Petadolex®

Supports Neurological Discomfort

#1 Neurologist recommended butterbur supplement

There are other butterbur products **but there is only one Petadolex®**

The ORIGINAL butterbur extract (Petasites) containing at least 15% of the active ingredients petasin and isopetasin. It is the only butterbur product used in research and scientific studies, because of the patented purification and toxin-elimination used in their manufacture,

Try Petadolex gelcaps with confidence

- ✓ Standardized Formula: Truly contains 15% Petasites Hybridus Petasin Extract
- ✓ PA-free: zero detectable pyrrolizidine alkaloids (detection limit 0.035 ppm)
- ✓ The only butterbur supplement used in medical research
- ✓ Cited by medical standard-of-care guidelines
- ✓ Patented butterbur root extract process
- ✓ 20+ years, 1 million+ users, no adverse effects

Gluten & Wheat Free

Milk & Lactose Free

No Artificial flavors, sweeteners, colors or preservatives

Vegetarian Capsule

linpharma

To order, go to www.petadolex.com Or Call 1-888-301-1084

Migraine Treatments of the Month

A root, a spray and an intravenous infusion: 3 different approaches to migraine relief

A Root (Petadolex)

Butterbur (scientific name *Petasites hybridus*) is a member of the sunflower family that grows in marshes and is largely found in southern Europe and parts of Asia. There was a time when its large leaves were used to wrap butter during warm weather, and its medicinal value was recognized as long ago as the Middle Ages, when it was a common remedy for fever.

More recently butterburr has been used to treat migraine. A specific extract made from the roots of the plant is marketed as "Petadolex", and for years European neurologists recommended Petadolex to their patients for migraine prevention. Petadolex appears to have multiple mechanisms of action by which it may stabilize the biologic circuitry that produces migraine, chief of which may reside in its anti-inflammatory properties.

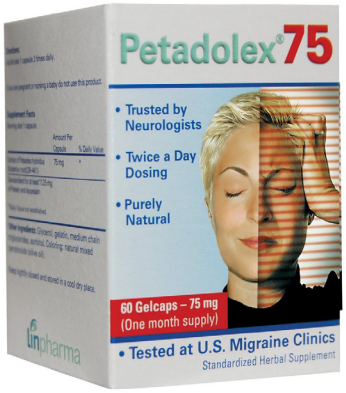
Supporting such clinical use of the butterbur root extract is compelling evidence from research undertaken by leading American neuroscientists. In one notable study conducted by Lipton et al, Petadolex taken at a dose of 75 mg twice daily reduced migraine attack frequency by almost 50%. As has been characteristic of other Petadolex treatment studies, the most common side effect reported was burping.

In an analysis performed by Diener and colleagues that used a somewhat different endpoint for treatment response, almost half of patients receiving Petadolex enjoyed a 50% or greater reduction in migraine frequency. This was in contrast to a response rate of only 15% in patients receiving placebo.

One important word of caution: some products marketed as Petadolex may contain alkaloids that can seriously harm your liver. Alkaloids are nitrogen-containing organic compounds derived from plants which may have a profoundly negative physiologic action effect on humans. An extreme example is the poison, strychnine.

As with many nutraceuticals which are available direct to consumer, the various products marketed as "Petadolex" may differ significantly from one another. Some "Petadolex" may promise much in terms of migraine relief... but is in fact biologically inactive and thus nothing more than a placebo. Again, of much greater concern is the potential for unregulated products to contain toxic alkaloids that can cause great harm.

So, a rose is not necessarily a rose. Do not use butterbur products unless they are certified to be free of pyrrolizidine alkaloids.



Ask your healthcare provider to recommend a trusted brand. Having knowledge that the Petadolex brand produced by Linpharma has been investigated thoroughly by the FDA and the equivalent regulatory agency in Germany for its safety and biologic activity, the editor recommends this specific brand to his patients.

In summary: When a well-investigated and trusted brand is used, Petadolex can serve as safe, well-tolerated and effective non-prescription therapy for migraine prevention.

A Spray (Trudhesa)

Even prior to the advent of injectable sumatriptan (*Imitrex*) 30 years ago, investigators had been searching for an acute migraine therapy that could bypass the tricky landscape of the gastrointestinal tract so as to reach its therapeutic target more rapidly and consistently. Inhalant devices similar to those used by asthmatics, intranasal sprays and even rectal suppositories were investigated and in some cases introduced into clinical practice, but no breakthroughs were forthcoming…until now.

Now we may have an attractive alternative to orally administered medication or injectable sumatriptan for self-treatment of moderate to severe migraine headache. Dihydroergotamine (DHE) is an old drug, arguably the first of the "designer drugs" for migraine (its synthesis involves tinkering with the naturally occurring ergot). Because it is rapidly metabolized within the gut and broken down into therapeutically inactive fragments, DHE is not suitable for oral administration. Given intravenously or subcutaneously it can be remarkably effective for treating acute migraine headache, but intravenous administration requires a healthcare provider, and – in contrast to sumatriptan – there is no autoinjector available for subcutaneous self-administration.

But there is the nose. The effectiveness of DHE delivered via nasal spray appears to be heavily dependent upon the specific section of the nose towards which the spray is directed. Only a portion of spray directed towards the lower portion of the nasal cavity will be absorbed into the circulation and thus reach its therapeutic target, and a substantial portion may simply drip down into the back of the throat and ultimately into the stomach, where, as previously mentioned, it cannot survive to be absorbed into the bloodstream with its therapeutic potential remaining intact.

Now there is an intranasal formulation of DHE (*Trudhesa*) employing a novel delivery device. *Trudhesa's* "precision olfactory delivery" (POD) system ensures the spray is directed towards the superior portion of the nasal cavity, an area richly supplied by blood vessels which readily absorb the medication into the circulation. Research studies have demonstrated that the concentration of *Trudhesa* in the bloodstream reaches a therapeutic level very rapidly following administration, and both its effectiveness and the rapidity with which headache relief is achieved approaches what is experienced with injectable sumatriptan.

Another attractive feature of *Trudhesa*: as a consequence of its longer half-life in the body, the frequency of early recurrent headache after initially successful treatment is much lower with DHE/*Trudhesa* than with injectable sumatriptan or the other triptans. Thus *Trudhesa* may represent a particularly attractive option for those whose more severe migraine headaches temporarily respond to their

usual treatment but consistently recur within the following 24 hours (for more on this topic see Doctor on Call in this issue).

Downside? Not much. Occasionally *Trudhesa* can induce nausea or a runny nose. Another important consideration: because both DHE/*Trudhesa* and the triptans possess some potential for causing constriction of arteries, it is recommended that one avoid using a triptan within 24 hours of administering *Trudhesa* and avoid using *Trudhesa* within 24 hours of administering a triptan.

In summary: *Trudhesa* represents a most welcome and very nice alternative to orally administered medication, to other intranasally administered medications currently available and to injectable sumatriptan for the acute treatment of moderate to severe migraine headache.

An intravenous infusion

The biologic circuitry which produces migraine is driven by electrochemical transmission of a head pain signal. The two chemicals that play a major role in that transmission are serotonin and calcitonin gene related peptide (CGRP). If serotonin receptors that block the transmission of head pain signal can be activated or CGRP can be disabled, the migraine circuit can be "short-circuited"…resulting in reduced migraine burden.

2018 marked the arrival of erenumab (*Aimovig*), the first of the synthesized monoclonal antibodies (Mabs) intended to hit the CGRP target. Aimovig blocks the receptor to CGRP within the migraine circuitry, preventing the CGRP molecule from docking with its receptor and thus blocking transmission of head pain signal. Fremanezumab (*Ajovy*) and galcanezumab (*Emgality*), also CGRP Mabs, soon followed. Their mechanism of action is a bit different from that of *Aimovig* in that they attack the CGRP molecule directly and disable it rather than block its receptor. All three medications typically are self-administered subcutaneously once a month.

The next anti-CGRP Mab to become available is interestingly different. Epitenzumab (*Vyepti*) is administered intravenously once every three months for either prevention of episodic migraine or suppression of chronic migraine. Clinical research involving Vyepti has demonstrated that the therapy is effective not only for reducing monthly migraine days but also for providing a positive and lasting impact on the migraine symptoms experienced by migraineurs in the "real world".

Why would one favor *Vyepti* over the subcutaneously self-administered anti-CGRP Mabs or the orally administered anti-CGRP "gepants"? One obvious reason: some patients prefer to avoid taking a pill daily or every other day and also shun the prospect of self-injection. Particularly for patients prone to noncompliance with treatment, the simplicity of a 30 minute infusion every three months may serve to help keep them on therapeutic track.

Less obvious reasons for admiring *Vyepti* include the rapidity with which it begins to exert a positive treatment response effect in those destined to respond. In the large scale, placebo-controlled clinical research studies that earned Vyepti its FDA approval, for patients with chronic migraine the evidence of benefit was present as early as the first 24 hours following initial intravenous infusion, and a sizable proportion of responders began to experience a reduction in headache burden within the first week following treatment. This rapidity of action may result from the intravenous administration of the drug. Whereas the absorption of orally, intranasally and subcutaneously administered medications may be erratic, because of its intravenous route *Vyepti* is 100% "bioavailable". This presumably results in a high concentration of the drug rapidly reaching its CGRP target, disabling that target and continuing to exert that therapeutic action for an extended period.

Aside from occasional rhinitis (runny nose) or rarely occurring hypersensitivity reactions, side effects are extremely uncommon with Vyepti. This is perhaps the most well-tolerated of all the new "designer drugs" for migraine treatment.

In summary: Given that the drug so well tolerated, often effective and rapidly so, for patients with episodic or chronic migraine whose headache burden is sufficiently high to require prevention therapy, intravenous infusion of Vyepti every three months is a reasonable and attractive option. M