Baclofen

Essential medicine status

Section: 5. Medicines for neurological disorders > 5.1. Medicines for central nervous system disorders > 5.1.4. Medicines for cerebral palsy

EMLc | ATC codes: M03BX01

Indication	Spastic cerebral palsy ICD11 code: 8D20
INN	Baclofen
Medicine type	Chemical agent
List type	Complementary (EML) (EMLc)
Formulations	Oral > Liquid: 10 mg per 5 mL Parenteral > Locoregional injections > Intrathecal: 500 µg per mL in ampoule Oral > Solid > tablet: 10 mg
EML status history	First added in 2025 (TRS 1064)
Sex	All
Age	Also recommended for children
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Baclofen
DrugBank	Baclofen

Expert Committee recommendation

The Expert Committee recognized the significant public health burden associated with cerebral palsy. Effective management of spasticity in people with cerebral palsy is essential to improve mobility, posture, comfort and quality of life, particularly in children. The Committee noted that baclofen is widely used in clinical practice for this indication but had not previously been evaluated for inclusion on the Model Lists. No other pharmacological treatments for spasticity in cerebral palsy are currently included on the EML or EMLc. The Committee reviewed evidence from multiple systematic reviews and clinical studies. Most of the available evidence focused on use in children and adolescents up to 18 years. For intrathecal baclofen, the Committee noted evidence of significant benefit in reducing spasticity. Improvements in motor function were more modest. However, the quality of evidence was generally low, with concerns about heterogeneity of effect sizes across studies and risk of bias. The Committee also noted the risks of harms associated with intrathecal therapy, including infections, seizures and device-related complications. Overall, the Committee considered intrathecal baclofen to have a favourable balance of benefits to harms in reducing spasticity, a critical outcome. The Committee also highlighted the importance of integrating pharmacological treatment with rehabilitation and supportive care. For oral baclofen, the Committee noted the weakness of the available evidence with limited and inconsistent findings from small, methodologically flawed studies. However, the Committee recognized the important role of oral baclofen: in assessing responsiveness to treatment before surgical placement of an intrathecal pump; as a complementary therapy during the intrathecal dose titration when the pump is installed; as a supportive therapy when intrathecal therapy is discontinued; and to prevent and treat baclofen withdrawal, which can be severe and life-threatening. The Committee considered cost–effectiveness analyses from high-income settings, which suggested that intrathecal baclofen may be cost-effective in selected patients despite high initial and maintenance costs. However, the need for neurosurgical expertise and long-term device management may limit feasibility in many low- and middle-income countries. Furthermore, anatomical constraints for pump placement in very young

children may mean intrathecal use is unsuitable for this age group. Oral baclofen is more affordable and widely available in generic form, although no recent cost–effectiveness studies were identified. Based on these considerations, the Expert Committee recommended the addition of intrathecal baclofen to the complementary list of the EML and EMLc for the treatment of spasticity associated with cerebral palsy based on evidence of a favourable balance of benefits to harms in reducing spasticity. The Committee also recommended addition of oral baclofen, recognizing its role in assessing suitability for intrathecal treatment, and dose titration and cessation. The Committee also considered that oral baclofen may be the only available and affordable option in some resource-constrained settings. Given the importance of specialist oversight in people receiving baclofen, the Committee considered that listing it on the complementary list, rather than the core list, was appropriate.

Background

Baclofen has not previously been evaluated for inclusion on the Model Lists. Diazepam, included on the Model Lists for other indications, may be used in the treatment of spastic cerebral palsy.

Public health relevance

The overall birth prevalence of cerebral palsy is about 2 per 1000 live births (1). In 2019, the global prevalence of cerebral palsy was estimated at 50 million (2). Individuals with cerebral palsy may have varying degrees of neurological impairments such as weakness, sensory deficits, cognitive impairments, loss of selective motor control, incoordination and hypertonia including spasticity, dystonia, and choreoathetosis. These deficits can impair motor function and interfere with care, comfort and positioning (3). Hypertonia, or spasticity, can also lead to hip subluxation, torsional deformities, gait abnormalities, contractures, higher energy expenditure and pain (4, 5). There is no cure for cerebral palsy but early diagnosis and intervention, coupled with regular treatment, can have a meaningful impact on an individual's overall function and quality of life. The treatments that are available for hypertonia are able to minimize the long term impact of some of the neurological impairments and improve function (3). The goal of hypertonia or spasticity management is to improve function, not only to reduce muscle tone. Optimum and early management of spasticity can help achieve developmental milestones, improve function, prevent contractures, increase tolerance of braces, help with care, comfort and positioning, and improve weight gain velocity (6).

Benefits

Intrathecal baclofen versus placebo A 2024 systematic review and meta-analysis evaluated the effect of intrathecal baclofen therapy delivered via spinal implant on severe spasticity and motor function in patients with cerebral palsy (7). The review included 19 studies (343 participants) on severity of spasticity and six studies (117 participants) on motor function. Intrathecal baclofen therapy was associated with a significant reduction in spasticity levels, as measured using Ashworth Scale or Modified Ashworth Scale scores (pooled standardized mean difference (SMD) −1.70, 95% confidence interval (CI) −2.15 to −1.25; P < 0.0001). For motor function, as assessed using the Gross Motor Function Measure (GMFM), intrathecal baclofen therapy was associated with a small but significant improvement in GMFM scores (SMD 0.15, 95% CI 0.08 to 0.22; P = 0.003). The authors reported that asymmetrical funnel plots and Egger tests indicated the presence of publication bias among the included studies. A 2015 Cochrane systematic review of six studies (95 participants) evaluated intrathecal baclofen for the treatment of spasticity in children 0 to 18 years with cerebral palsy (8). One study did not report sufficient results to determine the effect of intrathecal baclofen compared with placebo. Of the remaining five studies, four used lumbar puncture or another short-term administration method to deliver intrathecal baclofen, and one used implantable baclofen pumps over 6 months. The data obtained were unsuitable for meta-analysis, so a qualitative summary was presented. The review reported that the results of all included studies suggested a beneficial effect of intrathecal baclofen in reducing spasticity in children with cerebral palsy. Reported outcomes included: a significant difference in muscle tone in lower extremities (but not upper extremities) between baclofen and placebo; significant differences in mean Ashworth Scale scores in the lower limbs between baclofen and placebo 4 hours post-injection; small but statistically significant changes in Ashworth Scale score in the upper limbs at time points up to 8 hours post-injection; decreased Ashworth Scale scores from baseline at time points up to 6 hours post-injection for all muscle groups except hip flexors at 2 hours post-injection; significantly reduced spasticity in four of 22 muscle groups assessed compared with control at 6 months; and positive differences in gross motor function scores favouring baclofen. The authors noted that the validity of the evidence was limited by the small sample sizes and methodological issues (including high or unclear risk of bias) in the studies. The authors concluded that there was limited short-term evidence of the effectiveness of intrathecal baclofen in reducing spasticity in children

with cerebral palsy; however, the effect of treatment on long-term outcomes is uncertain. Intrathecal baclofen versus other therapies A 2020 systematic review of 47 studies investigated the use of intrathecal baclofen pump therapy for treatment of spasticity in cerebral palsy (14 studies, 312 participants) compared with selective dorsal rhizotomy – a surgical procedure that involves severing the lumbosacral sensory nerves in the spine to relieve pain (28 studies, 1016 participants) – and extracorporeal shockwave therapy – delivery of therapeutic electric shocks of varying frequencies at different time intervals to relieve pain (8 studies, 251 participants) (9). Each treatment intervention was associated with improvements in spasticity, measured variously as changes in Modified Ashworth Scale and GMFM scores. However, the review did not include a meta-analysis, so direct comparisons between treatments could not be made. The authors concluded that intrathecal baclofen pump therapy was a less invasive treatment option that could be titrated to individual patient needs, while noting the disadvantage of long-term maintenance requirements. Selective dorsal rhizotomy offers an effective method for permanent spasticity relief in young patients, however, its implementation is limited as only a few centres globally are able to perform this treatment. Extracorporeal shockwave therapy offers relief of spasticity with minimal invasiveness but is relatively new and further studies are needed to establish optimal frequencies and application sites. Oral baclofen versus placebo A 2015 systematic review of six randomized controlled trials (130 participants) evaluated the effectiveness of oral baclofen for treatment of spasticity in children and adolescents with cerebral palsy (10). The overall methodological quality of the included studies was low. The motor classification, baclofen dosage and outcome measures varied widely across studies. The authors found conflicting evidence for the effectiveness of oral baclofen in reducing muscle tone or improving motor function or level of activity and concluded that the data were insufficient to support or refute use of oral baclofen in children and adolescents with spastic cerebral palsy. The application included brief summaries of the findings of the included individual trials. The application stated that oral baclofen is commonly used to predict or 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. Oral baclofen versus other therapies Alternative oral therapies to baclofen include diazepam 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 were mostly conducted in the immediate years after the approval of baclofen by the United States Food and Drug Administration. In addition, most of the studies focused on patients with multiple sclerosis and showed very little difference between oral therapies. A 1985 double-blind crossover study compared oral baclofen and oral diazepam for spasticity reduction in 13 patients over a period of 19 weeks. Both medicines were associated with overall improvement, with no significant difference in preference for either treatment (11). A 1988 randomized double-blind crossover study compared baclofen and tizanidine for treatment of spasticity in 48 patients with multiple sclerosis. No statistically significant difference in efficacy was reported, however, efficacy was judged to be good or excellent by 24% of patients receiving tizanidine and 39% of patients receiving baclofen (12). More recently, a randomized, prospective follow-up study compared diazepam and oral baclofen in 67 children with cerebral palsy. For the outcome measure of change in mean Modified Ashworth Scale scores, no significant difference was found between treatment groups (13).

Harms

Commonly reported adverse effects of oral baclofen include somnolence, confusion, ataxia, polyuria and headache. Adverse reactions can occur with sudden discontinuation of baclofen, such as hallucinations, seizures, increased muscle tone or, in rare cases, more severe complications. Therefore, it is generally recommended to taper the dosage gradually, unless a clinical situation necessitates otherwise. In the 2024 systematic review of intrathecal baclofen versus placebo, 501 participants (including some without cerebral palsy) were evaluated for safety outcomes (7). Adverse events reported included 75 catheter or pump complications and 203 medical complications. Seizure-related adverse events were of particular concern, including six reports of new-onset seizures, and seven reports of increased seizure frequency. There were 33 reports of infections, including eight reports of meningitis. There were 16 reports of cerebrospinal fluid leaks associated with intrathecal baclofen therapy. The most commonly reported adverse events (75 cases) were delivery system complications (dislocations, malfunctions and disconnections). In the 2015 systematic review of oral baclofen versus placebo, three of the studies did not show a significant difference in adverse effects between treatment groups, while two studies reported a higher rate of adverse effects in baclofen treated patients (sedation and reduced muscle tone) (10). The review also highlighted several disadvantages that limit the use of oral baclofen in children including: the large (> 90%) interindividual variability in oral absorption and elimination creating difficulties in determining the appropriate dosage in paediatric patients; poor blood–brain barrier penetration and a short half-life of 3–4 hours, necessitating

repeated daily dosing; moderate systemic side-effects such as somnolence, confusion, polyuria, headache, weakness, memory deficits, orthostatic hypotension; and severe neurological side-effects such as sudden withdrawal syndrome, baclofen overdose and risk of seizures (10). Neonates born to mothers taking baclofen regularly 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. Some individuals with certain pre-existing conditions may need closer monitoring when using baclofen. Patients with a history of stroke may not experience significant improvement in spasticity and may have reduced tolerance for the drug. Patients with psychiatric conditions 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 of autonomic dysreflexia, while individuals with epilepsy may experience some variability in seizure control (10). 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 maintenance of functional stability. Additionally, some women using baclofen long-term have reported the development of ovarian cysts, although these typically resolve without intervention. Intrathecal baclofen pump therapy also has risks associated with the surgical procedure required to place the pump, as well as the injections required to refill the pump.

Cost / cost effectiveness

A French study modelled the cost–effectiveness of intrathecal baclofen versus other conventional treatment options as first-line treatment for disabling spasticity caused by any neurological disease (18). The study found that intrathecal baclofen as first-line therapy was associated with a higher treatment success rate (defined as a combination of increased patient and care-giver satisfaction as assessed by goal attainment scaling, and at least 1-point decrease in the Ashworth score) than conventional medical management despite having the highest acquisition cost of antispastic treatments. Over a 2-year time horizon, intrathecal baclofen therapy was associated with lower total medical costs than conventional treatments and was considered the dominant strategy. Mean cost–effectiveness ratios per treatment success were 75 204 euros (€) for intrathecal baclofen therapy versus €148 822 for conventional treatment. A Dutch study conducted a cost-effectiveness analysis of intrathecal baclofen therapy versus standard treatment in children with spastic cerebral palsy from the health-care perspective over a 1-year time horizon (19). Intrathecal baclofen therapy was more effective and more costly than standard treatment with an incremental cost per quality-adjusted life year (QALY) gained of €32 737 using the Dutch EuroQol-5D index and €28 273 using the United Kingdom's EuroQol-5D index. The authors concluded that given a willingness-to-pay threshold of €80 000, intrathecal baclofen therapy was a cost-effective intervention for certain children with spastic cerebral palsy. A study in the United States of America assessed the cost–effectiveness of intrathecal baclofen in children with severe spasticity of cerebral origin who were unresponsive to less invasive treatments (e.g. oral medicines) relative to alternative medical and surgical therapy from a health-system perspective over a 5-year time horizon (20). Intrathecal baclofen was associated with increased treatment costs and an average gain of 1.2 QALYs compared with alternative treatments, resulting in an incremental cost–effectiveness ratio of 42 000 United States dollars (US$) per QALY, which is within the range considered acceptable as offering good value for money. In addition to the cost of the medicine, intrathecal baclofen requires a surgical procedure to install the pump and regular interventions to refill and maintain the pump, as well as further surgical procedures to replace the pump every 5–8 years. However, the additional cost and the need for surgical expertise mean that intrathecal baclofen is not available in many low- and middle-income countries. No information on the cost of intrathecal baclofen ampoules was presented in the application. Oral baclofen is widely available globally, including in generic forms. The application stated that no recent studies were available on its cost–effectiveness compared with other treatments. The application presented a summary of comparative costs for baclofen 10 mg tablets in multiple countries, which ranged from US$ 0.07 per tablet (US$ 6.30 per month) in Nigeria to US$ 0.40 per tablet (US$ 36.00 per month) in Argentina and the United States. No price information was presented in the application for baclofen oral liquid.

WHO guidelines

The WHO package of interventions for rehabilitation outlines the most essential rehabilitation interventions for 20 health conditions that have high prevalence rates and high levels of associated disability, including for cerebral palsy. The package includes, among other things, oral muscle relaxants (benzodiazepines and baclofen) as pharmacological interventions for children, adolescents and adults with cerebral palsy (14). The package does not currently include intrathecal baclofen. Inclusion of the oral muscle relaxant interventions in the package was based on a review of clinical practice guidelines for rehabilitation in cerebral palsy. The United Kingdom National Institute for Health and Care Excellence (NICE) clinical guidelines for management of

spasticity in people younger than 19 years with non-progressive brain disorders informed the inclusion of oral muscle relaxants in the package of interventions (15). The NICE guidelines include the following recommendations (16). • Consider oral diazepam or baclofen in children and young people if spasticity is contributing to one or more of the following: discomfort or pain; muscle spasms, for example, night-time muscle spasms; and functional disability. Diazepam is particularly useful if a rapid effect is desirable (e.g. in a pain crisis). Baclofen is particularly useful if a sustained long-term effect is desired, for example, to relieve continuous discomfort or to improve motor function (conditional recommendations, moderate-certainty evidence). • Give oral diazepam treatment as a bedtime dose. If the response is unsatisfactory, consider increasing the dose or adding a daytime dose (conditional recommendation, moderate-certainty evidence). • If oral diazepam is initially used because of its rapid onset of action, consider changing to oral baclofen if long-term treatment is indicated (conditional recommendations, moderate-certainty evidence). • Start oral baclofen treatment with a low dose and increase the dose stepwise over about 4 weeks to achieve the optimum therapeutic effect (strong recommendation, low to moderate-certainty evidence). • 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: pain or muscle spasms; posture or function; and self-care (or ease of care by parents or carers). The NICE guidelines for cerebral palsy in adults include recommendations to consider: (i) enteral baclofen as the first-line pharmacological treatment for adults with cerebral palsy and generalized spasticity causing functional impairment, pain or muscle spasm; and (ii) referring adults with cerebral palsy to a tone or spasticity management service offering continuous pump-administered intrathecal baclofen therapy, if they still have difficulties with spasticity despite enteral muscle relaxant treatment or botulinum toxin type A treatment (17). Other international guidelines include various recommendations for the use of oral and/or intrathecal baclofen in patients with spastic cerebral palsy.

Availability

Baclofen tablets are widely available globally. The availability of the oral liquid and intrathecal injection formulations does not appear to be as widespread. According to the WHO Global essential medicines dashboard (21), baclofen is currently included in the national EML of 46 countries. The dashboard does not differentiate between different dosage forms.

Other considerations

The Department of Mental Health, Brain Health and Substance Use provided comments on the application which expressed support for the inclusion of baclofen on the Model Lists for the proposed indication. It was the view of the technical department that including baclofen on the Model Lists would support countries in prioritizing its inclusion in national EMLs, standard treatment guidelines, health service packages and procurement plans, which may help to improve appropriate use, availability and affordability, especially in low- and middle-income countries.

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