PDL DRUG REVIEW

Proprietary Name: Gemtesa®
Common Name: vibegron
PDL Category: Antispasmodics- Long Acting

Comparable Products	Preferred Drug List Status
Myrbetriq	Non-Preferred
Solifenacin	Preferred

Summary

Pharmacology/Usage: Vibegron, the active ingredient of Gemtesa®, is a selective beta-3 adrenergic receptor agonist. Activation of the beta-3 adrenergic receptor increases bladder capacity by relaxing the detrusor smooth muscle during bladder filling.

Indication: For the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency in adults

There is no pregnancy category for this medication; however, the risk summary indicates that there are no available data on use in pregnant women to assess for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. The safety and efficacy of use in the pediatric population have not been established.

Dosage Form: Film-Coated Tablets: 75mg

Recommended Dosage: Take one tablet PO QD with or without food. Swallow tablets whole with a glass of water. However, in adults, Gemtesa® tablets may also be crushed and mixed with a tablespoon (about 15ml) of applesauce. The mixture must be taken immediately with a glass of water.

Dosage adjustment is not required for renal impairment; however, use has not been studied in patients with eGFR<15ml/min/1.73m^2 (with or without dialysis) and is not recommended in this patient population. Dosage adjustment is not required with mild to moderate hepatic impairment; however, use has not been studied in patients with severe hepatic impairment and is not recommended in this patient population.

Drug Interactions: Concomitant use of Gemtesa® increases digoxin maximal concentrations and systemic exposure as assessed by area under the concentration-time curve (AUC). Serum digoxin concentrations should be monitored before starting and during therapy with Gemtesa® and used for titration of the digoxin dose to obtain the desired clinical effect. Continue monitoring digoxin concentrations upon discontinuation of Gemtesa® and adjust the digoxin dose as needed.

Box Warning: There is no box warning listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Gemtesa®) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was*

the same as or less than placebo. The most frequently reported adverse event included headache (1.6%), nasopharyngitis (1.1%), diarrhea (1.1%), nausea (1.1%), and upper respiratory tract infection (1.3%).

Urinary retention has been reported in patients taking Gemtesa®. The risk of urinary retention may be increased in patients with bladder outlet obstruction and also in patients taking muscarinic antagonist medications for the treatment of OAB. Monitor patients for signs and symptoms of urinary retention, especially in patients with bladder outlet obstruction and patients taking muscarinic antagonist medications for the treatment of OAB. Discontinue Gemtesa® in patients who develop urinary retention.

Contraindications: With known hypersensitivity to vibegron or any of the components of the product.

Manufacturer: Urovant Sciences, Inc

Analysis: The safety and efficacy of Gemtesa® were assessed in a 12-week double-blind, randomized, placebo-controlled and active-controlled study that included patients with OAB (N=1,515). Patients were randomized to receive either Gemtesa® 75mg, placebo, or active control PO once daily for 12 weeks. For study entry, patients had to have symptoms of OAB for at least 3 months with an average of 8 or more micturitions per day and at least 1 urge urinary incontinence (UUI) per day, or an average of 8 or more micturitions per day and an average of at least 3 urgency episodes per day. UUI was defined as a leakage of urine of any amount because the patient felt an urge or need to urinate immediately.

This study population included OAB medication-naïve patients as well as patients who had received prior therapy with OAB medications. Most patients in the study were Caucasians (78%) and female (85%) and had a mean age of 60 years (range 18 to 93 years).

The co-primary endpoints were the change from baseline in average daily number of micturitions and average daily number of UUI episodes at week 12. Additional endpoints included change from baseline in average daily number of 'need to urinate immediately' (urgency) episodes and average volume voided per micturition. Please note that data regarding the active control was not noted in the prescribing information. Results can be seen in the table below, which was adapted from the prescribing information.

Parameter	Gemtesa® 75mg	Placebo
Average daily number of micturitions		
Baseline mean (n)	11.3 (526)	11.8 (520)
Change from baseline (n)	-1.8 (492)	-1.3 (475)
Difference from placebo; p-value	-0.5; p<0.001	
Average daily number of UUI episodes		
Baseline mean (n)	3.4 (403)	3.5 (405)
Change from baseline (n)	-2.0 (383)	-1.4 (372)
Difference from placebo; p-value	-0.6; p<0.0001	
Average daily number of 'need to urinate immediately' (urgency) episodes		
Baseline mean (n)	8.1 (526)	8.1 (520)
Change from baseline (n)	-2.7 (492)	-2.0 (475)

Parameter	Gemtesa® 75mg	Placebo
Difference from placebo; p-value	-0.7; p=0.002	
Average volume voided (ml) per micturition		
Baseline mean (n)	155 (524)	148 (514)
Change from baseline (n)	23 (490)	2 (478)
Difference from placebo; p-value	21; p<0.0001	

Per the full-text study by Staskin et al[2] tolterodine ER 4mg was used as the active control. The average daily number of micturitions decreased by 1.6 for tolterodine, which was a least square mean difference of -0.3 from placebo (p=0.0988). UUI episodes decreased by an adjusted mean of 1.8 for tolterodine, which was a least square mean difference of -0.4 from placebo (p=0.0123). Furthermore, the authors indicated that efficacy responses to vibegron in patients with prior OAB pharmacotherapy were similar to treatment naïve patients.

Place in Therapy: Gemtesa® is indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency in adults. It is an oral selective beta-3 adrenergic receptor agonist. In a 2021 meta-analysis by Su et al[4], the authors concluded that the therapeutic effect of vibegron was similar to that of antimuscarinic therapy, but that vibegron did not increase the risk of adverse events (e.g. dry mouth). Serious adverse events and discontinuations due to adverse events were not significantly different between treatment groups. In addition, while no formal comparators have been made, Gemtesa® does not have a warning regarding increased blood pressure as does Myrbetriq® (mirabegron), a previously FDA approved beta-3 adrenergic receptor agonist.

Although blood pressure increases, like those seen with Myrbetriq® (another FDA approved beta-3 adrenergic receptor agonist) were not observed during Gemtesa® trials, it is important to note that head-to-head studies between the two agents have not been performed. Therefore, it is concluded that while there is some preliminary data that vibegron may be better tolerated with regards to some side effects, the efficacy appears to be similar to antimuscarinics and the tolerability comparison should be demonstrated in head-to- head trials. It is therefore recommended that Gemtesa® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on more cost-effective, preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred**

References

[1] Gemtesa [package insert]. Irvine, CA: Urovant Sciences, Inc; 2020.
[2] Staskin D, Frankel J, Varano S, et al. International Phase III, randomized, double-blind, placebo and active controlled study to evaluate the safety and efficacy of vibegron in patients with symptoms of overactive bladder: EMPOWUR. *J Urol.* 2020; 204(2): 316-324.
[3] Myrbetriq [package insert]. Northbrook, IL: Astellas Pharma US, Inc; 2021.
[4] Su S, Liang L, Lin J, et al. Systematic review and meta-analysis of the efficacy and safety of vibegron vs antimuscarinic monotherapy for overactive bladder. Medicine. 2021; 100(5):e23171.