



## **CEDAC FINAL RECOMMENDATION and REASONS for RECOMMENDATION**

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### **TREPROSTINIL SODIUM (Remodulin™ --Northern Therapeutics Inc.)**

#### **Description**

Treprostinil is a tricyclic benzindene analog of prostacyclin, indicated for the long-term, subcutaneous treatment of pulmonary arterial hypertension in patients with New York Heart Association (NYHA) Class III and IV disease who do not respond adequately to conventional therapy.

#### **Recommendation**

CEDAC recommends that treprostinil not be listed.

#### **Reasons for recommendation**

1. Three randomized trials have compared treprostinil and placebo. One was a small 8 week pilot study; the two other studies each lasted 12 weeks. In the two larger studies, the median improvement in the six-minute walk test for treprostinil, compared with placebo, was sixteen meters which is less than what is usually considered the minimal clinically important difference.
2. To date, there is no definitive evidence that treprostinil improves survival.
3. Because of its subcutaneous administration, treprostinil offers an advantage over epoprostenol, which requires continuous IV infusion through a permanent central venous catheter. However, although treprostinil is administered subcutaneously, most recipients experience considerable pain at the injection site, which may limit the dose that can be utilized.
4. There has been no head-to-head comparison between treprostinil and either epoprostenol or bosentan. Thus, it is difficult to accurately assess the efficacy of treprostinil, compared with current standard of care. Treprostinil results in a smaller improvement in the six minute walk test, in comparison to the placebo controlled studies that were done with epoprostenol and bosentan. In part, this may be due to differences among patients studied, although it is possible that this relates to an inability to achieve high enough doses of treprostinil due to injection site pain.
5. The studies provide no data regarding the frequency of hospitalization with treprostinil compared to placebo.
6. Treprostinil is a very expensive medication, with drug cost varying from \$18,000 to more than \$70,000 per year, depending upon the dose used. While the comparator drugs, epoprostenol

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### **Common Drug Review**

and bosentan, are also expensive, the cost advantage reported for treprostinil compared to epoprostenol in the provided cost-effectiveness report assumed a substantially lower duration of hospitalization for treprostinil-treated patients. It is uncertain, given current practice patterns in managing patients with epoprostenol, whether this purported cost advantage actually exists.

7. In summary, there is no conclusive evidence that treprostinil improves clinically relevant outcomes. Nevertheless, the Committee felt that the use of treprostinil might be justified in patients with severe primary pulmonary hypertension or CREST syndrome-related pulmonary hypertension who have not responded to bosentan and who would meet criteria for reimbursement of a prostacyclin analogue but who are unable to operate the complicated delivery system of epoprostenol due to physical limitations or other contraindications.

**Of Note**

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