

**The UK Medicines and Healthcare products Regulatory Agency (MHRA)
Sativex Public Information Report (PIR)**

Q&A

1. Why has MHRA published this PIR?

The MHRA has taken this unprecedented step due to its view of the “huge public interest” in Sativex and the fact that approximately 1400 patients in the UK have so far received the medicine on prescription on a named patient basis. New patients continue to be prescribed Sativex every day. Hence, the MHRA considers that it is in the public interest for potential prescribers to have further information on the medicine in order to assist them with their prescribing decision.

2. What is a “named patient” prescription? How are patients currently entitled to receive Sativex?

Since Sativex was approved as a prescription medicine in Canada a couple of years ago, it has been possible for UK doctors and patients to prescribe Sativex as an unlicensed medicine on a “named patient” basis. Such prescriptions can be written by any UK doctor if he or she considers that a particular medicine may be of benefit to a specific “named” patient.

Sativex is classified as a controlled substance, and, prior to the Canadian approval, it was necessary for an individual doctor to apply for a patient-specific license from the Home Office. Since early 2006, the Home Office has put in place a licence to all UK doctors, patients and pharmacists permitting the possession and use of Sativex without a patient-specific license. In response to prescriptions, any pharmacist in the UK is able to arrange overnight delivery of Sativex from a UK distribution centre.

3. Which patients can currently receive Sativex on prescription? Are only people with MS eligible?

The decision about whether to prescribe Sativex as an unlicensed medicine is entirely a decision to be taken between the prescribing doctor and the patient. The situation is the same for people with MS as for those with any other medical condition – the suitability of any patient for Sativex is solely for a patient’s doctor to decide. GW Pharmaceuticals is able to provide product information only in response to a specific enquiry from a health care professional.

4. Does the NHS pay for Sativex prescriptions?

As with every medicine, licensed or unlicensed, the question of payment for the prescription is one for the paying authorities to decide. Experience to date suggests that a large proportion of Sativex prescriptions have been funded through the NHS.

5. How do I find out more information about prescribing/receiving Sativex?

Any decision to prescribe Sativex is entirely one to be taken between the prescribing doctor and the patient. GW Pharmaceuticals is able to provide product information only in response to a specific enquiry from a health care professional. GW is not able to provide any medical advice regarding any individual patient. Hence, any patient who wishes to receive information on Sativex can only do so through consultation with their doctor.

Doctors may contact GW for more information about Sativex, and how to prescribe it, either by phone on 01980 557026 or by email at enquiries@gwpharm.com

6. What information does the PIR contain?

The PIR contains the details of the recent assessment of Sativex, by the MHRA. The information in the assessment relates to an application made for the marketing authorisation of Sativex as a treatment for spasticity in multiple sclerosis. The PIR summarises the MHRAs view of the evidence presented in this recent regulatory application.

The PIR also contains a consensus statement prepared by a panel of clinical experts, chaired by Lord Walton, an eminent British neurologist. This statement expresses their independent view that the evidence supports the approval of Sativex for the relief of MS spasticity.

7. What are the principal conclusions of the PIR?

The Report states that the major issue to be overcome prior to approval of Sativex for the relief of spasticity in people with Multiple Sclerosis relates to the provision of specific additional efficacy data. Key summary conclusions of the Report are:

- All pharmaceutical points raised during the procedure have been resolved satisfactorily.
- There are no preclinical objections to the granting of a marketing authorisation.
- The safety profile is considered acceptable in principle for the proposed patient population and indication, providing sufficient efficacy is demonstrated.
- The key outstanding efficacy issue is to carry out a prospectively planned study to confirm GW's "post hoc analyses supporting an argument that non responders can be identified in a 4 week therapeutic trial, and that the mean treatment effect in the remaining patients who would continue to receive treatment, would be clinically significant."

In addition to the guidance disclosed in the assessment report on the additional required clinical trial, GW has separately received formal "Scientific Advice" from MHRA on the company's protocol design and statistical analysis plan.

8. Why was Sativex not approved in the last application?

The PIR concludes that the MHRA wish to see additional evidence of the efficacy of Sativex before issuing a marketing authorisation. Specifically, an additional clinical trial is required which clarifies the magnitude of the clinical effect over a three month period on patients who respond to the treatment in an initial four week “therapeutic trial” of therapy.

9. What does the PIR conclude about the quality of Sativex?

All points raised by the MHRA in respect of the quality of Sativex were resolved satisfactorily.

10. What does the PIR conclude about the safety of Sativex?

As with all medicines, Sativex is associated with unwanted effects (side-effects). The PIR concludes that the evidence of safety is sufficient to support approval, provided that efficacy is demonstrated.

Sativex has now been available as a prescription medicine in Canada, as an unlicensed medicine in the UK, and as part of a local government-sponsored compassionate use programme in Catalonia. This extensive ‘real-world’ experience has not revealed any unexpected new safety concerns.

11. What does the PIR conclude about the efficacy of Sativex?

The MHRA conclude that the evidence has not yet demonstrated sufficient evidence of efficacy. They identify the design of an additional clinical trial through which such compelling evidence of efficacy can be generated. An independent body of clinical experts, headed by Lord Walton, wrote to MHRA during the course of the application to disagree with the MHRA’s opinion.

12. What are the most common side effects of taking Sativex?

In order of frequency, the most common side effects are dizziness, fatigue and nausea. These are generally mild or moderate and resolve with continuing treatment. These side effects are seen at a similar frequency with many other medicines, particularly those which target the nervous system.

13. Who is Lord Walton? What does he and his fellow clinical experts say about Sativex?

Lord Walton of Detchant is an eminent British neurologist, formerly Professor of Neurology at The University of Newcastle upon Tyne. He was previously President of the Royal Society of Medicine, of the British Medical Association, of the General Medical Council, of The Association of British Neurologists and of the World

Federation of Neurology. The other authors of the report represent a cross section of patient representatives, experts in neurorehabilitation, in general practice and in clinical research in multiple sclerosis.

They conclude that the evidence supports the approval of Sativex for the relief of spasticity in people with MS.

14. Does the PIR contain any information about the use of Sativex other than for MS spasticity?

No. Although Sativex is approved as a prescription medicine in Canada for the relief of neuropathic pain in people with MS, and in the relief of chronic pain in patients with advanced cancer, the recent MHRA assessment was limited to the indication of spasticity in people with MS.

15. Will Sativex be approved by the MHRA in the future? What further data is GW generating to answer the MHRA's outstanding concern?

GW is committed to providing the necessary additional evidence to gain approval for Sativex from the MHRA. GW continues to conduct clinical studies which investigate the use of Sativex in people with MS, and also in cancer pain. GW anticipates being able to re-submit evidence to the MHRA during the course of 2008 or early in 2009. Our intention is to ensure that the evidence for the efficacy of Sativex meets the MHRA's outstanding requirement.

Specifically in respect of MS spasticity, GW has now started a new study, designed in consultation with the MHRA, which intends to address the remaining efficacy issue raised by the MHRA. This study should be completed towards the end of 2008.