PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

DIBENZYLINE
(phenoxybenzamine)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit ***Ref # 3673-C***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Dibenzyline is indicated in the treatment of pheochromocytoma, to control episodes of hypertension and sweating. If tachycardia is excessive, it may be necessary to use a beta-blocking agent concomitantly.

Compendial Uses
Paraganglioma[5,6]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the treatment of pheochromocytoma or paraganglioma to control episodes of hypertension and sweating
  AND
- The patient has experienced an inadequate treatment response to an alpha 1 selective adrenergic receptor blocker (e.g., doxazosin, prazosin, terazosin)
  OR
- The patient has experienced an intolerance to an alpha 1 selective adrenergic receptor blocker (e.g., doxazosin, prazosin, terazosin)
  OR
- The patient has a contraindication that would prohibit a trial of an alpha 1 selective adrenergic receptor blocker (e.g., doxazosin, prazosin, terazosin)

Quantity Limits apply.

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Dibenzyline (phenoxybenzamine) is indicated in the treatment of pheochromocytoma to control episodes of hypertension and sweating.[1-3]

In the 2017 World Health Organization (WHO) classification, pheochromocytoma is an adrenal tumor, and paraganglioma is an extraadrenal tumor. Since the two tumor types cannot be differentiated on the basis of histologic findings, anatomical location is used to distinguish them.[4]

According to the Endocrine Society Clinical Practice Guideline for Pheochromocytoma and Paraganglioma (PPGL), Dibenzyline (phenoxybenzamine) is effective in controlling hypertension before surgical resection of a PPGL. It is frequently given 10-14 days before surgery to bring hypertension under control and prevent any complications during surgery.[5] Additionally, the National Comprehensive Cancer Network (NCCN) Guidelines for Neuroendocrine and Adrenal Tumors recommends alpha blockade as first-line therapy for all hormonally secreting pheochromocytomas and

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paragangliomas. Therapy with alpha 1 selective receptor blockers, including terazosin, doxazosin, and prazosin, and non-selective blockers, Dibenzyline (phenoxybenzamine), is recommended for 7-14 days prior to surgical therapy.[6] Retrospective studies demonstrated that alpha 1 selective adrenergic receptor blockers were associated with lower preoperative diastolic pressure, a lower intra-operative heart rate, better postoperative hemodynamic recovery, and fewer adverse effects such as reactive tachycardia and sustained postoperative hypotension than nonselective adrenergic blockers.[5] Therefore, coverage will be provided for patients who have experienced an inadequate treatment response, intolerance, or contraindication to an alpha 1 selective adrenergic receptor blocker (e.g., doxazosin, prazosin, terazosin).

In the event that surgical resection of a pheochromocytoma is not feasible, Dibenzyline can be used chronically to control hypertension and sweating symptoms associated with the pheochromocytoma.[2] Chronic use of this medication must be weighed against the risk of cancer that is possibly associated with long term use.[1-3] Because paragangliomas are so closely related to pheochromocytomas, the criteria will also allow for extended coverage for a paraganglioma that may not be surgically resected.

The initial dose of Dibenzyline (phenoxybenzamine) is 10 mg twice daily. The dosage should be increased every other day, usually to 20 to 40 mg two to three times a day, until an optimal dosage is obtained, as judged by blood pressure control.[1-3] Although not usually necessary, some patients may need higher doses (1 mg/kg/day)[5]. Therefore, the approval quantity will allow for the upper range of the recommended daily dosage of 12 capsules per day.

REFERENCES

1. Dibenzyline [package insert]. Dublin 9, Ireland: Amdipharm Limited; April 2020.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online, Hudson, Ohio: UpToDate, Inc.; 2021; Accessed February 22, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed February 22, 2021.
4. Neumann HPH, Young WF, Eng C. Pheochromocytoma and Paraganglioma. *The New England Journal of Medicine* 2019;381:552-65.
5. Lenders JWM, Duh QY, Eisenhofer G, et al. Pheochromocytoma and Paraganglioma: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology and Metabolism* 2014;99(6):1915-1942.
6. Neuroendocrine and Adrenal Tumors. NCCN Guidelines version 2.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed February 2021.

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CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the treatment of pheochromocytoma or paraganglioma to control episodes of hypertension and sweating? [If no, then no further questions.]	Yes	No
2	Has the patient experienced an inadequate treatment response to an alpha 1 selective adrenergic receptor blocker (e.g., doxazosin, prazosin, terazosin)? [If yes, then skip to question 5.]	Yes	No
3	Has the patient experienced an intolerance to an alpha 1 selective adrenergic receptor blocker (e.g., doxazosin, prazosin, terazosin)?	Yes	No

	[If yes, then skip to question 5.]		
4	Does the patient have a contraindication that would prohibit a trial of an alpha 1 selective adrenergic receptor blocker (e.g., doxazosin, prazosin, terazosin)? [If no, then no further questions.]	Yes	No
5	Does the patient require MORE than the plan allowance of 12 capsules per day? [RPh Note: If yes, then deny and enter a partial approval for 360 capsules/25 days or 1080 capsules/75 days of the requested drug.]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are using it to help treat symptoms of pheochromocytoma or paraganglioma. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 5	Go to 3	
3.	Go to 5	Go to 4	
4.	Go to 5	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried an alpha 1 selective adrenergic receptor blocker and it either did not work for you or you cannot use it. Your request has been denied based on the information we have. [Short Description: No trial of artificial tears]
5.	Deny	Approve, 12 months 360 capsules/25 days or 1080 capsules/75 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 360 capsules/month of the requested drug and strength. You have been approved for the maximum quantity that your plan covers for a duration of 12 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity]

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*