CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

SODIUM OXYBATE RESUBMISSION
(Xyrem® – Valeant Canada Ltd.)

Description:
Sodium oxybate is the sodium salt of gamma-hydroxybutyrate (GHB) and is indicated for treatment of cataplexy in patients with narcolepsy. Sodium oxybate was previously submitted to the Common Drug Review, but the submission was withdrawn prior to the Canadian Expert Drug Advisory Committee (CEDAC) deliberations.

Dosage Forms:
Supplied as an oral solution containing sodium oxybate 500 mg/mL. The recommended starting dose is 4.5 grams per night, divided into two equal doses of 2.25 grams. The dose can be increased to a maximum of 9 grams per night.

Recommendation:
The Canadian Expert Drug Advisory Committee (CEDAC) recommends that sodium oxybate not be listed.

Reasons for the Recommendation:
1. At recommended doses, the daily cost of sodium oxybate ranges from $22.50 to $45. The manufacturer reported cost per quality adjusted life year (QALY) estimates ranging from $70,000 to $100,000. Based on uncertainty regarding clinical effectiveness, the Committee felt that the cost effectiveness of sodium oxybate had not been demonstrated.

2. Sodium oxybate reduced the incidence of total cataplexy attacks (includes both complete and partial attacks) relative to placebo, but there were no data provided that demonstrated a statistically significant reduction in complete attacks, relative to placebo. In view of the overall objective to decrease morbidity from complete attacks, knowing the effect of therapy on the incidence of complete attacks was considered essential.

Summary of Committee Considerations:
The Committee considered a systematic review of six double-blind randomized controlled trials (RCTs) evaluating the effects of sodium oxybate in patients diagnosed with narcolepsy with cataplexy (n=753). The trials were between 2 to 8 weeks in duration. All trials included placebo as a comparator; one trial also included modafinil and sodium oxybate plus modafinil. Sodium oxybate (9 grams daily) was associated with statistically significant reductions in the incidence of total cataplexy attacks, resulting in

approximately 10 fewer attacks per week compared to placebo. Lower doses of sodium oxybate had smaller effects on the frequency of total attacks. An estimate of the effect of sodium oxybate on the incidence of complete cataplexy attacks was provided for only one study, which did not demonstrate a statistically significant reduction relative to placebo. The effect on cataplexy was not measured in the trial that used modafinil as a comparator.

One trial reported statistically significant and clinically significant improvements in the physical component and the vitality index domain of the Short Form-36 (SF-36) for sodium oxybate compared to placebo. There is uncertainty whether these changes could be attributed to changes in cataplexy. Similarly, statistically significant improvements in the Functional Outcomes of Sleep Questionnaire (FOSQ) were seen in patients taking sodium oxybate, but the FOSQ does not measure functional outcomes related to cataplexy.

The manufacturer submitted a cost-utility analysis that compared sodium oxybate (6 or 9 grams daily) to no treatment. The manufacturer reported that the incremental cost per QALY for sodium oxybate is $106,607 for the 6 gram dose and $73,096 for the 9 gram dose. However, the manufacturer did not account for the benefits in the FOSQ scores for the group that received no treatment. When accounting for this, CDR estimated that the cost per QALY increased to $195,000 for 6 grams daily and $94,000 for 9 grams daily.

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.