

Current medical uses of nabiximols

1. Please outline for the committee the medical indications for which Sativex is currently being used, and the present state of research in relation to the medical potential of nabiximols.

Sativex (nabixamols) has approved therapeutic use in Australia as follows: treatment for symptom improvement in patients with moderate to severe spasticity due to multiple sclerosis (MS) who have not responded adequately to other anti spasticity medication and who demonstrate clinically significant improvement in spasticity related symptoms during an initial trial of therapy. Clinical trials are currently being undertaken by GW Pharma Ltd to investigate the use of Sativex in cancer pain and neuropathic pain.

2. What are the active ingredient(s) in nabiximols, and what relationship does it bear to the raw cannabis plant?

Sativex contains 80mg/mL nabiximols [each mL contains 80mg of extract Cannabis sativa L., corresponding to 56 mg total cannabinoids including 27 mg of delta-9-tetrahydrocannabinol (THC) and 25mg of cannabidiol (CBD). Nabiximols is a highly characterized botanical extract of Cannabis sativa L., containing delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) as the major constituents together with other cannabinoid and non-cannabinoid components. It is defined in the Standard for the Uniform Scheduling of Medicines and Poisons as a "botanical extract of Cannabis sativa, which includes the following cannabinoids: tetrahydrocannabinol, cannabidiol, cannabinol, cannabigerol, cannabichromene, cannabidiolic acid, tetrahydrocannabinolic acid, tetrahydrocannabivanol, and cannabidivanol, where tetrahydrocannabinol and cannabidiol (in approximately equal proportions) comprise not less than 90 per cent of the total cannabinoid content) in a buccal spray for human therapeutic use".

3. How is the consistency and quality of the medication guaranteed, given that Sativex incorporates a herbal starting product?

Sativex is a cannabis based medicine that contains consistent amounts of delta-9-tetrahydrocannabinol (THC), cannabidiol (CBD), as well as other named and specified cannabinoids, plant terpenes and other plant components. The composition reflects that of naturally occurring, Cannabis sativa L., which contains approximately equal quantities of the principal cannabinoids THC and CBD (as well as a variety of other plant components). Two chemotypes (or varieties) of Cannabis sativa L. that have the desired cannabinoid profile and chemical/chromatographic fingerprint are used in the manufacture of Sativex. GW Pharma Ltd, the developer and manufacturer of Sativex, has a specialist understanding of the plant genetics of Cannabis sativa L. that ensures stability of the selected chemotypes and secures a consistent raw material for production. The finished medicinal product is a blend of botanical extracts. In order to provide close control over both the production process and the final concentration of cannabinoids in Sativex, extracts from two defined chemotypes of Cannabis sativa L. plants, containing high THC or high CBD are used to manufacture Sativex. The separate extracts from each chemotype are used to accurately provide the desired levels of THC and CBD. The final product comprises specified and controlled quantities of the principal cannabinoids and has tightly controlled product specifications.

Global availability and use of Sativex

4. In which countries globally has Sativex been approved for use and made available to patients?

Sativex is approved in 28 countries globally. It is currently available on prescription in the UK, Spain, Germany, Canada, Denmark, Norway, Italy, Israel, Iceland, Austria, Poland, Sweden, Finland, Switzerland, Lichtenstein and New Zealand. Approvals have also been granted in Belgium, Czech Republic, Luxembourg, Netherlands, Portugal, Slovakia, France, Ireland, Kuwait, Malaysia and the United Arab Emirates.

5. How many patients are accessing Sativex globally at the present time?

As of 15th April 2015, it is estimated that there have been 45432 patient years of exposure to Sativex.

Availability of Sativex in Australia

6. What federal and State/Territory regulatory approvals are required in order for Sativex to be made available to patients in Australia? a. Which of these approvals (if any) have already been sought and completed?

Sativex was registered by the TGA on 26 November 2012. However, the product is subject to extensive RMP requirements, and cannot be marketed until these requirements have been fulfilled. They include the development of an educational accreditation program for prescribers, development of a Patient Registry for Sativex in Australia, and development and implementation of a mechanism that limits supply of Sativex to patients of a 'registered' prescriber population limited to neurologists and rehabilitation physicians who have successfully completed the educational module. In most instances, a registered prescriber requires an authority/permit to prescribe Sativex for more than 8 weeks from the respective State/Territory. The States/Territories also control the requirements for the storage and supply of Sativex by pharmacies. These requirements vary on a State-by-State basis. Novartis has had extensive consultations with the health authorities in each State and Territory regarding the storage and supply requirements for Sativex within Australia and, thus far, no satisfactory resolution has been found. Being a Schedule 8 (S8) medicine (drug of dependence), Sativex is required to be stored in a safe. It also requires storage in a refrigerator (store at 2-8°C). Pharmacies cannot generally accommodate a locked refrigerator. A central supply mechanism has been investigated by Novartis but certain States do not allow the transport of an S8 medicine across borders. If Sativex were to be made available to patients, issues of law-enforcement still remain to be resolved. For example, the impact of roadside drug testing on patients prescribed Sativex needs to be addressed.

7. Why is Sativex currently not being commercially supplied in Australia, and what barriers need to be overcome in order to make Sativex commercially available?

As identified above, the main barriers are: an acceptable mechanism of supply that can accommodate storage under cold chain and compliance with State storage and transportation requirements for a Schedule 8 medicine; the need for compliance with the RMP requirements, including the development of a Patient Registry; and lack of PBS listing.

8. Are any patients in Australia currently accessing Sativex through clinical trials, or other mechanisms?

Novartis is unable to comment as to whether Sativex is being sourced by individuals through other routes e.g. personal import or for clinical investigation direct from GW Pharma Ltd or an international pharmacy.

9. Is it possible for Australian consumers to purchase Sativex from outside of Australia?

There are strict requirements for the importation of a product such as Sativex. Novartis is unable to comment on whether Australian consumers are accessing Sativex from outside Australia.

10. Is Novartis seeking to start supplying Sativex on a commercial basis in Australia in the future? a. If so, what processes are being undertaken to make this happen, and what is the expected timeframe for Sativex to become commercially available?

Sativex is only approved for use in a limited patient population. There are currently too many barriers for Novartis to be able to supply, as identified above.

Retail cost of Sativex

- 11. What is the retail cost of Sativex in the jurisdictions in which it is currently available to patients?*
- 12. What would the likely cost be of Sativex prescriptions in Australia if it was to become commercially available in Australia?*
- 13. Has Sativex been approved as a government-subsidised medication in any of the jurisdictions in which it is currently used? If so, what is the quantum of the subsidy?*
- 14. Noting that the Pharmaceutical Benefits Advisory Committee rejected Novartis' submission seeking listing of nabiximols under the Pharmaceutical Benefits Scheme in July 2013, does Novartis have any plans to re-apply for nabiximols to be listed under the PBS, on the basis of emerging clinical evidence or other factors?*

Please see answers above with regard to questions concerning jurisdictions outside of Australia. With regards to pricing in Australia, were Sativex reimbursed via the PBS, then the cost would be the relevant patient co-payment as per all other items on the PBS.

Regulatory environment in Australia

- 15. Do you have any comment on the proposed Regulator of Medicinal Cannabis Bill 2014 currently under consideration by the committee?*
- 16. In your view, would establishing a standalone federal regulator for medicinal cannabis (as proposed by the Bill) impact on the ability of companies such as Novartis to develop and commercialise cannabinoid-based medicines in Australia? If so, what do you consider the impact would be?*

The proposal is worthy of exploration but it would be important that any new legislative regime successfully resolve the issues like the ones identified above.