficacy and registered on the Australian Register of Therapeutic Goods (ARTG).

In the globally accepted 'traffic light' system for categorising and evaluating effective treatments for cerebral palsy, intrathecal baclofen is considered a 'green light' intervention for treating spasticity. In other words, a systematic review of the best available evidence has found it to be an effective medical intervention for cerebral palsy, the most common lifelong physical disability globally. As a passionate supporter of global health equity, we are also supportive of baclofen's

addition to the EML and EMLc for the significant opportunity for improved access this will afford people with disabilities in low- and middle-income countries (LMICs).

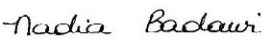
In many LMICs, access to medications like baclofen is limited, leaving millions of individuals with disabling conditions untreated or undertreated. By adding baclofen to the EML and EMLc, WHO can ensure greater accessibility to a cost-effective, essential therapy that significantly improves function and independence for those living with spasticity and related disorders. Furthermore, the addition of baclofen to the EML and EMLc aligns with WHO's mission of achieving universal health coverage, reducing health inequities, and improving the health and well-being of vulnerable populations.

We strongly support the addition of baclofen to the EML and EMLc. This is a meaningful step in reducing health disparities and improving access to this life-changing medication.

Please reach out for further information or if you would like to connect directly with experts in the area of cerebral palsy treatment, or with people with lived experience of cerebral palsy to speak to the effectiveness and benefits of baclofen.

Sincerely,

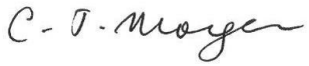
**Mr Rob White**
*Chief Executive Officer,*
*Cerebral Palsy Alliance*



**Professor Nadia Badawi AM**
*CP Alliance Chair of Research, The University of Sydney and Medical Director, Grace Centre for Newborn Intensive Care, The Children's Hospital at Westmead*

**Professor Iona Novak AM**
*Head of Research Translation, CPA Research Institute, The University of Sydney*

**Dr Simon Paget**
*Paediatric Rehabilitation Medicine Physician, the Children's Hospital at Westmead*



**Adj A/Prof Cathy Morgan**
*Principal Research Fellow and Program Lead Early Detection & Early Intervention, CPA Research Institute*

Call: 1300 888 378 (Mon-Fri 8:00am – 5:00pm)
Email: ask@cerebralpalsy.org.au
Visit: cerebralpalsy.org.au
ABN 45 000 062 288

Cerebral Palsy Alliance
PO Box 171
Forestville NSW 2087
Australia

World Health Organization

20 Avenue Appia
1211 Geneva
Switzerland

October 28, 2024

Dear Members of the Expert Committee,

We, the undersigned, write in support of the addition of baclofen to the World Health Organization's (WHO) Model Essential Medicines List (EML) and Model Essential Medicines List for Children (EMLc). Collectively, we have witnessed the profound impact that baclofen can have on the lives of individuals living with spasticity due to neuromuscular disorders, stroke, spinal cord injuries, traumatic brain injuries, and cerebral palsy. This medication can improve quality of life and functional outcomes for patients with these conditions.

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In many low- and middle-income countries, access to medications like baclofen is limited, leaving millions of individuals with disabling conditions untreated or under-treated. By adding baclofen to the EML and EMLc, WHO can ensure greater accessibility to a cost-effective, essential therapy that significantly improves function and independence for those living with spasticity and related disorders. Furthermore, the addition of baclofen to the EML and EMLc aligns with WHO's mission of achieving universal health coverage, reducing health inequities, and improving the health and well-being of vulnerable populations.

We strongly support the addition of baclofen to the EML and EMLc. This is a meaningful step in reducing health disparities and improving access to this life-changing medication.

Sincerely,

BEATRIZ SANTOS VIEIRA:35192977878

Assinado de forma digital por BEATRIZ SANTOS VIEIRA:35192977878
Dados: 2024.10.29 08:23:04 -03'00'

Beatriz Santos Vieira
President

Instituto Nossa Casa – Um lugar para falar sobre paralisia cerebral
Organização da Sociedade Civil
CNPJ: 29.116.990/0001-00
Rua Cumaru, 98, 13098-324, Campinas – SP
www.nossacasa.org.br

香港大学深圳医院
The University of Hong Kong-Shenzhen Hospital

World Health Organization
20 Avenue Appia
1211 Geneva
Switzerland
Oct.29th， 2024

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Sincerely,

Lin Feng
Assistant Consultant of Pediatric Orthopedics
Hongkong University, Shenzhen Hospital
Shenzhen, Guangdong Province
P.R.China

地址：深圳市福田区海园一路一号
1，Haiyuan1st Road,Futian District,Shenzhen
网站 ： www.hku-szh.org 电话 ： 0755-86913333
邮箱 ： info@hku-szh.org 传真 ： 0755-86913108
邮编 ： 518053 国际医疗中心 ： 8691 3388
预约电话 ： 0755-8691 3399

FONDATION PARALYSIE CÉRÉBRALE



World Health Organization
20 Avenue Appia
1211 Geneva
Switzerland

October 30th 2024

Dear Members of the Expert Committee,

We, the undersigned, write in support of the addition of baclofen to the World Health Organization's (WHO) Model Essential Medicines List (EML) and Model Essential Medicines List for Children (EMLc). Collectively, we have witnessed the profound impact that baclofen can have on the lives of individuals living with spasticity due to neuromuscular disorders, stroke, spinal cord injuries, traumatic brain injuries, and cerebral palsy. This medication can improve quality of life and functional outcomes for patients with these conditions.

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We strongly support the addition of baclofen to the EML and EMLc. This is a meaningful step in reducing health disparities and improving access to this life-changing medication.

Sincerely,

Dr Alain Chatelin
Chairman
ac@cerebrale.org

#fightthestroke

World Health Organization
20 Avenue Appia
1211 Geneva
Switzerland

*Milano, 26/10/2024*

Dear Members of the Expert Committee,

We, the undersigned, write in support of the addition of baclofen to the World Health Organization's (WHO) Model Essential Medicines List (EML) and Model Essential Medicines List for Children (EMLc). Collectively, we have witnessed the profound impact that baclofen can have on the lives of individuals living with spasticity due to neuromuscular disorders, stroke, spinal cord injuries, traumatic brain injuries, and cerebral palsy. This medication can improve quality of life and functional outcomes for patients with these conditions.

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In many low- and middle-income countries but also in our own country, access to medications like baclofen is limited, leaving millions of individuals with disabling conditions untreated or under-treated. By adding baclofen to the EML and EMLc, WHO can ensure greater accessibility to a cost-effective, essential therapy that significantly improves function and independence for those living with spasticity and related disorders. Furthermore, the addition of baclofen to the EML and EMLc aligns with WHO's mission of achieving universal health coverage, reducing health inequities, and improving the health and well-being of vulnerable populations.

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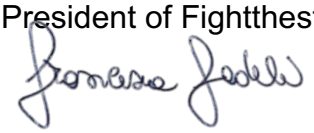
Sincerely,
Francesca Fedeli
President of Fightthestroke Foundation



Fight the Stroke Foundation E.T.S. – Via C. Gluck 35 – 20125 Milano (MI), Italy
www.fightthestroke.org tel.+39.333.2459267 Fax +39.02.66984153 C.F./P.IVA 97688330154
IBAN: IT51P0306909606100000131356
info@fightthestroke.org - fightthestroke@legalmail.it

Our Lady Of Peace Center
for Persons with Disabilities

مركز سيدة السلام
للأشخاص ذوي الإعاقة

World Health Organization
20 Avenue Appia
1211 Geneva
Switzerland

28/10/2024

Dear Members of the Expert Committee,

We, the undersigned, write in support of the addition of baclofen to the World Health Organization's (WHO) Model Essential Medicines List (EML) and Model Essential Medicines List for Children (EMLc). Collectively, we have witnessed the profound impact that baclofen can have on the lives of individuals living with spasticity due to neuromuscular disorders, stroke, spinal cord injuries, traumatic brain injuries, and cerebral palsy. This medication can improve quality of life and functional outcomes for patients with these conditions.

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We strongly support the addition of baclofen to the EML and EMLc. This is a meaningful step in reducing health disparities and improving access to this life-changing medication.

Sincerely,
Wafiqa Antone Deeb
Director of rehabilitation, education and development.
Our Lady Of Peace Center for persons with disabilities – Jordan.

Our Lady Of Peace Centre
Latin Vicariate Jordan

هاتف ٠٦-٤٢٩١٩٩٠ ٦ ٩٦٢+ - فاكس ٤٢٩١٩٩٢ ٦ ٩٦٢+ - ص.ب ٨٥١٣٧٩ عمان ١١١٨٥ الأردن
Phone: +(962-6) 4291990-1 - Fax: +(962-6) 4291992 - Facebook: Our Lady Of Peace Centre - P.O.B. 851379 Amman 11185 Jordan

THE AGA KHAN UNIVERSITY

*Faculty of Health Sciences*
*Medical College*

6th November 2024

WHO
Committee for the model list of essential medicines and model list of essential medicines for children.
Geneva, Switzerland

Dear Sir,

Subject: Advocacy for the Global Inclusion of Baclofen as an Essential Drug

I am a pediatric neurologist at the Aga Khan University Hospital in Nairobi, Kenya, where I have catered to over 2,500 patient visits each year for the last 14 years. A significant number of children and adolescents in this practice suffer from disabling spasticity that frequently results from birth asphyxia. A smaller proportion present with spasticity and weakness due to stroke related to Sickle cell disease. Oral baclofen, in our experience, has been a critical medication in relieving their pain and improving their daily functioning.

I am writing to urge the consideration of Baclofen as an essential drug in healthcare systems worldwide. Its accessibility in all facilities that receive these referrals can have profound implications for millions of patients' quality of life, mobility, and overall well-being.

1. Clinical Importance of Baclofen
Baclofen works by acting on the central nervous system to reduce muscle rigidity, spasms, and pain associated with spasticity. For individuals with neurological impairments, spasticity can severely limit mobility, independence, and daily functioning. In severe cases, untreated spasticity can lead to complications such as joint deformities, chronic pain, and pressure sores. Baclofen's ability to manage these symptoms is invaluable, providing relief and enabling more independent living.

2. Safety and Efficacy Profile
The safety and efficacy of Baclofen have been well-documented in clinical settings. Baclofen has been shown to significantly improve the quality of life, increase comfort, and reduce the risk of secondary complications in spasticity patients. It is generally well-tolerated, with a safety profile that makes it suitable for long-term management in adults and children.

AK 963

*3rd Parklands Avenue, off Limuru Road, P. O. Box 30270, GPO 00100, Nairobi, Kenya*
*Telephone: +254 20 366 2107/2109; Fax: +254 20 374 4035*

3. Cost-Effectiveness and Affordability

Baclofen is an affordable drug, making it accessible for inclusion in healthcare programs across developed and developing nations. Its cost-effectiveness is also beneficial to healthcare systems, as it reduces the need for more expensive interventions or hospitalizations associated with untreated spasticity.

4. Global Accessibility and Need

Despite its effectiveness, Baclofen remains inaccessible in many regions, particularly in low- and middle-income countries. The absence of Baclofen from essential drug lists in these areas creates a critical gap in care for individuals with spasticity. By including Baclofen as a crucial drug, global health organizations can play a pivotal role in reducing health disparities and improving the quality of life for individuals with neurological conditions.

Conclusion

In summary, including Baclofen as an essential medication can significantly improve health outcomes for patients with spasticity globally. Its proven efficacy, safety, affordability, and role in reducing healthcare costs make it a necessary addition to essential medicine lists worldwide. I strongly advocate for policy efforts to increase access to Baclofen to meet this vital health need.

Thank you for considering this request to recognize Baclofen as an essential global drug. I am confident that this measure will make a profound difference in the lives of those affected by spasticity and contribute to more equitable healthcare access. This action will encourage governments and other stakeholders likewise to support the provision of Baclofen.

Sincerely,

Dr. Pauline Samia
Chair, Department of Paediatrics and Child Health

AK 963

*3rd Parklands Avenue, off Limuru Road, P. O. Box 30270, GPO 00100, Nairobi, Kenya*
*Telephone: +254 20 366 2107/2109; Fax: +254 20 374 4035*

# CEREBRAL PALSY CENTER

CpCenter House. Eseosa Uwa Close. Lakowe, Ibeju-Lekki, Lagos
**T:** 234 803 348 2792, 0703 244 3664, 0802 124 3022
**E:** info@cpcenter.com.ng **W:** www.cpcenter.com.ng

*...improving the quality of lives of people with CP*


World Health Organization

20 Avenue Appia

1211 Geneva

Switzerland

DATE

Dear Members of the Expert Committee,

I, the undersigned, write in support of the addition of baclofen to the World Health Organization's (WHO) Model Essential Medicines List (EML) and Model Essential Medicines List for Children (EMLc). Collectively, we have witnessed the impact that baclofen can have on the lives of individuals living with spasticity due to neuromuscular disorders, stroke, spinal cord injuries, traumatic brain injuries, and cerebral palsy. This medication can improve quality of life and functional outcomes for patients with these conditions.

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We strongly support the addition of baclofen to the EML and EMLc. This is a meaningful step in reducing health disparities and improving access to this life-changing medication.

Sincerely,

Nonyelum Nweke (Founder/CVO)

ANGELS' HOME
WELFARE ORGANISATION
Centre For The People With Disabilities

World Health Organization
20 Avenue Appia
1211 Geneva
Switzerland

DATE October 28, 2024

Dear Members of the Expert Committee,

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Sincerely,

Morris Khurshid
Chief Executive officer
Angels Home Welfare organization

**dd:** Chamkani chowk, Inkalab Road: opp to Alied School Peshawar,
ear bara Bridge. **Ph:** +92 91 2604071.
angelshomepak@gmail.com
Angel's Home Welfare Organization
www.angelshomepak.info
Angel's Home Welfare Organization

10 November 2024

World Health Organization
Committee for the Model List of Essential Medicines and Model list of Essential Medicines for Children
20 Avenue Appia
1211 Geneva
Switzerland

Dear Members of the Expert Committee

**LETTER OF SUPPORT FOR THE ADDITION OF BACLOFEN TO THE WHO ESSENTIAL MEDICINES LIST**

The Southern African Academy of Childhood Disability (SA-ChilD) is a member of the International Alliance of Academies of Childhood Disability. SA-ChilD supports the addition of baclofen to the World Health Organization's (WHO) Model Essential Medicines List (EML) and Model Essential Medicines List for Children (EMLc).

In our context in Southern Africa, to make a medication more readily available and optimise pricing, it is desirable for it to be part of the national essential drugs list. Having it in the WHO drugs list helps national medicines control authorities more likely to consider a medication. This will improve access overall. Otherwise we end up with only benzodiazepines available for tone management in our low income settings. Whilst oral baclofen is not optimal in all cases it can improve quality of life for individuals and families and will hopefully pave the way for greater accessibility of other means of baclofen delivery.

Another issue is that in the event that baclofen is taken as an option for an individual patient at this time, there is no way to guarantee its availability if it is not on the national list and this risks children and adults who need it going into acute withdrawal with tone crises.

We strongly support the addition of baclofen to the EML and EMLc. This is a meaningful step in reducing health disparities and improving access to this life-changing medication.

Yours sincerely,

Gillian Saloojee

*Dr. Gillian Saloojee*
*Chairperson: SA-ChilD*

FUNDACIÓ aspace Catalunya

Barcelona, 10/20/2024

**Dear Members of the Expert Committee,**

We, as **Fundació Aspace Catalunya** write in support of the addition of baclofen to the World Health Organization's (WHO) Model Essential Medicines List (EML) and Model Essential Medicines List for Children (EMLc). Collectively, we have witnessed the profound impact that baclofen can have on the lives of individuals living with spasticity due to neuromuscular disorders, stroke, spinal cord injuries, traumatic brain injuries, and cerebral palsy. This medication can improve quality of life and functional outcomes for patients with these conditions.

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**Additional Information: Availability, Price, and Regulatory Status in Spain**

In Spain, oral baclofen 10 mg is available and is primarily used to treat spasticity associated with various neurological conditions, such as cerebral palsy, stroke, multiple sclerosis and spinal cord injuries.

- **Availability:** Baclofen is approved and accessible in pharmacies nationwide, typically by prescription only. It is available in both generic form and under specific brand names, with the 10 mg tablet being the most common formulation.
- **Price:** The price of 10 mg baclofen is relatively affordable, as it is partially covered by the Spanish social security system for patients with a prescription. This co-payment system significantly reduces costs for users, who only pay a portion based on their circumstances. However, prices can vary depending on the brand and the co-payment policy.
- **Regulatory Status:** In terms of regulation, baclofen is approved by the Spanish Agency of Medicines and Medical Devices (AEMPS). Its use requires a medical prescription due to potential side effects and the need for monitoring by a healthcare professional.

**Consultes Externes**

C. dels Tres Pins, 31-35 (Parc de Montjuïc) 08038, Barcelona

We strongly support the addition of baclofen to the EML and EMLc. This is a meaningful step in reducing health disparities and improving access to this life-changing medication.

**Sincerely,**

**DR. TAMARA BIEDERMANN VILLAGRA**
Md, PMR, EMDOS, BBA
Director of Health Services
Telf: 93 325 83 00
tbiedermann@aspace.cat/www.aspace.cat

FUNDACIÓ aspace Catalunya

World Health Organization
20 Avenue Appia
1211 Geneva
Switzerland

October 30th, 2024

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Sincerely,

Micah Niermann MD

Dr. Micah Niermann
Chief Medical Officer
Gillette Children's Specialty Healthcare

Shirley Ryan Abilitylab
355 E. Erie St., Chicago, IL 60611 | 844.355.ABLE (2253) | sralab.org

November 5, 2024

To: WHO
Committee for the Model List of Essential Medicine and Model List of Essential Medicine for Children
Geneva, Switzerland

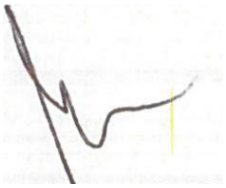
I am writing this letter to support the inclusion of baclofen for the treatment for spasticity in children with cp. Baclofen is standard of care within the United States and has been extensively studied by the NIH, Population Pharmacokinetics of Oral Baclofen in Pediatric Patients with Cerebral Palsy including safety and efficacy, J Pediatr. 2014 May; 164(5): 1181–1188.e8. doi:10.1016/j.jpeds.2014.01.029.

My colleagues and I at SRALAB have used baclofen for over 40 years in patients with cp with very few side effects and with much collaborative patient input. It has the potential to improve sleep, reduce pain and improve function for those with uncontrolled muscle tone.

The inclusion of this important medication for treatment in cerebral palsy assists with tone reduction and function not only for the ambulatory child as well as for those non-ambulatory needing assistance for dressing, transfers and positioning.

Spasticity is chronic and but may intermittently become exacerbated, Baclofen which can be both oral or intrathecal can meet the needs of the spectrum of clinical presentations that is characteristic of children and adults with cp.

I urge you to include Baclofen as an essential medication that is linked to body structure, function and quality of. Life.



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