



Therapeutic Class ReviewSM

Pulmonary arterial hypertension - Sildenafil (RevatioTM)

November 2005

New Product for Review:

sildenafil (RevatioTM) [Pfizer]

Dossier Provided by Manufacturer: No

Dossier Evaluation: not applicable

1 - dossier w/missing components

2 - all components, except pharmacoeconomic model

3 - all components, well done

Executive Summary

- Revatio is a new oral medication approved for use in the treatment of pulmonary arterial hypertension (PAH).
- Revatio contains the same active ingredient (sildenafil) as Viagra[®], a medication used to treat erectile dysfunction.
- The tablet strengths and dosing regimens used in treating these two conditions are different.
- There is a potential for off-label use of Revatio in the treatment of erectile dysfunction.
- For treatment of PAH, there are very few treatment options available.
- The role of the new treatment options in the treatment of PAH is still emerging.

Evidence:

- There is no published evidence that supports the use of Revatio in the treatment of PAH.
- There is unpublished data from a single pivotal trial with Revatio that demonstrated improvement in exercise capacity (6-minute walk test) in patients with PAH that had NYHA class II and III symptoms.
- The baseline symptoms of the patients studied in the Revatio trial were less severe than those studied in trials with other PAH agents (based on NYHA class).
- There are no RCTs that compare Revatio with other currently established treatments for PAH.
- There is no good evidence that the safety of Revatio is superior to other agents used to treat PAH.
- There is currently no evidence that Revatio provides additional benefit when given concomitantly with other PAH treatments.

Decision

- Add sildenafil (Revatio™) as preferred/formulary not based on evidence, but because:
 - it is an additional option in a condition with few treatment options,
 - it offers another step before progressing to more invasive therapies, and
 - it is available at a lower cost than other treatment options.

Products

Drug Product	Date of FDA Approval	FDA Approved Indications	Dose/Route	Potential Off-Label Uses
bosentan (Tracleer®) ^{1, 6}	11/2001	Treatment of pulmonary arterial hypertension (PAH) in patients with WHO class III or IV symptoms, to improve exercise ability and decrease the rate of clinical worsening.	125 mg orally twice daily	congestive heart failure; hypertension
epoprostenol (Flolan®) ^{2, 6}	09/1995	(1) Long-term intravenous treatment of primary PAH and (2) pulmonary hypertension associated with scleroderma spectrum of disease in NYHA Class III and IV patients who do not respond adequately to conventional therapy.	<i>initial/titration:</i> 2 ng/kg/min via intravenous infusion, then increase every 15 minutes by 2 ng/kg/min until adverse effects. (dose highly variable; typically in 20 to 40ng/kg/min range)	lung transplantation; cardiopulmonary bypass
iloprost (Ventavis®) ^{3, 6}	12/2004	Treatment of PAH (WHO group I) in patients with NYHA Class III or IV symptoms. (Ventavis has not been adequately studied with concomitant use of other approved therapies for PAH)	2.5 to 5 mcg via inhalation 6 to 9 times per day. <i>maximum:</i> 5mcg per dose; 45 mcg per day.	concomitant treatment with other PAH agents; peripheral vascular disease; angina pectoris
sildenafil (Revatio™) ^{4, 6}	06/2005	Treatment of PAH (WHO Group I) to improve exercise ability.	20 mg orally three times daily.	erectile dysfunction
treprostinil (Remodulin®) ^{5, 6}	05/2002	For the treatment of PAH in patients with NYHA Class II to IV symptoms to diminish symptoms associated with exercise.	1.25 ng/kg/min via subcutaneous or intravenous infusion. Increase in increments of 1.25 ng/kg/min per week; <i>maximum:</i> 40 ng/kg/min.	heart failure

WHO classification = World Health Organization classification of PAH (see *Appendix D* for group definitions)

NYHA classification= New York Heart Association functional classification by symptoms (see *Appendix D* for definitions)

References

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