

Prescribing information

Sativex® Oromucosal Spray Prescribing Information (refer to full Summary of Product Characteristics (SmPC) before prescribing).

Presentation: 1mL contains: 38-44mg & 35-42mg of two extracts from *Cannabis sativa* L., (Cannabis leaf and flower) corresponding to 27mg delta-9-tetrahydrocannabinol (THC) and 25mg cannabidiol (CBD). Each 100 microlitre spray contains: 2.7mg THC and 2.5mg CBD. **Indication(s):** 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. **Posology and method of administration:** treatment must be initiated and supervised by a physician with specialist expertise in MS. Intended to be used in addition to patient's current anti-spasticity medication. Oromucosal use only. Shake before use. Direct spray at different sites on the oromucosal surface changing site each time product is used. May take up to 2 weeks to find optimal dose, review response after 4 weeks of treatment. Re-evaluate long term treatment periodically. Standardise administration as far as possible in relation to food intake to minimise variability in bioavailability. **Adults:** titration period necessary; number/timing of sprays will vary between patients. Number of sprays increased daily according to SmPC table, up to maximum of 12 sprays per day with minimum 15 minutes between sprays. **Children and adolescents:** not recommended. **Elderly:** no specific studies but CNS side effects may be more likely (see Warnings and Precautions). **Significant hepatic or renal impairment:** no specific studies but effects of Sativex may be exaggerated or prolonged. Frequent clinical evaluation recommended. **Contraindications:** hypersensitivity to cannabinoids or excipients. Breast feeding. Known/suspected history or family history of schizophrenia/other psychotic illness. History of severe personality disorder/other significant psychiatric disorders other than depression associated with MS. **Warnings and precautions:** caution during initial titration essential since alterations in pulse rate and blood pressure observed following initial dosing. Fainting episodes observed. Not recommended in patients with serious cardiovascular disease. Caution in patients with history of epilepsy/recurrent seizures. Psychiatric symptoms (anxiety, illusions, mood changes, paranoid ideas) reported. Disorientation (or confusion), hallucinations, delusional beliefs or transient psychotic reactions reported and causal association with suicidal ideation not ruled out in few cases: in any of these circumstances stop treatment immediately and monitor until symptom completely resolved. THC and CBD are metabolised in the liver and approx. one third (parent drug and metabolites) excreted in urine. Several THC metabolites may be psychoactive. Frequent clinical evaluation recommended if significant impaired hepatic or renal function exists due to possible exaggerated or prolonged effects. Contains approx. 50% v/v ethanol. Risk of falls if spasticity/muscle strength no longer sufficient to maintain posture/gait. CNS side effects e.g. dizziness, somnolence could impact personal safety, e.g. hot food & drink preparation. Theoretical risk of additive effect with muscle-relaxing agents, not seen in clinical trials but warn patients risk of falls may increase. No effect seen on fertility but cannabinoids shown to affect spermatogenesis in animals. Female patients of child-bearing potential/male patients with a partner of child-bearing potential should use reliable contraception. Patients with a history of substance abuse may be more prone to abuse Sativex. Withdrawal symptoms following abrupt withdrawal of long-term Sativex are likely to be limited to transient disturbances of sleep, emotion or appetite. No increase in daily dosage observed in long-term use; self reported levels of 'intoxication' low; dependence on Sativex unlikely. Adverse reactions reported possibly associated with route of administration e.g. mild/moderate stinging at time of application and possible leukoplakia (unconfirmed or unrelated); prescribers should consult SmPC for

further information. Vary site of application if discomfort or ulceration observed. Do not continue spraying onto sore or inflamed mucous membrane. Perform regular inspection of oral mucosa in long-term administration. In cases of lesions or persistent soreness, interrupt medication until complete resolution. Advise patient to check legal status of medicine before travelling to other countries. **Interactions:** THC and CBD metabolised by cytochrome P450: inhibitory effects seen *in vitro* and in animal models only at doses significantly higher than max. in clinical trials. Co-administration with food results in mean increase in C_{max} and AUC. Concomitant ketoconazole increases C_{max} and AUC of THC & CBD. Starting or stopping of concomitant treatment with CYP3A4 inhibitors (e.g. ketoconazole, ritonavir, clarithromycin) or CYP3A4 inducers (e.g. rifampicin, carbamazepine, St John's Wort) may require new dose titration. Inhibition of p-glycoprotein cannot be excluded: caution recommended with concomitant digoxin and other p-glycoprotein substrates. Risk of additive sedation and muscle relaxing effects with hypnotics, sedatives and drugs with sedating effects. Sativex may interact with alcohol, affecting co-ordination, concentration and ability to respond quickly, could increase risk of falls/other accidents; advise patient accordingly. Recommend to avoid alcoholic beverages especially at beginning of treatment or when changing dose. **Pregnancy and lactation:** do not use in pregnancy unless benefit outweighs potential risks. Do not use if breast feeding. Insufficient experience of effects on reproduction - use reliable contraception during therapy and for 3 months after discontinuation. **Effects on ability to drive and use machines:** do not drive, operate machinery or engage in any hazardous activity if experiencing significant CNS side effects; warn patients may cause loss of consciousness. **Side effects:** very common - dizziness, fatigue; common - anorexia, decreased or increased appetite, depression, disorientation, dissociation, euphoria, amnesia, balance disorder, disturbance in attention, dysarthria, dysgeusia, lethargy, memory impairment, somnolence, blurred vision, vertigo, constipation, diarrhoea, dry mouth, glossodynia, mouth ulceration, nausea, oral discomfort/pain, vomiting, application site pain, asthenia, feeling abnormal/drunk, malaise, fall; uncommon - hallucination, illusion, paranoia, suicidal ideation, delusional perception, syncope, palpitations, tachycardia, hypertension, pharyngitis, throat irritation, upper abdominal pain, oral mucosal disorders e.g. discolouration, exfoliation, stomatitis, tooth discolouration, application site irritation. A single case of ventricular bigeminy has been reported although this was in the context of acute nut allergy. Prescribers should consult the SmPC for further information on side effects. **Overdose:** symptomatic and supportive treatment required. **Special Precautions for Storage:** refrigerate (2 to 8°C); once opened refrigeration is unnecessary but do not store above 25°C. **Legal Category:** POM. **Package Quantities and Basic NHS Costs:** 3 x 10mL £375.00. **MA holder:** GW Pharma Ltd, Porton Down Science Park, Salisbury, Wiltshire SP4 0JQ. **MA Number(s):** PL 18024/0009. **Further information available from:** Bayer plc, Bayer House, Strawberry Hill, Newbury, Berkshire RG14 1JA United Kingdom. Telephone: 01635 563000. **Date of preparation:** October 2011. Sativex® is a registered trademark of GW Pharma Ltd.

Adverse events should be reported. Reporting forms and information can be found at <http://www.mhra.gov.uk/yellowcard>. Adverse events should also be reported to GW Pharma Ltd. Tel: 01223 233410, Fax: 01223 233319