LIORESAL® Intrathecal Injection 50 micrograms/1 ml
LIORESAL® Intrathecal Infusion 10 mg/5 ml
LIORESAL® Intrathecal Infusion 10 mg/20 ml
(baclofen)

Patient Information Leaflet

The product will be called Lioresal Intrathecal in this leaflet

What you need to know about Lioresal Intrathecal

Your doctor has decided that you or your child needs this medicine to help treat your condition. **Please read this leaflet carefully before you start treatment. It contains important information.** Keep the leaflet in a safe place because you may want to read it again.
If you have any other questions, or if there is something you don't understand, please ask your doctor or nurse.
If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Lioresal Intrathecal is and what it's used for

Lioresal Intrathecal contains the active ingredient, baclofen. It is administered by intrathecal injection directly into the spinal fluid. It is available in three different sizes and strengths containing either 50 micrograms in 1 ml, 10 mg in 5 ml or 10 mg in 20 ml of baclofen.

Baclofen is a muscle-relaxant drug. Lioresal Intrathecal is intended for adults and children of 4 years and above and is used to reduce and relieve the excessive tension in your muscles (spasms) occurring in various illnesses such as cerebral palsy, multiple sclerosis, spinal cord diseases, cerebrovascular accidents, and other nervous system disorders. This injection is used in people who haven't responded to oral medicines or who get unacceptable side effects when they take baclofen by mouth.

2. Things to consider before you have Lioresal Intrathecal

Some people MUST NOT have Lioresal Intrathecal. Talk to your doctor if:

- you think you may be allergic to baclofen or to any of the other ingredients of the injection (these are listed at the end of the leaflet).

You should also ask yourself these questions before having Lioresal Intrathecal:

- Have you understood everything the doctor or nurse has told you about the risks associated with Lioresal Intrathecal?
- Do you understand how to use the injection pump?

If you are at all confused about either of these points, please ask the doctor or nurse. Get urgent medical help if you observe that your implanted device is not working and you also notice withdrawal symptoms (see "Section 3 having Lioresal Intrathecal")

- Are you having any other injections into the spine?
- Are you suffering from any infection?
- Have you had a head injury within the last year?
- Have you ever had a crisis caused by a condition called autonomic dysreflexia? (Your doctor will be able to explain this to you.)
- Have you had a stroke?
- Do you have epilepsy?
- Do you have a stomach ulcer or any other problem with your digestion?
- Do you suffer from any mental illness?
- Are you being treated for high blood pressure?
- Do you have Parkinson's disease?
- Do you suffer from any liver, kidney or lung disease?
- Do you have diabetes?
- Do you have difficulties in urinating?
- Are you pregnant or breast-feeding?

If the answer to any of this second list of questions is YES, tell your doctor or nurse because Lioresal Intrathecal may not be the right medicine for you.

Tell your doctor immediately if you get any of these symptoms during treatment with Lioresal Intrathecal:

- **If you have pain** in your back, shoulders, neck and buttock during the treatment (a type of spinal deformity called scoliosis).
- **If you have** thoughts of harming or killing yourself at any time, speak to your doctor straightaway or go to a hospital. Also, ask a relative or close friend to tell you if they are worried about any changes in your behaviour and ask them to read this leaflet.

Are you taking other medicines?

Some medicines can interfere with your treatment. Remind your doctor or nurse if you are taking any of the following:

- Other medicines for your spastic condition e.g. tizanidine or diazepam
- Antidepressants e.g. imipramine or amitriptyline
- Medicines for high blood pressure e.g. diltiazem or moxonidine
- Other drugs which also affect the kidney, e.g. ibuprofen
- Medicines for Parkinson's disease e.g. levodopa or carbidopa
- Medicines for epilepsy e.g. carbamazepine or clonazepam
- Opiates for pain relief e.g. morphine
- Medicines which slow down the nervous system, e.g. anti-histamines such as promethazine and sedatives such as temazepam. (Some of these can be bought over-the-counter.)

Always tell your doctor or nurse about all the medicines you are taking. *This means medicines you have bought yourself as well as medicines on prescription from your doctor.*

Will there be any problems with driving or using machinery?
Some people may feel drowsy and/or dizzy or have problems with their eyes while they are being treated with Lioresal Intrathecal. If this happens, you should not drive or do anything that requires you to be alert (such as operate tools or machinery) until these effects have worn off.

Other special warnings

- Be careful when drinking alcohol - it may affect you more than usual.
- Contact your doctor immediately if you think that Lioresal Intrathecal is not working as well as usual. It is important to make sure that there are no problems with the pump.
- Treatment with Lioresal Intrathecal must not stop suddenly because of the risk of withdrawal effects. You must make sure that you do not miss those hospital visits when the pump reservoir is being refilled.
- Your doctor may want to give you a check up from time to time while you are being treated with Lioresal Intrathecal.
- If you are going to have an operation of any kind, make sure that the doctor knows that you are being treated with Lioresal Intrathecal. Anaesthetics such as propofol may increase the risk of side effects.

Children and adolescents:
Lioresal Intrathecal formulation is intended for children of 4 years and above.

Lioresal Intrathecal contains Sodium chloride:

Lioresal 0.05mcg/ 1 mL Intrathecal Injection contains less than 1 mmol sodium (23 mg) in 1 mL, that is to say essentially 'sodium-free'.

Lioresal 10 mg/ 5 mL Intrathecal Infusion contains less than 1 mmol sodium (23 mg) in 5 milliliter, that is to say essentially 'sodium-free'.

Lioresal 10 mg/ 20 mL Intrathecal Infusion contains 70.81 mg sodium (main component of cooking/table salt) per dose. This is equivalent to 3.5% of the recommended maximum daily dietary intake of sodium for an adult.

3. Having Lioresal Intrathecal

Lioresal Intrathecal is administered by intrathecal injection. This means that the medicine is injected directly into the spinal fluid. The dose needed varies from person to person depending on their condition, and the doctor will decide what dose you need after he/she has tested your response to the drug.

First of all the doctor will find out, by giving you single doses of Lioresal Intrathecal, whether it is suitable for you. During this period your heart and lung functions will be closely monitored. If your symptoms improve, a special pump which can deliver the drug continuously, will be implanted into your chest or abdominal wall. The doctor will give you all of the information you need to use the pump and to get the correct dosage. Make sure that you understand everything.

The final dose of Lioresal Intrathecal depends on how each person responds to the drug. You will be started on a low dose, and this will be increased gradually over a few days, under the

supervision of the doctor, until you are having the dose which is right for you. If the starting dose is too high, or if the dose is increased too quickly, you are more likely to experience side effects.

To avoid unpleasant side effects which may be serious and even life-threatening, it is important that your pump does not run out. The pump must always be filled by a doctor or nurse, and you must make sure that you do not miss your clinic appointments.

You should not stop treatment suddenly. If the doctor decides to stop your treatment, the dose will be reduced gradually to prevent withdrawal symptoms such as muscle spasms and increased muscle rigidity, fast heart rate, fever, confusion, hallucinations, changes in mood and emotion, mental disorders, feeling persecuted or convulsions (fits), persistent painful erection of the penis (priapism). On rare occasions these symptoms could be life-threatening. If you or your carers notice any of these symptoms, contact your doctor immediately just in case something has gone wrong with the pump or delivery system.

During long-term treatment some patients find that Lioresal becomes less effective. You may require occasional breaks in treatment. Your doctor will advise you what to do.

Lioresal Intrathecal is not suitable for all children. The doctor will decide.

Overdose

It is very important that you, and anyone caring for you, can recognise the signs of overdose. These may appear if the pump is not working properly, and you must tell the doctor straight away.
Signs of overdose are:
Unusual muscle weakness (too little muscle tone)
Sleepiness
Dizziness or light-headedness
Excessive salivation
Nausea or vomiting
Difficulty in breathing
Convulsions
Loss of consciousness
Abnormally low body temperature.

4. Possible side effects

Lioresal Intrathecal is suitable for most people, but, like all medicines, it can sometimes cause side effects. Implanted drug delivery device or infusion system malfunction can lead to withdrawal symptoms including death.

The side effects listed below have been reported:
More than 1 in 10 people have experienced:
Feeling tired, drowsy or weak.

Up to 1 in 10 people have experienced:
Feeling lethargic (having no energy)
Headache, dizziness or light-headedness
Pain, fever or chills
Seizures

Tingling hands or feet
Problems with eyesight
Slurred speech
Insomnia
Breathing difficulties, pneumonia
Feeling confused, anxious, agitated or depressed
Low blood pressure (fainting)
Feeling or being sick, constipation and diarrhoea
Loss of appetite, dry mouth or excessive saliva
Rash and itching, swelling of the face or hands and feet
Urinary incontinence, or problems when urinating
Cramps
Sexual problems in men, e.g. impotence.

Up to 1 in 100 people have experienced:
Feeling abnormally cold
Memory loss
Mood swings and hallucinations, feeling suicidal
Stomach ache, difficulty in swallowing, loss of taste, dehydration
Loss of muscle control
Raised blood pressure
Slow heart beat
Deep vein thrombosis
Flushed or pale skin, excessive sweating
Hair loss.

Other side effects (how often they happen is not known)
Restlessness (dysphoria)
Abnormally slow breathing rate (bradypnoea)
Increase in sideways curvature of the spine (scoliosis)
Inability to achieve or maintain an erection (erectile dysfunction).

There have been rare reports of problems associated with the pump and delivery system e.g. infections, inflammation of the lining around the brain and spinal cord (meningitis) or a collection of immune cells at the tip of the delivery tube.

If any of the symptoms become troublesome, or if you notice anything else not mentioned here, please go and see your doctor. He/she may want to adjust the dose or give you a different medicine.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme (www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Lioresal Intrathecal

Keep this medicine out of the sight and reach of children.

Store below 30ºC.
It should not be used after the expiry date which is printed on the outside of the pack.

6. Further information

Lioresal Intrathecal is available in three different sizes and strengths containing either 50 micrograms in 1 ml, 10 mg in 5 ml or 10 mg in 20 ml of the active ingredient, baclofen. The ampoules also contain sodium chloride and water for injections.

Marketing Authorisation Holder and Manufacturer :

Novartis Pharmaceuticals UK Limited,
2nd Floor, The WestWorks Building, White City Place,
195 Wood Lane,
London,
W12 7FQ
United Kingdom.

This leaflet was revised in August 2021
If you would like any more information, or would like the leaflet in a different format, please contact Medical Information at Novartis Pharmaceuticals UK Ltd, telephone number 01276 698370.

Information for the healthcare professional
Please see the SPC for full details.

Therapeutic indications
Lioresal Intrathecal is indicated in patients with severe chronic spasticity of spinal or cerebral origin (associated with injury, multiple sclerosis, cerebral palsy) who are unresponsive to oral baclofen or other orally administered antispastic agents and/or those patients who experience unacceptable side-effects at effective oral doses.
In patients with spasticity due to head injury a delay of at least one year before treatment with Lioresal Intrathecal is recommended, to allow the symptoms of spasticity to stabilise.
Lioresal Intrathecal may be considered as an alternative to ablative neurosurgical procedures.

Paediatric population
Lioresal Intrathecal is indicated in patients aged 4 to <18 years with severe chronic spasticity of cerebral origin or of spinal origin (associated with injury, multiple sclerosis, or other spinal cord diseases) who are unresponsive to orally administered antispastics (including oral baclofen) and/or who experience unacceptable side effects at effective oral doses.

Posology and method of administration
Intrathecal administration of Lioresal through an implanted delivery system should only be undertaken by physicians with the necessary knowledge and experience. Specific instructions for

implantation, programming and/or refilling of the implantable pump are given by the pump manufacturers, and must be strictly adhered to.

Lioresal Intrathecal 50 micrograms/1ml is intended for administration in single bolus test doses (via spinal catheter or lumbar puncture) and, for chronic use, in implantable pumps suitable for continuous administration of Lioresal Intrathecal 10mg/20ml and 10mg/5ml into the intrathecal space (EU certified pumps). Establishment of the optimum dose schedule requires that each patient undergoes an initial screening phase with intrathecal bolus, followed by a very careful individual dose titration prior to maintenance therapy.

Respiratory function should be monitored and appropriate resuscitation facilities should be available during the introduction of treatment with Lioresal Intrathecal. Intrathecal administration using an implanted delivery system should only be undertaken by physicians with appropriate knowledge and experience. Specific instructions for using the implantable pump should be obtained from the pump manufacturers. Only pumps constructed of material known to be compatible with the product and incorporating an in-line bacterial retentive filter should be used.

Adult Screening Phase

Prior to initiation of a chronic infusion, the patient's response to intrathecal bolus doses administered via a catheter or lumbar puncture must be assessed. Low concentration ampoules containing 50 micrograms baclofen in 1ml are available for the purpose. Patients should be infection-free prior to screening, as the presence of a systemic infection may prevent an accurate assessment of the response.

The usual initial test dose in adults is 25 or 50 micrograms, increasing step-wise by 25 microgram increments at intervals of not less than 24 hours until a response of approximately 4 to 8 hours duration is observed. Each dose should be given **slowly** (over at least one minute). In order to be considered a responder the patient must demonstrate a significant decrease in muscle tone and/or frequency and/or severity of muscle spasms.

The variability in sensitivity to intrathecal baclofen between patients is emphasised. Signs of severe overdose (coma) have been observed in an adult after a single test dose of 25 micrograms. It is recommended that the initial test dose is administered with resuscitative equipment on hand.

Patients who do not respond to a 100 micrograms test dose should not be given further dose increments or considered for continuous intrathecal infusion.

Monitoring of respiratory and cardiac function is essential during this phase, especially in patients with cardiopulmonary disease and respiratory muscle weakness or those being treated with benzodiazepine-type preparations or opiates, who are at higher risk of respiratory depression.

Paediatric population Screening Phase

The initial lumbar puncture test dose for patients 4 to <18 years of age should be 25-50 micrograms/day based upon age and size of the child. Patients who do not experience a response may receive a 25 micrograms/day dose escalation every 24 hours. The maximum screening dose should not exceed 100 micrograms/day in paediatric patients.

Dose-Titration Phase

Once the patient's responsiveness to Lioresal Intrathecal has been established, an intrathecal infusion may be introduced. Lioresal Intrathecal is most often administered using an infusion

pump which is implanted in the chest wall or abdominal wall tissues. Implantation of pumps should only be performed in experienced centres to minimise risks during the perioperative phase.

Infection may increase the risk of surgical complications and complicate attempts to adjust the dose.

The initial total daily infused dose is determined by doubling the bolus dose which gave a significant response in the initial screening phase and administering it over a 24 hour period. However, if a prolonged effect (i.e. lasting more than 12 hours) is observed during screening the starting dose should be the unchanged screening dose delivered over 24 hours. No dose increases should be attempted during the first 24 hours.

After the initial 24 hour period dosage should be adjusted slowly to achieve the desired clinical effect. If a programmable pump is used the dose should be increased only once every 24 hours; for non-programmable multi-dose reservoir pumps intervals of 48 hours between dose adjustments are recommended. In either case increments should be limited as follows to avoid possible overdosage:

Patients with spasticity of spinal origin:	10-30% of the previous daily dose
Patients with spasticity of cerebral origin:	5-15% of the previous daily dose.

If the dose has been significantly increased without apparent clinical effect pump function and catheter patency should be investigated.

There is limited clinical experience using doses greater than 1000 micrograms/day.
It is important that patients are monitored closely in an appropriately equipped and staffed environment during screening and immediately following pump implantation. Resuscitative equipment should be available for immediate use in case of life-threatening adverse reactions.

Adult Maintenance Therapy
The clinical goal is to maintain as normal a muscle tone as possible, and to minimise the frequency and severity of spasms without inducing intolerable side effects. The lowest dose producing an adequate response should be used. The retention of some spasticity is desirable to avoid a sensation of "paralysis" on the part of the patient. In addition, a degree of muscle tone and occasional spasms may help support circulatory function and possibly prevent the formation of deep vein thrombosis.

In patients with spasticity of spinal origin: maintenance dosing for long-term continuous infusions of intrathecal baclofen has been found to range from 12 to 2003 micrograms/day, with most patients being adequately maintained on 300 to 800 micrograms/day.

In patients with spasticity of cerebral origin: maintenance dosage has been found to range from 22 to 1400 micrograms/day, with a mean daily dosage of 276 micrograms per day at 12 months and 307 micrograms per day at 24 months.

Paediatric population Maintenance Therapy
In children aged 4 to <18 years with spasticity of cerebral and spinal origin, the initial maintenance dosage for long-term continuous infusion of Lioresal Intrathecal ranges from 25 to 200 micrograms/day (median dose: 100 micrograms/day). The total daily dose tends to increase over the first year of therapy, therefore the maintenance dose needs to be adjusted based on

individual clinical response. There is limited experience with doses greater than 1,000 micrograms/day.

The safety and efficacy of Lioresal Intrathecal for the treatment of severe spasticity of cerebral or spinal origin in children younger than 4 years of age have not been established.

Delivery specifications
Lioresal Intrathecal ampoules of 20ml containing 500 micrograms/ml and 5ml containing 2mg (2000micrograms)/ml are intended for use with infusion pumps. The concentration to be used depends on the dose requirements and size of pump reservoir. Use of the more concentrated solution obviates the need for frequent refilling in patients with high dosage requirements.

Delivery regimen
Lioresal Intrathecal is most often administered in a continuous infusion mode immediately following implant. After the patient has stabilised with regard to daily dose and functional status, and provided the pump allows it, a more complex mode of delivery may be started to optimise control of spasticity at different times of the day. For example, patients who have increased spasm at night may require a 20% increase in their hourly infusion rate. Changes in flow rate should be programmed to start two hours before the desired onset of clinical effect.

Most patients require gradual dose increases to maintain optimum response during chronic therapy due to decreased responsiveness or disease progression. In patients with spasticity of spinal origin the daily dose may be increased gradually by 10-30% to maintain adequate symptom control. Where the spasticity is of cerebral origin any increase in dose should be limited to 20% (range: 5-20%). In both cases the daily dose may also be reduced by 10-20% if patients suffer side effects.

A sudden requirement for substantial dose escalation is indicative of a catheter complication (i.e. a kink or dislodgement) or pump malfunction.

In order to prevent excessive weakness the dosage of Lioresal Intrathecal should be adjusted with caution whenever spasticity is required to maintain function.

During long-term treatment approximately 5% of patients become refractory to increasing doses due to tolerance or drug delivery failure (see Special Warnings and Precautions for Use “Treatment Withdrawal” section). This “tolerance” may be treated by gradually reducing Lioresal Intrathecal dose over 2 to 4 week period and switching to alternative methods of spasticity management (e.g. Intrathecal preservative-free morphine sulphate). Lioresal Intrathecal should be resumed at the initial continuous infusion dose. Caution should be exercised when switching from Lioresal Intrathecal to morphine and vice versa.

Discontinuation
Except in overdose-related emergencies, the treatment with Lioresal Intrathecal should always be gradually discontinued by successively reducing the dosage. Lioresal Intrathecal should not be discontinued suddenly (see below).

Special populations

Renal impairment
Because baclofen is primarily excreted unchanged by the kidneys it should be given with special care and caution in patients with impaired renal function.

Hepatic impairment
No dosage adjustment is recommended as the liver does not play any significant role in the metabolism of baclofen after intrathecal administration of Lioresal. Therefore, hepatic impairment is not expected to impact the drug systemic exposure.

Elderly population
Several patients over the age of 65 years have been treated with Lioresal Intrathecal during the clinical trials without increased risks compared to younger patients. Problems specific to this age group are not expected as doses are individually titrated.

Special warnings and precautions for use
Intrathecal baclofen therapy is valuable but hazardous. Careful pre-operative assessment is mandatory.

The patient must be given adequate information regarding the risks of this mode of treatment, and be physically and psychologically able to cope with the pump. It is essential that the responsible physicians and all those involved in the care of the patient receive adequate instruction on the signs and symptoms of overdose, procedures to be followed in the event of an overdose and the proper home care of the pump and insertion site.

Inflammatory mass at the tip of the implanted catheter: cases of inflammatory mass at the tip of the implanted catheter that can result in serious neurological impairment, including paralysis, have been reported. Although they have been reported with Lioresal intrathecal, they have not been confirmed by contrast MRI or histopathology. The most frequent symptoms associated with inflammatory mass are: 1) decreased therapeutic response (worsening spasticity, return of spasticity when previously well controlled, withdrawal symptoms, poor response to escalating doses, or frequent or large dosage increases), 2) pain, 3) neurological deficit/dysfunction. Clinicians should monitor patients on intraspinal therapy carefully for any new neurological signs or symptoms. Clinicians should use their medical judgement regarding the most appropriate monitoring specific to their patients' medical needs to identify prodromal signs and symptoms for inflammatory mass especially if using pharmacy compounded drugs or admixtures that include opioids. In patients with new neurological signs or symptoms suggestive of an inflammatory mass, consider a neurosurgical consultation since many of the symptoms of inflammatory mass are not unlike the symptoms experienced by patients with severe spasticity from their disease. In some cases, performance of an imaging procedure may be appropriate to confirm or rule-out the diagnosis of an inflammatory mass.

Pump Implantation
Patients should be infection-free prior to pump implantation because the presence of infection may increase the risk of surgical complications. Moreover, a systemic infection may complicate attempts to adjust the dose. A local infection or catheter malplacement can also lead to drug delivery failure, which may result in sudden Lioresal Intrathecal withdrawal and its related symptoms (see "Treatment Withdrawal" section).

Reservoir refilling
Reservoir refilling must be performed by trained and qualified personnel in accordance with the instructions provided by the pump manufacturer. Refills should be timed to avoid excessive depletion of the reservoir, as this would result in the return of spasticity or potentially life-threatening symptoms of Lioresal Intrathecal withdrawal (see "Treatment Withdrawal" section).

When refilling the pump care should be taken to avoid discharging the contents of the catheter into the intrathecal space.

Strict asepsis is required to avoid microbial contamination and infection.

Extreme caution must be taken when filling a pump equipped with an injection port that allows direct access to the intrathecal catheter as a direct injection into the catheter through the access port could cause a life-threatening overdose.

Precautions in paediatric patients
For patients with spasticity due to head injury, it is recommended not to proceed to long-term Lioresal Intrathecal therapy until the symptoms of spasticity are stable (i.e. at least one year after the injury).

Children should be of sufficient body mass to accommodate the implantable pump for chronic infusion. Use of Lioresal Intrathecal in the paediatric population should be only prescribed by medical specialists with the necessary knowledge and experience. There is very limited clinical data regarding the safety and efficacy of the use of Lioresal Intrathecal in children under the age of four years.

Precautions in special patient populations
In patients with **abnormal CSF flow** the circulation of drug and hence antispastic activity may be inadequate.

Psychotic disorders, schizophrenia, confusional states or Parkinson's disease may be exacerbated by treatment with oral Lioresal. Patients suffering from these conditions should therefore be treated cautiously and kept under close surveillance.

Special attention should be given to patients known to suffer from **epilepsy** as seizures have occasionally been reported during overdose with, and withdrawal from, Lioresal Intrathecal as well as in patients maintained on therapeutic doses.

Lioresal Intrathecal should be used with caution in patients with a history of **autonomic dysreflexia.** The presence of nociceptive stimuli or abrupt withdrawal of Lioresal Intrathecal may precipitate an autonomic dysreflexic episode.

Lioresal should be used with caution in patients with **cerebrovascular or respiratory insufficiency.**

An effect of Lioresal Intrathecal on **underlying, non-CNS related diseases** is unlikely because its systemic availability is substantially lower than after oral administration. Observations after oral baclofen therapy suggest that caution should be exercised in patients with a history of peptic ulcers and pre-existing sphincter hypertonia.

Renal impairment
After **oral** Lioresal dosing severe neurological outcomes have been reported in patients with renal impairment. Thus caution should be exercised while administering Lioresal Intrathecal in patients with renal impairment.

In rare instances elevated SGOT, alkaline phosphatase and glucose levels in the serum have been recorded when using oral Lioresal.

Treatment withdrawal
Abrupt discontinuation of Lioresal Intrathecal, regardless of cause, manifested by increased spasticity, pruritus, paraesthesia and hypotension, has resulted in sequelae including a hyperactive state with rapid uncontrolled spasms, hyperthermia and symptoms consistent with neuroleptic malignant syndrome, e.g. altered mental status and muscle rigidity. In rare cases this has advanced to seizures/status epilepticus, rhabdomyolysis, coagulopathy, multiple organ failure and death. All patients receiving intrathecal baclofen therapy are potentially at risk for withdrawal.

Some clinical characteristics associated with intrathecal baclofen withdrawal may resemble autonomic dysreflexia, infection (sepsis), malignant hyperthermia, neuroleptic-malignant syndrome, or other conditions associated with a hypermetabolic state or widespread rhabdomyolysis.

Patients and caregivers should be advised of the importance of keeping scheduled refill visits and should be educated on the signs and symptoms of baclofen withdrawal particularly those seen early in the withdrawal syndrome (e.g. priapism).

In most cases, symptoms of withdrawal appeared within hours to a few days following interruption of baclofen therapy. Common reasons for abrupt interruption of intrathecal baclofen therapy included malfunction of the catheter (especially disconnection), low volume in the pump reservoir and end of pump battery life.

Prevention of abrupt discontinuation of intrathecal baclofen requires careful attention to programming and monitoring of the infusion system, refill scheduling and procedures, and pump alarms. The suggested treatment for intrathecal Lioresal withdrawal is the restoration of intrathecal Lioresal at or near the same dosage as before therapy was interrupted. However, if restoration of intrathecal delivery is delayed, treatment with GABA-ergic agonist drugs such as oral or enteral Lioresal, or oral, enteral, or intravenous benzodiazepines may prevent potentially fatal sequelae. Oral or enteral Lioresal alone should not be relied upon to halt the progression of intrathecal baclofen withdrawal.

Scoliosis
The onset of scoliosis or worsening of a pre-existing scoliosis has been reported in patient treated with Lioresal Intrathecal. Signs of scoliosis should be monitored during treatment with Lioresal Intrathecal.

Incompatibilities
If alternative baclofen concentrations are required Lioresal Intrathecal may be diluted under aseptic conditions with sterile preservative-free sodium chloride for injections. The ampoules should not be mixed with other solutions for injection or infusion (dextrose has proved to be incompatible due to a chemical reaction with baclofen).

The compatibility of Lioresal Intrathecal with the components of the infusion pump (including the chemical stability of baclofen in the reservoir) and the presence of an in-line bacterial retentive filter should be confirmed with the pump manufacturer prior to use.

Shelf life
LIORESAL® Intrathecal Injection 50 micrograms/1 ml: 3 years
LIORESAL® Intrathecal Infusion 10 mg/5 ml: 3 years
LIORESAL® Intrathecal Infusion 10 mg/20 ml: 3 years

Special precautions for storage
Keep this medicine out of the sight and reach of children.
Store below 30°C.

Nature and content of container
Colourless glass ampoules, glass type I, according to Ph. Eur.

Instructions for use / handling
Each ampoule is intended for single use only, and any unused solution should be discarded.
Ampoules should not be either frozen or autoclaved.

Date of revision: December 2020