



CEDAC FINAL RECOMMENDATION and REASONS for RECOMMENDATION

BUPRENORPHINE/NALOXONE (Suboxone™ – Schering-Plough Canada Inc.)

Description:

Suboxone™ is a fixed dose combination of buprenorphine and naloxone which is approved for substitution treatment in opioid dependence in adults. Buprenorphine is a partial agonist at the mu-opioid receptor. The naloxone component is intended to deter intravenous injection.

Dosage Forms:

Buprenorphine/naloxone supplied as 2 mg/0.5 mg and 8 mg/2 mg sublingual tablets. The recommended initial dose is 4 mg of buprenorphine on day one and is increased progressively according to individual patient need. The maximum daily dose is 24 mg of buprenorphine.

Recommendation:

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that Suboxone™ be listed for the treatment of opioid dependence for patients in whom methadone is contraindicated (e.g. patients at high risk of, or with QT prolongation, or hypersensitivity to methadone). Accordingly, CEDAC recommends that prescribing of Suboxone™ be limited to physicians with a license to prescribe methadone in treating opioid dependence.

Reason for the Recommendation:

1. While buprenorphine/naloxone was more effective than placebo in flexible-dose randomized controlled trials (RCTs), it was less effective than methadone in retaining opioid dependent patients in therapy.

Summary of Committee Considerations:

The Committee considered a systematic review of double-blind RCTs evaluating buprenorphine, alone or in combination with naloxone, compared to methadone or placebo in adult patients with opioid dependence. Seventeen of the 24 RCTs included in a published meta-analysis and three double-blind RCTs completed after the period covered by the meta-analysis met the inclusion criteria for the systematic review. All 20 RCTs compared buprenorphine to methadone or placebo and only two evaluated the buprenorphine/naloxone combination formulation. Primary outcomes included retention in treatment at the end of the study and the use of heroin measured by

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urinalysis and self-reports. Subjects in the trials were using multiple drugs and had varying levels of experience with methadone.

Compared to placebo, buprenorphine with or without naloxone, increased the likelihood of retaining subjects on treatment and patients using doses higher than 6 mg per day had a decreased likelihood of having a morphine-positive urine sample. Thirteen trials used fixed doses of buprenorphine with or without naloxone, and methadone while seven trials compared flexible dosing regimens. Flexible doses of buprenorphine/naloxone were associated with statistically significantly lower retention rates when compared to methadone. Depending on the fixed dose comparison, buprenorphine/naloxone was similar, or inferior to methadone at retaining patients in clinical trials. The RCTs did not provide evidence for using buprenorphine/naloxone preferentially over methadone in any particular subgroup of opioid user.

Rates of adverse events were similar in buprenorphine/naloxone and methadone-treated patients in the clinical trials.

At recommended doses, the daily drug cost of Suboxone™ (\$5.34 for 4 mg/1 mg and \$14.19 for 24 mg/6 mg) is more expensive than methadone. The Committee did not consider the economic evaluation submitted by the manufacturer to be valid since it assumed that buprenorphine/naloxone and methadone have equal rates of treatment retention, which is not supported by the systematic review, and since additional assumptions around the dosing and required monitoring of methadone may have further underestimated the cost per quality adjusted life year associated with buprenorphine/naloxone.

Of Note:

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.

Background:

CEDAC provides formulary listing recommendations to publicly funded drug plans. Recommendations are based on an evidence-based review of the medication's effectiveness and safety and an assessment of its cost-effectiveness in comparison to other available treatment options. For example, if a new medication is more expensive than other treatments, the Committee considers whether any advantages of the new medication justify the higher price. If the recommendation is not to list a drug, the Committee has concerns regarding the balance between benefit and harm for the medication, and/or concerns about whether the medication provides good value for public drug plans.

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