



**Gold Coast
Health Plan**SM
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Gold Coast Health Plan Pharmacy Services Newsletter

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CMO Message

by Charles Cho, M.D.

The Comprehensive Diabetes Care (CDC) is a measure that Gold Coast Health Plan (GCHP) audits and reports annually to the National Committee for Quality Assurance (NCQA) for the HEDIS[®] quality of care performance reviews. A sub-measure of the CDC is compliance with testing the HbA1c level of diabetic members.

The results of the HEDIS[®] 2012 Measurement Year audit show that GCHP ranked above the minimum performance level national percentile for compliance with HbA1c testing of diabetic members. However, GCHP ranked below the minimum performance level for good diabetic control based on the HbA1c test results below 8.0. I would like to encourage our providers to continue HbA1c testing as often as 3 months, if necessary, in order to obtain more optimum level of diabetic control even below 7.0. For successful HEDIS reporting, it is essential that GCHP staff gets good cooperation from you and your staff. In that regard, I cannot thank you enough. We especially thank your staff.

Important Notice: As many of you may be aware, there will be a transition of more than 16,000 Healthy Family members into Gold Coast Health Plan (GCHP), as of August 1, 2013. These are children and young adults who have been under the care of other health plans including the Ventura County Health Care Plan, Anthem Blue Shield and Kaiser. For a smooth transition and continuity of care, there will be a 60 day (or 2 months) grace period in which the same medications that the members are on will be allowed. I suggest that you refill these medications for one month (30 or 31 days) with another refill. You must convert all medications to conform to the GCHP formulary policy during the time frame mentioned above. I really appreciate your cooperation.



Understanding HbA1c

Also Known As

Hemoglobin A1c; HbA1c; Glycohemoglobin; Glycated Hemoglobin; Glycosylated Hemoglobin

Formal Name

A1c

AT A GLANCE

Why Get Tested?

To monitor a person's diabetes and to aid in treatment decisions; to diagnose diabetes; to help identify those at an increased risk of developing diabetes.

When to Get Tested?

When first diagnosed with diabetes and then 2 to 4 times per year, as part of a health checkup, or when a patient has symptoms of diabetes.

Sample Required?

A blood sample either from a vein or from a finger stick.

Test Preparation Needed?

None

THE TEST SAMPLE

What is being tested?

The A1c test evaluates the average amount of glucose in the blood over the last 2 to 3 months. It does this by measuring the concentration of glycated (also often called glycosylated) hemoglobin A1c. Hemoglobin is an oxygen-transporting protein found inside red blood cells (RBCs). There are several types of normal hemoglobin, but the predominant form – about 95-98% – is hemoglobin A. As glucose circulates in the blood, some of it spontaneously binds to hemoglobin A. The hemoglobin molecules with attached glucose are called glycated hemoglobin. The higher the concentration of glucose in the blood, the more glycated hemoglobin is formed. Once the glucose binds to the hemoglobin, it remains there for the life of the red blood cell – normally about 120 days. The predominant form of glycated hemoglobin is referred to as HbA1c or A1c. A1c is



produced on a daily basis and slowly cleared from the blood as older RBCs die and younger RBCs (with non-glycated hemoglobin) take their place.

This test is used to monitor treatment in someone who has been diagnosed with diabetes. It helps to evaluate how well their glucose levels have been controlled by treatment over time. This test may be used to screen for and diagnose diabetes or risk of developing diabetes. In 2010, clinical practice guidelines from the American Diabetes Association (ADA) stated that A1c may be added to fasting plasma glucose (FPG) and oral glucose tolerance test (OGTT) as an option for diabetes screening and diagnosis.

For monitoring purposes, an A1c of less than 7% indicates good glucose control and a lower risk of diabetic complications for the majority of diabetics. However, in 2012, the ADA and the European Association for the Study of Diabetes (EASD) issued a position statement recommending that the management of glucose control in type 2 diabetes be more “patient-centered.” Data from recent studies have shown that low blood sugar (hypoglycemia) can cause complications and that people with risk of severe hypoglycemia, underlying health conditions, complications, and a limited life expectancy do not necessarily benefit from having a stringent goal of less than 7% for their A1c. The statement recommends that people work closely with their doctor to select a goal that reflects each person’s individual health status and that balances risks and benefits.

THE TEST

How is it used?

The A1c test is used to monitor the glucose control of diabetics over time. The goal of those with diabetes is to keep their blood glucose levels as close to normal as possible. This helps to minimize the complications caused by chronically elevated glucose levels, such as progressive damage to body organs like the kidneys, eyes, cardiovascular system and nerves. The A1c test result gives a picture of the average amount of glucose in the blood over the last few months. This can help the diabetic person and his doctor know if the measures that are being taken to control his diabetes are successful or need to be adjusted.

A1c is frequently used to help newly diagnosed diabetics determine how elevated their uncontrolled blood glucose levels have been over the last 2-3 months. The A1c test may be used to screen for and diagnose diabetes; however, A1c should not be used for diagnosis in pregnant women, people who have had recent severe bleeding or blood transfusions, those with chronic kidney or liver disease and people with blood disorders such as iron-deficiency anemia, vitamin



B12 deficiency anemia and some hemoglobin variants (e.g., patients with sickle cell disease or thalassemia). In these cases, a fasting plasma glucose or oral glucose tolerance test should be used for screening or diagnosing diabetes.

Only A1c tests that have been referenced to an accepted laboratory method (standardized) should be used for diagnostic or screening purposes. Currently, point-of-care tests, such as those that may be used at a doctor's office or a patient's bedside, are not accurate enough for use in diagnosis but can be used to monitor treatment (lifestyle and drug therapies).

When is it ordered?

Depending on the type of diabetes that a person has, how well their diabetes is controlled and on doctor recommendations, the A1c test may be measured 2 to 4 times each year. **The ADA recommends A1c testing in diabetics at least twice a year. Typically, the test is ordered every 3 months while a patient's diabetes is being controlled and then less often once their blood glucose level is stable at satisfactory levels.**

An individual with type 2 diabetes, however, may have an A1c goal selected by the person and his doctor. The goal may depend on several factors, such as length of time since diagnosis, the presence of other diseases as well as diabetes complications (e.g., vision impairment or loss, kidney damage), risk of complications from low blood glucose (hypoglycemia) and whether or not the person has a support system and health care resources readily available. For example, a person with heart disease who has lived with type 2 diabetes for many years without diabetic complications may have a higher A1c target (e.g., 7.5%-8.0%) set by their doctor, while someone who is otherwise healthy and just diagnosed may have a lower target (e.g., 6.0%-6.5%) as long as low blood sugar is not a significant risk.

Is there anything else one should know?

If an individual has a hemoglobin variant, such as sickle cell hemoglobin (hemoglobin S), they will have a decreased amount of hemoglobin A. This may limit the usefulness of the A1c test in diagnosing and/or monitoring this person's diabetes, depending on the method used.

If a person has anemia, hemolysis, or heavy bleeding, A1c test results may be falsely low if someone is iron-deficient.

If a person has had a recent blood transfusion, the A1c may be inaccurate and may not accurately reflect glucose control for 2 to 3 months.

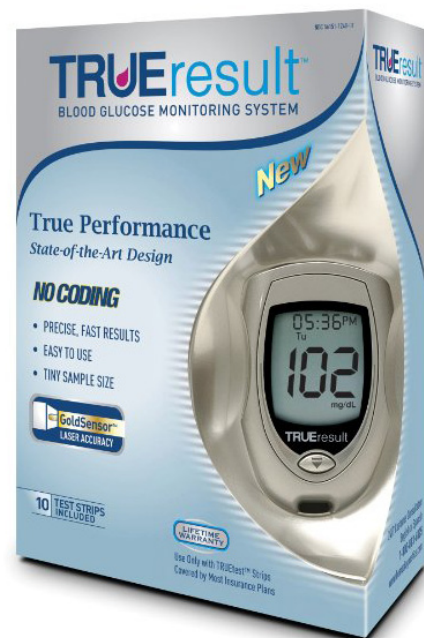


TRUEresult™ Product Review

The TRUEresult™ blood glucose meter is the only meter covered by GCHP. Below is a quick overview of some of its features.

Advanced Features

- No coding required
- 7- 14- and 30-day averaging
- 4 testing reminder alarms
- Audible fill detection
- Weekday display
- Glucose control detection
- Hematocrit range – 20-60%
- Ketone test reminder
- Alternate site testing
- Strip release button
- Automatic on/off



TRUEmanager™ PRO Software

TRUEmanager™ PRO diabetes management software is an easy-to-use tool to assist you in identifying and understanding how your patient's daily choices and actions affect their blood glucose levels. The design makes it easy and convenient to quickly identify glucose results that out of target range, so you can consult with your patients to help them understand various lifestyle and behavior choices affecting their blood glucose levels. TRUEmanager™ PRO offers seven comprehensive reports. Each report interprets test results from varied, valuable perspectives and packages them in easy-to-view, printable reports for evaluation and discussion.

[Click here to learn more about TRUEmanager™ PRO Diabetes Management Software](#)



List of Covered Drugs New Additions

The Pharmacy and Therapeutics Committee of GCHP has added Linaclotide to the List of Covered Drugs as step one for the treatment of irritable bowel syndrome (IBS) and chronic idiopathic constipation after a review of the extensive trial and clinical data. Linaclotide presents as a strong value proposition and adds another agent for IBS to the GCHP List of Covered Drugs along with lubiprostone (Amitiza). Lubiprostone is a step two agent if linaclotide is not effective.

Linzess (Linaclotide) Review for the Treatment of Irritable Bowel Syndrome

IBS-C and CIC are chronic functional gastrointestinal disorders that affect as many as 13 million children and 35 million adult Americans, respectively. Symptoms associated with IBS-C include abdominal pain and constipation; symptoms associated with CIC include constipation (infrequent stools, hard stools and incomplete evacuation). There are few treatment options for these conditions, particularly options that relieve abdominal pain associated with IBS-C. “The symptoms experienced by patients with IBS-C and chronic idiopathic constipation can have a significant impact on affected individuals,” said William D. Chey, M.D., professor of gastroenterology at the University of Michigan Health System. “The approval of LINZESS provides physicians with a new, evidence-based, effective treatment option for their adult patients with IBS-C and chronic idiopathic constipation.”

Linaclotide, the active ingredient in LINZESS, is a first-in-class guanylate cyclase-C (GC-C) agonist and acts locally in the intestine with minimal systemic exposure. In nonclinical studies, linaclotide has been shown to reduce intestinal pain and accelerate gastrointestinal transit. Linaclotide-induced intestinal pain reduction is thought to result from an increase in cyclic guanosine monophosphate (cGMP), which has been shown to decrease the activity of pain sensing nerves. In placebo-controlled Phase III clinical trials of more than 2,800 adults, LINZESS was shown to significantly reduce abdominal pain in IBS-C patients and significantly increase bowel movement frequency in both IBS-C patients and CIC patients. Improvements were reported in the first week of treatment and maintained throughout the treatment period. When a subset of LINZESS-treated patients in the trials were switched to placebo, they reported their symptoms returned toward pretreatment levels within one week, while placebo-treated patients switched to LINZESS reported symptom improvements. LINZESS has not been studied in pediatric patients. LINZESS is contraindicated in pediatric patients up to 6 years of age. The use of LINZESS in pediatric patients 6 through 17 years of age should be avoided.



Data Highlights: Irritable Bowel Syndrome with Constipation (IBS-C)

The safety and efficacy of LINZESS to treat IBS-C were evaluated in two double-blind, placebo-controlled Phase III clinical trials in which LINZESS met all four primary endpoints examining changes in abdominal pain and constipation in each trial. The trials involved 1,605 patients aged 18 to 87 years old, of which 807 were treated with LINZESS 290 mcg.

Combined Responder

In both trials, the proportion of LINZESS-treated patients who were combined responders was statistically significantly higher than placebo-treated patients. Two definitions of combined responder were used. A 9 of 12 week combined responder is a patient who reported at least a 30% reduction from baseline in abdominal pain, at least three CSBMS, and an increase of at least one CSBM from baseline, all in the same week for at least 9 out of 12 weeks. A 6 out of 12 week responder is a patient who reported at least a 30% reduction from baseline in abdominal pain and an increase of at least one CSBM from baseline, all in the same week for at least 6 out of 12 weeks. This second definition is consistent with the FDA guidance document on IBS and was one of the four pre-specified primary endpoints in the LINZESS Phase III IBS-C trials. In 9 out of 12 weeks, 12% (Study 1) and 13% (Study 2) of LINZESS-treated patients were combined responders, versus 5% (Study 1) and 3% (Study 2) of placebo-treated patients. In 6 out of 12 weeks, 34% (Study 1) and 34% (Study 2) of LINZESS-treated patients were combined responders, versus 21% (Study 1) and 14% (Study 2) of placebo-treated patients. During a two week pre-treatment period, these patients reported a mean abdominal pain score of at least 3 on a 0-to-10-point scale and less than three CSBMs per week.

Abdominal Pain

LINZESS 290 mcg was proven to significantly reduce abdominal pain; effects were seen within the first week of treatment and improvements were maintained throughout the treatment period. In the two trials, 34% (Study 1) and 39% (Study 2) of patients treated with LINZESS experienced at least a 30% reduction in abdominal pain from baseline for at least 9 out of 12 weeks versus 27% (Study 1) and 20% (Study 2) of placebo-treated patients. For at least 6 out of 12 weeks (a secondary endpoint), 50% (Study 1) and 49% (Study 2) of LINZESS-treated patients versus 38% (Study 1) and 35% (Study 2) of placebo-treated patients experienced at least a 30% reduction in abdominal pain from baseline.



Constipation Symptoms

LINZESS significantly increased the frequency of complete spontaneous bowel movements (CSBMs), with 20% (Study 1) and 18% (Study 2) of patients treated with LINZESS experiencing an increase of at least one CSBM from baseline for at least 9 out of 12 weeks versus 6% (Study 1) and 5% (Study 2) of placebo-treated patients. For at least 6 out of 12 weeks (secondary endpoint), 49% (Study 1) and 48% (Study 2) of LINZESS-treated patients versus 30% (Study 1) and 23% (Study 2) of placebo-treated patients experienced at least three CSBMs and an increase of at least one CSBM from baseline. In each trial, the drug reached maximum effectiveness within the first week of treatment, and improvements were maintained throughout the treatment period.

Data Highlights: Chronic Idiopathic Constipation (CIC)

The efficacy of LINZESS for the management of CIC was established in two double-blind, placebo-controlled Phase III clinical trials in which LINZESS met the primary endpoint in both trials. The primary endpoint in these trials examined changes in bowel function. The trials involved 1,275 patients aged 18 to 85 years old, of which 430 received LINZESS 145 mcg and 422 received LINZESS 290 mcg. During a two-week pretreatment period at the beginning of the trials, these patients reported less than three CSBMs per week.

Constipation Symptoms

LINZESS significantly increased the frequency of CSBMs in treated patients. At the 145 mcg dose, 20% (Study 3) and 16% (Study 4) of LINZESS-treated patients experienced at least 3 CSBMs and an increase of at least one CSBM from baseline in the same week for at least 9 of the 12 weeks (CSBM responder) versus 3% (Study 3) and 6% (Study 4) of placebo patients. In each trial, the drug reached maximum effectiveness within the first week of treatment, and improvements were maintained throughout the treatment period. Patients taking LINZESS experienced significant improvement in stool frequency and hardness of stool compared to placebo.

Safety

The most common adverse reactions in IBS-C or CIC patients were diarrhea, abdominal pain, flatulence and abdominal distension.



About LINZESS

LINZESS is the first and only guanylate cyclase-C (GC-C) agonist approved by the FDA for the treatment of both irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC) in adults. LINZESS is a once-daily capsule that helps relieve the chronic abdominal pain and constipation associated with IBS-C and constipation and hard stools associated with CIC. The recommended dose is 290 mcg for IBS-C patients and 145 mcg for CIC patients. LINZESS binds to the GC-C receptor locally in the intestine, with no measurable blood plasma concentrations, resulting in an increase in both intracellular and extracellular concentrations of cyclic guanosine monophosphate (cGMP). Elevations in intracellular cGMP are believed to stimulate secretion of intestinal fluid and accelerate gastrointestinal transit resulting in increased frequency of bowel movements. Elevations in extracellular cGMP are believed to decrease activity of pain-sensing nerves, which is thought to be responsible for a reduction in intestinal pain, according to nonclinical models.

About Irritable Bowel Syndrome with Constipation

Irritable bowel syndrome with constipation (IBS-C) is a chronic functional gastrointestinal disorder that affects as many as 13 million people in the United States. IBS-C can have a negative impact on daily living; patients often experience recurring abdominal pain or discomfort, constipation, and bowel symptoms including hard or lumpy stools in more than 25% of bowel movements, and soft or watery stools in less than 25% of bowel movements. There are currently few available therapies to treat this disorder.

About Chronic Idiopathic Constipation

Chronic idiopathic constipation (CIC) is a functional gastrointestinal disorder in which individuals experience infrequent bowel movements (less than three times per week) for at least three months. Patients who suffer from CIC may also experience a sensation of incomplete evacuation and hard stools. As many as 35 million Americans may suffer from symptoms associated with CIC

Contraindications

- LINZESS is contraindicated in pediatric patients up to 6 years of age.
- LINZESS is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction.



Warnings and Precautions

Pediatric Risk

- LINZESS is contraindicated in pediatric patients up to 6 years of age. In nonclinical studies, deaths occurred within 24 hours in young juvenile mice (1 to 3 week-old mice; approximately equivalent to human pediatric patients less than 2 years of age) following administration of one or two daily oral doses of linaclotide.
- Use of LINZESS should be avoided in pediatric patients 6 through 17 years of age. Linaclotide did not cause deaths in older juvenile mice (approximately equivalent to humans age 12 to 17 years). Although there were no deaths in older juvenile mice, given the deaths in young juvenile mice and the lack of clinical safety and efficacy data in pediatric patients, use of LINZESS should be avoided in pediatric patients 6 through 17 years of age.

Diarrhea

- Diarrhea was the most common adverse reaction of LINZESS-treated patients in the pooled IBS-C and CIC double-blind placebo-controlled trials. Severe diarrhea was reported in 2% of LINZESS-treated patients. The incidence of diarrhea was similar in the IBS-C and CIC populations.
- Patients should be instructed to stop LINZESS if severe diarrhea occurs and to contact their healthcare provider, who should consider dose suspension.

Adverse Reactions

- In IBS-C clinical trials, the most common adverse reactions in LINZESS-treated patients (incidence $\geq 2\%$ and greater than placebo) were diarrhea (20% vs 3% placebo), abdominal pain (7% vs 5%), flatulence (4% vs 2%), headache (4% vs 3%), viral gastroenteritis (3% vs 1%) and abdominal distension (2% vs 1%).
- In CIC clinical trials, the most common adverse reactions in LINZESS-treated patient (incidence $\geq 2\%$ and greater than placebo) were diarrhea (16% vs 5% placebo), abdominal pain (7% vs 6%), flatulence (6% vs 5%), upper respiratory tract infection (5% vs 4%), sinusitis (3% vs 2%) and abdominal distension (3% vs 2%).



Drug Interactions

No drug-drug interaction studies have been conducted with LINZESS. Linaclotide and its active metabolite are not measurable in plasma following administration of the recommended clinical doses; hence, no systemic drug-drug interactions or drug interactions mediated by plasma protein binding of linaclotide or its metabolite are anticipated. Linaclotide does not interact with the cytochrome P450 enzyme system based on the results of in vitro studies. In addition, linaclotide is neither a substrate nor an inhibitor of the efflux transporter P-glycoprotein (P-gp).

References

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