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Stable dose cannabinoid medicine (Sativex®; THC+CBD) can provide sustained efficacy in the treatment of refractory painful diabetic neuropathy or other peripheral neuropathic pain associated with allodynia.

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» BACKGROUND
Neuropathic Pain (NP) poses a major challenge:
• Most common long-term complication of diabetes mellitus
• Leads to great morbidity and mortality
• Results in a huge economic burden for diabetes care
• Can be a disabling and painful symptom
• Existing treatments afford only partial relief and have unpleasant side-effects

Study drug: Sativex® (THC/CBD) endocannabinoid system modulator
• Approved in Canada for relief of central neuropathic pain in Multiple Sclerosis and cancer pain
• Produced from selected strains of cloned Cannabis sativa plants formulated into a spray for oromucosal administration
• Highly standardised formulation; each 100µl spray of Sativex® contains 2.7 mg delta-9-tetrahydrocannabinol (THC), 2.5 mg cannabidiol (CBD), minor cannabinoids (5-6%) and small amounts of other plant extracts such as terpenes
• Subjects self-titrated to their optimal dose on the basis of their individual efficacy and tolerability response, up to a maximum of 24 sprays/day

Rationale for Treatment:
• Previous clinical trials have shown that Sativex has efficacious properties that are effective in relieving neuropathic pain
• These studies also suggested that Sativex is well tolerated and may also improve sleep and quality of life
• Pain resulting from diabetic neuropathy is often not satisfactorily alleviated by existing therapies

» METHODS
Study Design:
• 12-week open-label, follow-on study
Study Objectives:
• To evaluate maintenance of efficacy and development of tolerance through exposure to, and safety of open-label Sativex therapy in subjects with peripheral neuropathic pain (PNP)

Study Population:
• 385 subjects who had participated in one of two 3-month (GW25050 and GW25427), double blind, randomised controlled trials (parent RCT) designed to investigate the role of Sativex in the treatment of PNP secondary to diabetes or associated with allodynia

Assessments:
• Primary endpoint was pain severity scores recorded using a 0-10 Numerical Rating Scale (NRS-11)
• Secondary endpoints included the Neuropathic Pain Scale (NPS), sleep disturbance-NRS-11, Subject Global Impression of Change (SGIC), Intoxication NRS-11 and a quality of life EQ-5D health questionnaire
• Safety was assessed by monitoring adverse events (AEs) and serial clinical chemistry and vital signs

» RESULTS
1. Disposition of Subjects

2. Baseline Subject Characteristics

3. Mean NRS Pain Scores
There was an improvement over the initial weeks of treatment and subsequent maintenance of benefit.

4. Responders at the 30% and 50% Level of Improvement
After 3 months of open-label Sativex treatment, 141 (81%) completing subjects reported pain scores that were improved by ≥30% from the parent RCT baseline 12 months earlier.

5. Dosing Data

6. Secondary Endpoints

7. Safety
Common adverse events (occurring in 5% or more subjects)

» CONCLUSION
• Sativex remained well tolerated and beneficial for the majority of subjects with peripheral neuropathic pain secondary to diabetes or associated with allodynia over nine months.
• Maintenance in pain relief was achieved without an increase in dose of Sativex.
• The study raised no new safety concerns for Sativex.