Prescribing guide for baclofen in the treatment of alcoholism

For use by physicians

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Version 2

Preamble: How to read this guide?

The purpose of this guide is to help doctors prescribe baclofen in the treatment of alcohol problems as there is, to date, no standardized way to prescribe this molecule in the treatment of alcohol dependence. The Recommended Medical Practices in respect of baclofen prescription generally proposes, for neurological treatment, increasing dosage by 15mg every 3 days, while suggesting flexibility, that is to say, adapting dosages individually. The proposals below reflect the experience of the signatories to this paper, experience which itself has been based on the original method described by Olivier Ameisen (1 page 218, 2). The authors have, between them, treated more than 1500 patients with this medication, and they have learned gradually and empirically how to use baclofen to help patients in the best possible way with alcohol problems. You will frequently notice that there is no absolute consensus and that prescribers have different approaches and practices in the conduct of treatment. At the present time, it is impossible to give a definitive answer to the question.

Our bibliography (see References) includes three papers describing clinical experiences in which the authors have compiled their results allowing us to base prescription on the results they have described (3, 4, 5). There are also articles reporting single cases or a small number of cases (6, 7, 8). These recommendations are intended to help you prescribe baclofen in full confidence that you will find, as we have, that this treatment is superior to all others.

1 – Ameisen’s postulate for the high dose prescription of baclofen.

Alcoholism is a neurobiological disease whose symptoms constitute the disease; the elimination of these symptoms (loss of control of consumption, for example) suppresses the disease. Baclofen is, to date, the single molecule that has shown an ability to remove the motivation to drink in experiments with rats; the use in humans should give similar results (2). We invite you to read the book as a way to familiarize yourself with baclofen.
2 – For whom to prescribe and when to prescribe baclofen? As the first treatment? When all else has failed?

The latest release of the French Society for Studies in Alcoholism states that baclofen could be a therapeutic option when all other treatments properly conducted have failed (9). This is what happened to Olivier Ameisen when he, almost in desperation, self-administered 270 mg of baclofen. Since 2006, when prescription of baclofen for alcoholism started, it has been mainly for patients who had tried repeatedly but failed to achieve sobriety. But with the media interest, more and more therapeutically “new” patients are asking for treatment with baclofen. Must we comply with their requests? Certainly an increase in prescribing is to be foreseen as a consequence of the results of ongoing tests, of controlled studies and of the clinical experience of prescribers. Some of us prescribe baclofen as a primary treatment for alcoholism, others only after other therapeutic approaches have failed, but in the absence of formal comparisons of baclofen with other the treatments for alcohol dependence, it is difficult to give a categorical answer to this question. Here are some points which may help you in making your decision to prescribe:

- What is the history of the patient’s alcohol use?
- What is the impact of alcohol consumption in the patient’s life; severe? minimal?
- Has the patient ever followed non-drug treatments, alcohol “cures” for example, for his alcohol problems? Which? How long? With what results?
- Has the patient ever taken medication to treat his alcohol problems? Which? With what results?
- Is the patient requesting baclofen? What does he know of this medication? What does he expect from it? Does he know that the treatment is experimental and has not received formal approval from the authorities for use in alcohol problems?
- Has the patient been diagnosed with any psychopathological disorders: depression, anxiety, bipolar disorder? personality disorders?
- Is the patient taking any psychotropic medication? Which? Since when? With what effects?
- Does the patient have any current medical problems or a history, notably, of epilepsy, liver, kidney, heart disorders, history of incipient or active stomach ulcers?
- What is his daily environment? Social network? Family support? Employment status?

Taking into account these parameters, you can decide if you want to proceed with prescribing high doses of baclofen in the knowledge that the contra-indications are only of relative importance, with the exception of severe kidney disease and epilepsy. Considerations weighing in the decision are primarily the history of the patient’s attempts and failures at alcohol treatment, and the patient’s motivation to take baclofen.
3 - What information is it essential to give your patient before prescribing baclofen?

1. Treatment with baclofen is intended to make one indifferent to alcohol, that is to say, to make the preoccupation with alcohol disappear from one’s mind. Alcohol will gradually become a thought like any other, one which is no longer perpetually fixed in one’s brain. The ultimate goal is to feel free from the urge to drink. Strict and permanent abstinence from alcohol is no longer systematically the goal sought after.

2. Baclofen is an "old" drug which has been on the market for over 40 years. It is used to decrease muscular, spasticity that is to say, the muscle stiffness related to inactivity observed, for example, in individuals with paralyzed lower limbs. As a result, we have a good understanding of the adverse side effects and experience with its use over a sufficient length of time. There are also some studies of the use of baclofen at high doses (10, 11) and its potential interactions with alcohol (12). We therefore know pretty much what is to be expected with this medication.

3. The dose needed for one to reach the stage of indifference is not standard and will be determined based on one’s reactions and feelings during the administration of the medication and the progressive increase of dosage. The patient himself will know when they feel they are at the right dose. The effective dose and the adverse side effects cannot be predicted before initiating treatment.

4. The dose the patient takes will be much higher than the doses usually prescribed for this medication and will often vary between 0.5 mg / kg / day to 4 mg / kg / day or more. That is, for a person weighing 70kg, from 30 mg to 280 mg per day.

5. A gradual increase in the dosage of the medication is essential to alleviate the adverse side effects that occur when increasing the dose too quickly. On average, it takes 6 to 12 weeks to reach the required dose.

6. The adverse side effects are well known but do not follow the same pattern in everyone. One may not have any adverse reaction, or, on the other hand several that may be more or less unpleasant. Their development is variable but overall they tend to fade over time. They are reversible, in any event, as soon as you reduce the dose or, as the case may be stop the medication.

7. The duration of treatment will depend on the patient’s feelings. Some patients stop after a few months and have no further problem with alcohol without taking baclofen, but in most cases they must continue the treatment because they relapse if they stop baclofen.

8. Generally the patient will stay for several weeks or even months at the maximum, then he will reduce gradually until he finds his maintenance dose. We lack experience to be more precise.

4 - How to prescribe baclofen?

Initiating treatment

There is a consensus that it is necessary to increase the dosage gradually and at a sufficiently slow rate. Generally one starts with small daily doses of about 15mg, then one increases to 30 mg 3-4 days later and then increases by 10 mg every 3 to 5 days until one reaches the therapeutic, which varies from one person to another and is unpredictable. Some prescribers even question that there is a proven correlation between weight and dose.
Most prescribers recommend **not increasing too quickly, even if the drug is well tolerated**. Some, however, use a faster increase of 20 mg every 3-4 days during the first two weeks, and often the second fortnight, and then slow the progression after the first month to a the slower rate of increase of 10 mg every 3 to 4 days or 20 mg per week.

**When side effects become too severe**, it is advisable to remain at the same dosage. Two options are then available to the prescriber: if the adverse reaction improves one can increase dose; if it does not improve, it will be wise to return to the lower dose that did not cause the side effect. We can then try again to increase after one to two weeks if the dose is not sufficient.

Some prescribers **remain longer at certain dosages**: 30mg, 60mg, 100mg, 150mg, ...

Studies have shown that the average dose is around 150 mg /day and ranged from 30 mg / day to 400 mg/day. It is the clinical view and the feeling of the patient that must guide dose adjustment. The treatment is totally customized to the individual patient after the first two weeks of treatment in accordance with the patient’s response to therapy.

Experience has shown that it is not necessary to be sober to start treatment with baclofen. This decision will be discussed with the patient based on his clinical situation and the advantages or disadvantages of withdrawal. In case of prior withdrawal, it is useful to remember that baclofen lowers the epileptic seizure threshold. Patients may be asked to deliberately moderate alcohol consumption during the first weeks of treatment, till “indifference” sets in. This will make the patient feel that he is actively involved in his treatment: he avoids social occasions for drinking, he becomes aware of his rituals and habits related to alcohol and frees himself of them and seeks other ways than taking alcohol to cope with life’s stresses.

**Continuing treatment**

When the desired dose is reached and it is well tolerated, it is recommended to stay at that dose for 2 to 3 months (sometimes less and sometimes more) and then try to reduce the dose to find the lowest effective dose. There is no established pattern as to how to reduce the dose. One way to determine the effective dose is to reduce the dose until the urge to drink returns, and then increase the dosage one level above this dose. The decrease can be done either very slowly (10 mg per week) or in larger increments (back to two-thirds of the dose) and stay at that level for 1 or 2 months. The maintenance dose is often between one third and half the maximum dose reached.

**Maintain lifelong treatment?**

Baclofen has not been prescribed for long enough that we have the necessary clinical experience to be able to say how long the treatment will last. Experience has shown that it has been possible for some people to stop baclofen after a few months or years of treatment, but this is a minority of patients, while others must wait and see.

**5 - What are the adverse side effects of baclofen and how to mitigate them?**

Side effects (SEs) are potentially numerous and clearly unpredictable in their occurrence during treatment, apart from the drowsiness that is the most common SE during this treatment. The list below is not exhaustive but represents both the main effects encountered during the administration of baclofen and the ways to mitigate them.
Continued treatment has a favourable effect on many SEs. The have a fortunate tenancy to disappear or lessen with a reduction in dose. They are also always reversible upon discontinuation of treatment.

It is curious but nonetheless remarkable that many patients continue their treatment in spite of suffering from some potentially very unpleasant side effects.

The most common side effects

**Sleepiness**: the best known and most anticipated of SEs. Patients frequently describe a sudden and almost irresistible desire to sleep rather than true sleepiness. It usually occurs during the first days of treatment. It tends to lessen as time passes. It is sometimes very troublesome especially among working people. It is often reported as having a maximum effect after lunch, so much so that some patients start taking their tablets after lunch to avoid the postprandial sleepiness. Car drivers must be carefully warned not to use their vehicles, especially early in treatment.

**Fatigue**: This is another commonly reported effect whose development is similar to that of somnolence. Patients may report the feeling of fatigue or of somnolence or both simultaneously. Like somnolence, fatigue resolves favourably over time. Some patients sometimes complain of real aching, especially in the lower limbs.

**Dizziness**: Of variable intensity, patients describe this as an uncomfortable sensation during which they are afraid of falling. In terms of symptomatology this is a false vertigo. These sensations of dizziness often occur in the morning and resolve during the day. When they are too troublesome, it may be necessary to reduce the dose temporarily or permanently.

**Headaches**: These are reported as mainly occurring in the morning, in the skull and sometimes throbbing; they fade during the day. They respond well to conventional analgesics. They usually diminish with continued treatment.

**Nausea, vomiting, gastrointestinal disorders**: The frequent complaints are difficult to relate to baclofen, especially in early treatment because they are often symptoms described by patients at that time and especially if they stop drinking. It seems nonetheless that nausea in particular is the subject of numerous but temporary.

**Sleep disorders**: A paradoxical effect. Patients may complain of daytime sleepiness and sleep disorders. The addition of a hypnotic is desirable when the sleep deficit is too high. These sleep disorders may be accompanied by psychomotor agitation of variable intensity and sometimes painfully felt by those around them (also verbal diarrhoea). Time does not always improve these symptoms. There are sometimes very realistic or even frightening dreams or nightmares which can be very destabilizing.

The least frequent SEs

**Tremors**: in the upper extremities, they are typically mild. They do not reduce much with continued treatment

**Double vision**: highly related to muscle-relaxant properties of baclofen, it resolves well with continued treatment.
Painful paraesthesia in arms and legs: Occurring generally at night, they can be quite debilitating and seriously jeopardize the continuation of treatment. Patients report a sensation of tightness or even crushing in the upper and lower limbs accompanied by paraesthesia of varying intensity. This often persists and usually requires a temporary reduction or sometimes permanent reduction in dose.

Nocturnal apnoea: A temporary cessation of breathing during sleep. These brief apnoeas should lead the physician to examine the possibility of a true sleep apnoea syndrome which may have been revealed or even triggered by taking baclofen.

Mania or hypomania mood shift: This is probably infrequent but nevertheless rather “disturbing” clinically. It takes the form of a reduction in the duration of sleep, nocturnal agitation, a tachypsychia (acceleration of the succession of thoughts), behavioural disinhibition, verbal diarrhoea and sometimes confused ideas. These symptoms may occur for the first time in patients with no history of bipolar disorder. They necessitate the reduction or cessation of the treatment. It is sometimes necessary to prescribe a sedative, or better still a mood regulator (such as valproic acid) until symptoms disappear.

Confusional syndrome/delirium: Onset may be sudden or gradual. The patient may present in a disturbing manner to those around him yet be unaware of his condition. This syndrome necessitates a reduction in dosage or cessation of the treatment or admission to hospital. The syndrome always disappears when the treatment is discontinued.

Morbid thoughts: They may reveal an underlying depression hitherto offset by the consumption of alcohol or be the result of a sudden and painful awareness (painful lucidity) of a particularly deteriorated somatic, mental, emotional or social condition.

Other adverse effects: Some patients have complained of pain in the gums, of slurred speech, unilateral or bilateral tinnitus, chest tightness, oedema of the lower limbs or urinary problems.

Anorgasmia/loss of libido: This side effect, not described in published studies seems in fact to be frequent but is not always reported in the lists of SEs. Future studies should seek to search for it and assess its frequency.

6 – Baclofen: Is it sufficient on its own? Is there a place for other approaches along with this prescription?

Baclofen is intended to eliminate craving and free patients from their addiction to alcohol. Olivier Ameisen, having followed a large number of treatments and attended thousands of AA meetings before taking baclofen, has written very clearly in his book (Le Dernier Verre), that baclofen had allowed him to put into practice what he had learned during his cognitive behavioural psychotherapy and his AA meetings. Baclofen gave him the space to reflect and to redirect his life. He was able to do this by applying all the strategies he had learned so far but could not use because his cravings were too intrusive.

Many of us have been struck by the nature of consultations with patients on HD Baclofen. Very often, and certainly in the early stages, they are simply pharmacotherapy consultations during which there is no mention of adverse side effects, doses of baclofen or variations of craving. When the effective dosage is reached at the cost of minimal adverse effects, many difficulties remain particularly psycho-social difficulties. Baclofen, even when it is very effective, does not cure
solitude, the sheer pain of living, difficulties with interpersonal relations, or unemployment, but it allows one to take one’s distance and face reality thus sometimes to suffer acutely as one becomes aware of the mess one has made of one’s life. In this context, it is essential that the patients continue to get support on their journeys towards their psycho-social recovery. And it is appropriate at this stage to encourage and help patients to improve their psychological state, to overcome their isolation or to find pleasure in life. To do this, a multidisciplinary approach is essential.

In the presence of anxiety, depression, bipolar disorder, or borderline states where alcoholism is a symptom, psychiatric treatment adapted to these conditions will be maintained. Baclofen does not present contra-indicated with the usual psychotropic drugs (benzodiazepines, hypnotics, SSRIs, neuroleptics ...)

Psychotherapy, cognitive-behavioural or not, and participation in support groups is of great help, although this will be difficult for the group when patients have not chosen abstinence. All this remains to be developed. The paradigm shift brought about by HD Baclofen treatment requires rethinking the therapeutic methods for the whole field of alcoholism.

The value of baclofen consists in this new space that it gives patients, to rethink and reorganize their lives.

As with any withdrawal, a period of moderate or severe depression occurs. The patient finds himself facing his own reality which was hiding behind alcohol. To accompany him on this personal journey is part of the treatment plan.

The patient’s entourage, those close to the patient, must also move from an insistence on abstinence with its attendant pressures to an encouragement to reduce consumption. Some prescribers will find it useful to establish systematic contact with the patient’s immediate family and friends, even having them attend at their offices, so as to assist them with this change of attitude.

7 - What are the risks of prescribing baclofen: off-licence prescribing?

Prescribing a drug outside of its usual and accepted uses is widely practiced in medicine regardless of the specialty (General Medicine, Paediatrics, Psychiatry ...). It has often happened that it is discovered that a molecule can have unsuspected properties in an unexpected therapeutic area (Aspirin/cardio, carbamazepine as a mood stabilizer, antidepressants in chronic pain, etc.).

Legislators have foreseen this situation and provided for it (13.14). Off-licence prescribing (without authorization marketing) is permitted under the following conditions:

- Scientific data justify this therapeutic use.
- It is required as a treatment due to the failure of properly conducted conventional therapies.
- The patient has been given comprehensive information concerning the potential benefits and risks of the treatment.
- Informed consent of the patient and his written acceptance to take this treatment with full knowledge of the risks involved.
- Appropriate medical monitoring.
- Possibility of non-reimbursement of prescription

Under these conditions, the off-licence prescription is legitimate and ethically defensible, but it will remain an off-licence prescription and in this sense always entails some risk if something goes wrong and there are serious adverse reactions (e.g., a drowsy patient who falls asleep at the wheel of his car and causes a fatal accident).
Consent for Treatment with baclofen

- I hereby certify that I have received from Dr. XXXXX detailed information regarding the treatment with baclofen in high doses (HD) to treat my problems with alcohol.

- I know that this treatment has not received formal authorization from the competent authorities. I want to take this treatment despite the potential side effects because so far I have not found any effective solution to my problems with alcohol.

- I understand that the main side effects are: drowsiness, fatigue, headaches, dizziness and sleep disturbance; in rare cases, delirium may occur. Dr. XXXXX has informed me that this state of mental confusion requires stopping the increase of doses and perhaps stopping treatment.

- I have clearly informed Dr. XXXX of all my medical history, so that he could determine whether particular rules of caution should be applied to my baclofen prescription.

- Due to possible withdrawal symptoms upon discontinuation of baclofen, I know that one should not abruptly stop taking baclofen, but gradually decrease as instructed by Dr. XXXXX.

- I undertake not to drive my car or use dangerous machinery for at least the time of the increase in dosage and to resume such activities only in consultation with Dr. XXXX.

- I undertake to follow scrupulously the directions and prescriptions made by Dr. XXXXX and to keep him/her informed of the difficulties and problems that may occur during this treatment.

- Should I encounter serious problems related to this treatment, I strongly urge my relatives not to initiate legal proceedings against Dr. XXXXX (this point is not unanimous among prescribers).

- I have had time to make my decision to undergo this treatment.

________________ “read and approved”

NAME
Date

There is no prescription schedule (titration) for baclofen which has absolute validity and each doctor can prescribe it differently. The prescription schedule proposed here is a pattern we have adopted by consensus, without claiming that this is necessarily the best regimen.
Scheme with four doses per day

Baclofen (Liorésal ®) 10 mg
Theoretical therapeutic Dose: 200mg/day

<table>
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<th>Day</th>
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<th>13h</th>
<th>18h</th>
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<td>/</td>
<td>/</td>
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<td>½</td>
<td>½</td>
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<td>1</td>
<td>1</td>
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<tr>
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<td>1</td>
<td>1</td>
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<tr>
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<td>1½</td>
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<tr>
<td>D31 D32 D33 D34 D35</td>
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<td>1½</td>
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<td>2</td>
<td>7</td>
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<td>D36 D37 D38 D39 D40</td>
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<td>2</td>
<td>2</td>
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<td>8</td>
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<tr>
<td>D41 D42 D43 D44 D45</td>
<td>2½</td>
<td>2</td>
<td>2½</td>
<td>2½</td>
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<td>D46 D47 D48 D49 D50</td>
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<td>D51 D52 D53 D54 D55</td>
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Do not shorten the stages from 5 days even if treatment is well tolerated.
- Extend the duration of the stages beyond 5 days if levels of drowsiness or some other bothersome side effect has not disappeared.
- The most common side effects are drowsiness, muscle fatigue, dizziness. These may also occur, though less frequently, headaches, tremors, nausea, double vision, slurred speech, disturbed sleep, tinnitus, paraesthesia (ants) in the hands or feet, a sensation of agitation. These side effects tend to disappear gradually as and when the ascension of doses. They are reversible upon reduction or discontinuation of treatment.
- In rare cases some patients have complained of difficulty sleeping, restlessness at night or have been known to exhibit periods of confused ideas. In these cases one must go back to the previous dose of baclofen and not increase again until 7 days later. Then one should try again to reach the next step. In case of recurrence of these events, you must not increase the dose and must stick to the dose that does not cause these effects.
- Do not stop taking baclofen abruptly gradually decrease over 10-15 days.
- If there is a strong urge to drink, take 10 mg (1 tab.) of baclofen.
- Do not drive your car during the increase of dosage.
Bibliographical references:

5. Rigal L, Alexandre-Dubroeucq C., de Beaurepaire R., Le Jeunne C., Jaury P. Abstinence and 'low risk' consumption one year after the initiation of high-dose baclofen: a retrospective study among 'high risk' drinkers. Alcohol and Alcoholism, 2012 (in Press)

Annotations of the translators:

- The original French document was found here: http://www.alcool-et-baclofene.fr/pdf/guide-de-prescription-du-baclofene.pdf
- The original document is not dated. The timestamp of the original French pdf-file is 03-26-2012

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