Indications For Use

AspyreRx™ is a prescription-only digital therapeutic device intended to provide cognitive behavioral therapy to patients 18 years or older with type 2 diabetes. The device targets behavior to aid in the management of type 2 diabetes in patients who are under the care of a healthcare provider. AspyreRx provides cognitive behavioral therapy as a treatment that should be used adjunctively with standard of care.

Notes Regarding Indications For Use

- The device is not intended for use as a stand-alone therapy.
- The device is not a substitute for a patient's prescribed therapy or medication.
- The benefit of treatment with the device was not evaluated beyond 180 days of treatment. The ability of the device to prevent potential relapse into prior behaviors after treatment discontinuation has not been studied.
- The benefit of the device without the use of study-related compensation for glycemic monitoring has not been evaluated.
- The device should not be used by people with unstable psychiatric disorders.
- The device should not be used by people with severe psychiatric disorders and is not intended for use as a treatment for any psychiatric disorder or symptom.

Who Should Not Use AspyreRx

AspyreRx delivers cognitive behavioral therapy (CBT) to target the behaviors that contribute to type 2 diabetes. This type of treatment should not be used for patients with other serious underlying health risks or conditions or for patients requiring highly personalized medical nutrition therapy.

Patients with the following conditions should not use AspyreRx:

Contraindications

- Unstable psychiatric illness, such as severe and poorly controlled anxiety or depression, or active suicidal ideation.
- Unstable or life threatening medical illness which might prevent use of AspyreRx or require a need for more personalized medical nutrition therapy (e.g. patients on dialysis, hospitalized patients, patients with end-stage liver disease, patients with recent bariatric surgery).

Important Patient Information

Please use your clinical judgment to determine whether AspyreRx is right for your patient. Important considerations include:

Safety

- AspyreRx is not meant to be used as a treatment without the supervision of a healthcare provider.
- AspyreRx is meant to be adjunctive to pharmacotherapy; pharmacotherapy should be adjusted as medically appropriate.
- AspyreRx has not been evaluated in patients currently taking prandial insulin and does not offer insulin titration.
- AspyreRx has not been evaluated in patients with HbA1c levels >11%.
- AspyreRx has not been evaluated in patients who have undergone prior bariatric surgery.
- AspyreRx has not been evaluated in patients with advanced heart failure.
- AspyreRx has not been evaluated in patients who are pregnant or planning to become pregnant.
- AspyreRx is not intended for real-time monitoring of patient biometrics such as real-time blood glucose levels.

Effectiveness

- The majority of patients have observed reduction in HbA1c after 90 days of use, with continued benefits demonstrated after 180 days of use. Improved outcomes were observed with increased usage, with greater HbA1c reduction, on average, occurring as more CBT lessons were completed. The observed reduction in HbA1c occurred when used adjunctively with changes in patients' glycemic control medications and standard of care medical visits. A greater HbA1c reduction also occurred in patients with more frequent interaction with health care providers.
- The device was not studied past 180 days of use and benefits past the study period are not yet established.

Patient Eligibility

- AspyreRx is intended to be used alongside standard of care as part of a licensed healthcare provider's treatment of type 2 diabetes.
- AspyreRx is intended for patients aged 18 years and older whose primary language is English and are able to read at a 7th grade level or above.

- During AspyreRx use, patients should be willing to use an FDA-cleared glucometer for self-monitoring blood glucose.
- During AspyreRx use, patients will need access to an Android/iOS smartphone and must be familiar with use of smartphone apps.

Usage

- Compared to standard of care treatment alone, consistent use of AspyreRx for 90 days has been shown, on average, to result in greater improvements in blood glucose control, fewer diabetes-related risks to the patient, and more durable results, with benefits shown to persist up to 6 months with continued use of the app.
- Please instruct the patient to complete weekly lessons as directed by AspyreRx, and to complete a minimum of 10 lessons during the 90 day treatment period to achieve the best possible results.
- Alongside AspyreRx use, standard of care HbA1c monitoring should be conducted to determine appropriate antihyperglycemic medication type and dosage, and to make adjustments as needed.

Pivotal Study Summary

A 6 month randomized controlled study enrolled 726 subjects with type 2 diabetes with a BMI of ≥ 25 kg/m2 and baseline HbA1c between 7% and 11%. Subjects who used AspyreRx demonstrated reduced HbA1c (-0.41% at 90 days and -0.30% at 180 days), and had fewer medication increases compared to subjects who did not use AspyreRx. On average, subjects who used AspyreRx also experienced improved fasting blood glucose, reduced systolic blood pressure, reduced weight, improved mood, and improved quality of life scores, compared to subjects who did not use AspyreRx. All subjects were treated by their physicians according to standard of care during the study and medication management was continued during AspyreRx usage. Subjects who completed more AspyreRx lessons had greater HbA1c reduction on average. For example, those who completed 10 or more lessons in the first 90 days achieved an average 0.4% reduction from baseline at 90 days and an average 0.6% reduction from baseline at 180 days. A statistically significant fewer number of adverse events and serious adverse events were reported among subjects who used AspyreRx compared to subjects who did not use AspyreRx.

Among those assigned to AspyreRx, the average change in %HbA1c observed in the clinical study was -0.27% compared to baseline after 90 days of app use, and -0.37% compared to baseline after 180 days.

- After 90 days of app use, while 179 patients (60%) saw numerically improved glycemic control (%HbA1c decreased compared to baseline), there were 118 patients (40%) who saw no change or numerically worsened glycemic control (%HbA1c increased compared to baseline). In comparison, 136 patients (43%) in the control group saw HbA1c improvement and 177 (57%) saw no change or worsened glycemic control. These differences between the app and control group were statistically significant ($p<0.0001$).
- After 180 days of app use, while 159 patients (65%) saw numerically improved glycemic control after 180 days of app use (%HbA1c decreased compared to baseline), there were 85 patients (35%) who saw no change or numerically worsened glycemic control (%HbA1c increased compared to baseline). In comparison, 122 patients (45%) in the control group saw HbA1c improvement and 149 (55%) saw no change or worsened glycemic control. These differences between the device and control group were statistically significant ($p<0.0001$).

In the clinical study with AspyreRx, observed reduction in HbA1c was correlated with increased usage of the app. In addition, for patients who used the app, those with additional medical visits to a health care provider had average HbA1c reductions of -0.40% at day 90 and -0.38% at day 180. In comparison, patients in the control group with additional medical visits had an average HbA1c increase of +0.06% at day 90 and an average reduction of -0.07% at day 180. The difference between groups was -0.46% at day 90 and -0.31% at day 180. Patients without additional medical visits who used the app had average HbA1c reductions of -0.05% at day 90, and an average increase of +0.01% at day 180. In comparison, patients in the control group without additional medical visits had an average HbA1c increase of +0.27% at day 90 and +0.17% at day 180. The difference between groups was -0.32% at day 90 and -0.16% at day 180.

The AspyreRx pivotal study did not evaluate safety and effectiveness with continued 90-day treatments beyond 180 days.

Patients who used the app were financially compensated for taking frequent blood glucose measurements, whereas patients who used a control app were treated according to standard of care. Patients who used a control app did not take study-directed blood glucose measurements, thus their compensation was not associated with blood glucose measurements. Total compensation was equal for subjects who used the app and those who did not use the app.

What is AspyreRx?

AspyreRx is a 90-day prescription digital therapeutic treatment that delivers cognitive behavioral therapy to treat patients 18 years or older with type 2 diabetes. AspyreRx targets behaviors to aid in the management of type 2 diabetes. AspyreRx should be used adjunctively with standard of care diabetes treatments. AspyreRx is used by the patient on a smartphone and is available by prescription only by a licensed healthcare provider.

There are 3 core components of AspyreRx cognitive behavioral therapy:

1. **Lessons** - Help patients identify maladaptive thoughts that lead to diabetes-promoting behaviors and introduce adaptive thoughts that lead to positive behavioral changes. Core components of lessons include journaling exercises, relevant patient vignettes, and other interactive CBT techniques. Patients are instructed to complete a minimum of 1 lesson per week *(~12 minutes per lesson)*.
2. **Skills** - Help patients by improving their capacity to solve problems, reinforce healthy new behaviors, plan activities, and cope with interfering thoughts and emotions. Patients are instructed to complete a minimum of 1 skill per week *(~13 minutes per skill)*.
3. **Goal Setting** - Patients are instructed to set goals for key daily behaviors, biometric tracking, and completion of core CBT components, such as lessons. Goals are initially established based on each patient's baseline behaviors, and while goal increases are recommended by AspyreRx to encourage continued improvements in daily behaviors, biometric tracking, and CBT adherence, patients have the autonomy to increase or decrease their goals based on their personal readiness. Patients are instructed to goal set once per week *(~5 minutes per goal setting)*.

How to Start Using AspyreRx

AspyreRx is an app that is available in the Apple App and Google Play Stores but must be prescribed by a healthcare provider to be used.

Once an AspyreRx prescription has been processed by a pharmacy, an email or text message containing a link and a unique activation code is sent to the patient's smartphone. To prepare for use, the patient must have a WiFi or data connection and then complete the following steps:

1. The patient will tap on the link provided in the email or text message. Depending on what type of smartphone the patient has, the link will go to the AspyreRx app in either the Google Play or Apple App Store.
2. The patient will download the AspyreRx app.
3. Once the app has been downloaded to the patient's smartphone, the patient will open the app.
4. If the patient taps the link as instructed, they will not be prompted to enter their activation code. If the patient does not click the link, they will be prompted to enter the activation code provided in the email or text message from the pharmacy.
5. The patient will be asked to create an account by entering their first and last name, email, and date of birth. This information is used to verify their identity.
6. Next, the patient must to set a strong password that meets the following criteria:
   - 8+ character length
   - 1+ uppercase letter
   - 1 lowercase letter
   - 1 number
   - 1 special character (e.g. #, @, !, &)
7. Once the password is set, the patient will be prompted to complete a mandatory onboarding experience in AspyreRx. Once completed, the patient's treatment will begin.

If patients encounter issues with downloading the app or setting up an account, they are instructed to contact **1-888-ASPYRE-1 (1-888-277-9731)**.

Prescriptions

AspyreRx is prescribed to eligible patients with type 2 diabetes. AspyreRx delivers cognitive behavioral therapy to target behaviors to aid in the management of type 2 diabetes. AspyreRx is not intended to replace care by a licensed healthcare provider.

Dosage

- Patients are instructed to complete a minimum of one lesson per week, as part of their core CBT therapy.
- On average, patients who complete 10 or more lessons in a 90-day treatment period have demonstrated better and more durable HbA1c reduction as compared to patients who complete less than 10 lessons in 90 days.

Duration

- Patients with a prescription will access AspyreRx for a 90-day treatment period. The prescription may be refilled for an additional 90-day treatment period. An additional 90-day treatment period, for up to 180 days, is likely to offer further benefit to the patient, as CBT works by promoting long-lasting changes in the underlying core beliefs that lead to diabetes-promoting behaviors.
- After the treatment period has ended, the patient's app will no longer allow progression or access to their in-app content. Patients will have access to a summary of their accomplishments from treatment.

Operating System Support for AspyreRx

AspyreRx is supported on the following mobile operating systems:

- Apple iOS14+
- Android OS 9+
- The app does not support Unihertz Jelly smartphones or devices.

Security

AspyreRx stores and transmits Protected Health Information (PHI) in compliance with the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and the Health Information Technology for Economic and Clinical Health Act (HITECH) and Personally Identifiable Information (PII) in accordance with applicable state and federal privacy laws.

AspyreRx uses industry best practices and security features in order to protect patient data. Individual mobile devices should incorporate the following settings to maximize the security and data integrity:

- Configure with a strong passcode, pin code, Face ID, or Touch ID.
- Configure to automatically lock after a period of inactivity.
- Configure to not trust downloads from untrusted sources.
- Connect to secure wireless networks with a passcode and encryption.
- Configure to show notifications only when the device is unlocked.
- Check with the mobile device manufacturer to see whether it is safe and feasible to update the operating system on the device.
- Do not jailbreak or root the mobile device.

AspyreRx requires the patient to enter a username and password prior to use. A strong password should be used to safeguard patient data and the username and password should not be shared with others.

Patients should be vigilant and investigate unusual behavior of apps on their mobile devices. If any unexpected behavior is suspected or noticed, the patient’s mobile device manufacturer should be contacted as soon as possible. Patients should consider using anti-virus software and a firewall on their mobile device to further safeguard data.

Additional Support Available
For additional support with any aspect of the AspyreRx app, contact us by phone at **1-888-ASPYRE-1 (1-888-277-9731)**.

To access an electronic copy of the AspyreRx Instructions for Use (IFU), visit: **www.aspyrerx.com**

To request a hard copy of the IFU:
Call: **1-888-ASPYRE-1 (1-888-277-9731)**

or

Send a request to receive within 7 days:
Better Therapeutics, Inc.
548 Market St #49404
San Francisco, California 94104

Better
THERAPEUTICS

Manufacturer Address
Better Therapeutics, Inc.
548 Market St #49404
San Francisco, California 94104

℞

AspyreRx™ is only available for prescription use.