

Payers may require prior authorization or supporting documentation to process and cover a claim for the requested therapy. A prior authorization allows the payer to review the reason for the requested therapy and to determine medical appropriateness. The following are sample formulary exception talking points that can be customized based on your patient's medical history and physical examination. It may also be used to explain why a glucagon stimulation test (GST) may not be medically appropriate for your patient. Please note that some payers may have specific forms that must be completed to request formulary exception, prior authorization or to document medical necessity.

Please see Important Safety Information on the last page of this document.

Macrilen Medical Necessity Talking Points and Glucagon Stimulation Test Concerns

If a payer requests that a glucagon stimulation test (GST) be used in place of Macrilen, you may be able to appeal that decision. Below are sample talking points that may help to support your medical decision to use Macrilen.

- Any letter of medical necessity sent to a payer should include the patient's name, policy and group number, and diagnosis.
- The letter should be submitted on office letterhead and provide contact information for the physician.

Introduction, Product Summary, and Formal Request

- I am writing to request coverage for stimulation testing with Macrilen™ (macimorelin) for [Patient Name]. [Patient Name] has been under my care for [X months] for the treatment of [disease or symptoms].
- Provide a brief medical history, attach clinical records documenting that growth hormone deficiency is a result of hypothalamic-pituitary disease from organic or known causes (e.g., damage from surgery, cranial irradiation, head trauma, or subarachnoid hemorrhage), and/or document previously failed evocative AGHD stimulation tests.
- Macrilen (macimorelin) oral solution is a synthetic growth hormone secretagogue receptor agonist. It is a prescription drug that has been granted orphan drug designation in the U.S. and is the only FDA-approved (December 2017) oral growth hormone secretagogue receptor agonist indicated for the diagnosis of Adult Growth Hormone Deficiency (AGHD).

Limitations and Caveats of the GST: (Sample Discussion Points)

- The GST test results are affected by the presence of a high body mass index and/or glucose intolerance. There is no accepted protocol for how to adjust for these factors, leaving substantial variability in how tests are interpreted.¹
- The GST is administered via intramuscular injection, which may bother some patients.²

¹ Yuen KCJ, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Disease State clinical review: Update on growth hormone stimulation testing and proposed revised cut-point for the glucagon stimulation test in the diagnosis of adult growth hormone deficiency. *Endoc Pract.* 2016;22:1235-44.

- Delayed hypoglycemia is a serious adverse event associated with the GST.¹
- In addition to the risk of delayed hypoglycemia, the test can be unpleasant to the subject, with nausea and vomiting, headache, excessive sweating (diaphoresis), and abdominal cramps known to be side effects in up to one-third of patients. Severe symptomatic hypotension, hypoglycemia, and seizures have been reported in elderly subjects.^{1,3}
- The test is time-consuming: 3-4 hours for the test, several hours of post-test safety monitoring; and requires up to 10 blood draws. Therefore, the test is not appropriate for some patients due to testing limitations or adverse events and also may be inconvenient and unpleasant.²
- Add other statements to explain reasons why Macrilen is more medically appropriate for your patient over GST.

Conclusion

- I am a board-certified endocrinologist, and I believe that Macrilen is the appropriate agent for stimulation testing in the diagnosis of AGHD in this patient. It is imperative that a formulary exception be made.
- In my clinical judgement, diagnosing AGHD with Macrilen stimulation testing is medically necessary because of the product's diagnostic accuracy, safety profile, and labeled indication.
- Discuss rationale for using Macrilen over other non-FDA approved tests like the insulin tolerance test or glucagon stimulation test, including clinical factors, time required to safely administer each test, number of blood draws, test accuracy and repeatability, and physician work required.

Additional Document Recommendations

- For your immediate review, I have enclosed additional documentation that supports Macrilen as an appropriate evocative agent for adult growth hormone stimulation testing.
- Please consider coverage of Macrilen for my patient. If you have further questions, please feel free to call me at [telephone number] to discuss.
- Enclosures: Full Prescribing Information (additional suggested: include original Prior Authorization Form, Denial/EOB, patient medical history, additional supporting documents)

² Agrawal V, Garcia JM. The macimorelin-stimulated growth hormone test for adult growth hormone deficiency diagnosis. *Expert Rev Mol Diagn.* 2014;14:647-54.

³ Yuen KCJ. Growth hormone stimulation tests in assessing adult growth hormone deficiency. *Endotext.* NCBI Bookshelf. Last Update: August 1, 2016. <https://www.ncbi.nlm.nih.gov/books/NBK395585>. Accessed February 16, 2018.

Important Safety Information for Macrilen

Indication

Macrilen is indicated for the diagnosis of adult growth hormone deficiency (AGHD).

Limitations of Use

The safety and diagnostic performance of Macrilen have not been established for subjects with a body mass index (BMI) > 40 kg/m².

Warnings and Precautions

QT Prolongation

Macrilen causes an increase of about 11 msec in the corrected QT (QTc) interval. QT prolongation can lead to development of torsade de pointes-type ventricular tachycardia with the risk increasing as the degree of prolongation increases. The concomitant use of Macrilen with drugs that are known to prolong the QT interval should be avoided.

Potential for False Positive Test Results with Use of Strong CYP3A4 Inducers

Concomitant use of strong CYP3A4 inducers with Macrilen can decrease macimorelin plasma levels significantly and **thereby lead to a false positive result. Strong CYP3A4 inducers should be discontinued and enough time should be given to allow washout of CYP3A4 inducers prior to test administration.**

Potential for False Negative Test Results in Recent Onset Hypothalamic Disease

Adult growth hormone (GH) deficiency caused by a hypothalamic lesion may not be detected early in the disease process. Macimorelin acts downstream from the hypothalamus and macimorelin stimulated release of stored GH reserves from the anterior pituitary could produce a false negative result early when the lesion involves the hypothalamus. Repeat testing may be warranted in this situation.

Adverse Reactions

The most common adverse reactions were dysgeusia, dizziness, headache, fatigue, nausea, hunger, diarrhea, upper respiratory tract infection, feeling hot, hyperhidrosis, nasopharyngitis, and sinus bradycardia.

Please see [Full Prescribing Information](#).