THE US FOOD AND DRUG ADMINISTRATION (FDA) has granted 510(k) clearance to smart pen caps for insulin pens used to treat type 1 diabetes (T1D) and type 2 diabetes (T2D).

The clearance was granted to Big Foot Biomedical for their Bigfoot Unity Diabetes Management System, which uses smart pen caps to provide on-demand insulin doses for patients using multiple daily injection (MDI) therapy.

It is the first FDA granted dose decision support system that has minute-by-minute hypoglycemia alerts through integrated continuous glucose monitoring system (iCGM) data to provide dose recommendations.

The system will display a physician recommended dose using iCGM data on the pen cap, while also integrating with the Abbot FreeStyleLibre 2 system for glucose monitoring.

Patients can scan the FreeStyle Libre 2 sensor which will display the current glucose value, trend arrow, and a recommended correction dose. The system will also show patients the suggested meal insulin dose from their provider.

This treatment notified patients if they have missed their usual long-acting insulin dose. A low glucose alert will appear when a patient’s glucose level has fallen below 55 mg/dL, as well as an option alert when the glucose levels fall below 70 mg/dL.

Data from the iCGM and time-of-dose data from the system are uploaded to the cloud when it is possible, where health care providers can access the data through a secure web portal.

The FDA clearance system focuses on assisting clinicians deliver individualized care to patients with insulin-requiring diabetes.

Jim Malone, MD, chief medical officer for Bigfoot Biomedical said the clearance for the program “could be a game changer”.

“By replacing guesswork and complexity with connectivity and simplicity, the Bigfoot Unity program is truly serving as that real-time partner for both patients and providers when it comes to dose decision support and overall diabetes management,” said Malone in a statement.

Clinicians and health care providers can deliver care remotely, while also providing an accessible system for new patients and support to make insulin-dosing decisions.

In a statement accompanying the approval, Jeffrey Brewer, CEO of Bigfoot Biomedical expressed his pride in the company’s “advancements for this hugely underserved market.”

“Bigfoot Unity is specifically designed to be simple and accessible – no matter the person’s level of technical expertise – removing a key barrier to health equity,” Brewer said.

Connor Iapoce
**PATIENT-REPORTED OUTCOMES (PRO)** in the treatment of opioid dependence may be affected by the method of treatment.

Investigators, led by Fredrik Tiberg, PhD, of Camurus, found that patients in treatment receiving depot buprenorphine self-reported an improved treatment satisfaction compared to those receiving daily sublingual (SL) buprenorphine.

According to investigators, there is an increased interest in using PRO as an alternative end point for assessment and comparison of different medication in addiction outcome studies.

**Study Outlines**

The team compared depot buprenorphine versus daily SL buprenorphine, using the primary end point Treatment Satisfaction Questionnaire for Medication (TSQM).

As a result, the Depot Evaluation-Buprenorphine Utilization Trial (DEBUT) was an open-label, parallel group randomized clinical trial.

It was conducted in 6 outpatient drug treatment centers in Australia from October 2018 to September 2019.

Participants included patients aged ≥18 years who met criteria for opioid dependence. Excluded patients included those with severe respiratory and hepatic insufficiency and pregnancy.

Investigators used the primary efficacy outcome measure in global treatment satisfaction in the TSQM, with a range of 0 – 100, with higher scores showing greater satisfaction.

It was comprised of 14 items across 4 categories, including effectiveness, side effects, convenience, and global satisfaction. Each item was scored on a 5- or 7-point Likert scale, except for side effects (yes or no).

The secondary outcomes included other patient reported outcomes including satisfaction ratings (0 – 100), Patient Global Impression of Improvement (1 – 7, lower score indicating more improvement) and Treatment Burden Questionnaire (TBQ; 1 – 150, lower score indicating lower burden).

Other secondary outcomes included measures of opioid use, retention in treatment, and safety, including treatment-emergent adverse events (TEAEs), adverse drug reactions (ADRs), and serious AEs (SAEs).

**Treatment Results**

During the treatment period, 131 patients with opioid dependence were screened for eligibility, with 119 patients enrolled in the study. The patients included 70 (58.8%) men with a mean age of 44.4 years. Patients were receiving SL buprenorphine treatment prior to the study start.

After randomization, 60 participants (50.4%) received depot buprenorphine and 59 participants received SL buprenorphine (49.6%). A participant in the SL buprenorphine group withdrew consent and did not participate in the study.

Investigators found the mean duration since diagnosis of opioid dependence before randomization was 13.0 years and the mean duration from the first illicit use of opioids to randomization was 19.3 years.

Data show the mean daily dose of SL buprenorphine was 15.6 mg/d and the mean weekly depot buprenorphine dose was 21.5 mg/week and mean monthly dose was 107.4mg/month.

The team found the primary outcome TSQM Satisfaction Score had a mean at baseline of 71.2 in
the depot buprenorphine group and 73.8 in the SL buprenorphine group.

At week 24 in the mixed model for repeated measure (MMRM), investigators found the mean TSQM satisfaction score was significantly higher for the depot treatment group versus the sublingual group.

The mean score for depot buprenorphine was 82.5 versus a mean score of 74.3 in the SL buprenorphine group, with a difference of 8.2 (95% CI, 1.7 – 14.6; P = .01).

The overall study period had a mean score of 82.4 for the depot buprenorphine group and 73.8 for the SL buprenorphine group, with a difference of 8.6 (95% CI, 3.3 – 13.9; P = .002).

The team also noted improved results in the secondary outcomes after depot buprenorphine treatment. The treatment burden in the TBQ global score was (13.2 vs 28.6; 95% CI, −22.6 to −8.2; P < .001).

Data show 39 participants (65%) in the depot buprenorphine group experienced 117 adverse drug reactions, with most involving mild injection site reactions. In the sublingual buprenorphine group, the team saw 21 adverse drug reactions.

However, no participants in the trial withdrew due to adverse effects.

**Conclusion**

Investigators concluded that the study showed higher satisfaction in treatment with depot buprenorphine than SL buprenorphine, as well as improvement in treatment convenience, effectiveness, patient satisfaction, and treatment burden.

“In this study, participants randomized to receive depot buprenorphine administered weekly or monthly reported significantly higher and more sustained treatment global satisfaction than those randomized to continue to receive SL buprenorphine, adding to the evidence regarding depot buprenorphine from earlier double-blind RCTs,” investigators wrote.

The study, “Patient-Reported Outcomes of Treatment of Opioid Dependence With Weekly and Monthly Subcutaneous Depot vs Daily Sublingual Buprenorphine,” was published online in *JAMA Network Open.*
NEW DATA SHOW THAT A GENE THERAPY for hemophilia A may reduce the treatment burden for patients and clinicians, while also eliminating the need for factor VIII (FVIII) prophylaxis.

The BAY 2599023 is an adeno-associated virus (AAV) vector with capsid serotype hu37 (AAVhu37) that has demonstrated ability to achieve FVIII expressions at therapeutic levels with a good safety profile, according to investigators.

Thus, investigators, led by Stephen W. Pipe, MD of the University of Michigan, found BAY 2599023 resulted in sustained expression of endogenous FVII in all patients with indications of hemostatic efficacy.

The study was presented at the American Society of Gene & Cell Therapy (ASGCT) Virtual Meeting.

Study
The analysis aimed to report the safety and FVII activity achieved to data with BAY 2599023 in a six-patient population. Patients were enrolled sequentially in 3 cohorts.

Investigators used a phase 1/2, open-label, dose-finding study that included male patients with severe hemophilia A. Each patient received a single intravenous infusion of AAVhu37.

Further, the patient group was ≥18 years and >150 exposure days to FVII products, with no history of FVIII inhibitors and no detectable immunity to the AAVhu37 capsid.

Investigators primary endpoints for the study were adverse events (S/AESIs), while the secondary endpoint was FVII activity over time.

Results
The 3 cohorts included 2 patients each (n = 6) enrolled sequentially.

At the cutoff in January 2021, Cohort 1 (0.5 x 1013 GC/kg) reported no severe adverse events (SAE), drug-related adverse events (AE) or S/AESIs in a follow-up of 23 months.

After 12 months from treatment, a patient dropped out of the study.

Consequently, investigators enrolled two additional patients into the second (1.0 x 1013 GC/kg) and third (2.0 x 1013 GC/kg) dose cohorts. Study completion included 17 and 13 months of observation, respectively.

Investigators found in Cohort 2, an AESI event and mild elevation in alanine aminotransferase (ALT) was found. However, no loss of FVII activity levels were found and a short course of corticosteroid treatment returned the ALT to a normal range.

The team found both patients in Cohort 3 had mild or moderate increases in transaminases without associated symptoms or loss of FVIII expression with ongoing corticosteroid treatment.

There were no SAEs reported in any of the cohorts and patients with evaluable FVIII activity data showed durable and sustained levels over time. There were no bleeds observed after patients achieving FVIII levels >11%.

Conclusion
Investigators concluded in the first in-human study, escalating doses of BAY 2599023 were effective and few adverse effects were observed.

“Mild to moderate elevations of ALT, managed with corticosteroids, were the only observed AEs related to BAY 2599023,” investigators wrote. “Sustained expression of endogenous FVIII was observed in all patients with indications of hemostatic efficacy.”

The study, “First-in-Human Gene Therapy Study of BAY 2599023 in Severe Hemophilia A: Long-Term Safety and FVIII Activity Results,” was published online by the ASGCT.
DIRECT-ACTING ANTIVIRALS EFFECTIVE AGAINST HCV FOLLOWING LIVER TRANSPLANT SURGERY

Kenny Walter

A regimen of direct-acting antiviral (DAA) treatments is safe and efficacious against hepatitis C virus (HCV) infections following liver transplantation.

A team, led by Eric Kauffman-Ortega, MD, Hepatology and Liver Transplantation Unit, Department of Gastroenterology, Instituto Nacional de Ciencias Médicas y Nutrición “Salvador Zubirán,” identified the efficacy and safety of DAA treatment following liver transplantation hepatitis C virus recurrence in a cohort based in Mexico.

HCV infections represent 1 of the most frequent causes of liver transplants globally. Patients with HCV viremia at the time of transplantation universally develop recurrent HCV in the allograft, which causes accelerated fibrosis and graft loss.

However, treatment with direct-acting antivirals are highly effective and safe in this patient population.

The Study
In the retrospective cohort, the researchers examined all liver transplant patients between 2000-2019 with HCV recurrence following liver transplantation who received DAA.

The team collected clinical and biochemical characteristics from clinical records. The researchers also excluded patients who received treatment prior to a liver transplantation and patients who received interferon-based therapies after liver transplantation achieving sustained viral response at 12 weeks and eliminated patients who did not complete DAA therapy.

The investigators sought primary outcomes of SVR-12. The final analysis included 56 patients receiving DAA after the transplantation, with 98% SVR-12.

The most frequent genotypes were 1b (54%) and 1a (34%) and the most common antiviral scheme used was sofosbuvir/ledipasvir for 12 weeks in 59% of the patients.

Safety
The safety profile was positive, with no severe adverse effects observed.

Ribavirin was used in 82% of the patients. While 23.9% of this patient subgroup suffered from adverse effects, the majority were deemed mild.

In addition, the median follow-up after the transplant surgery was 55 months (IQR, 43-51), with a global and graft survival at 1 and 3 years of 100%.

“In a Mexican cohort, DAA therapy in LT patients with recurrence of HCV infection showed high efficacy and an acceptable safety profile,” the authors wrote.

Pediatric Patients with HCV
Recent data show a pediatric formulation of the direct-acting antiviral therapy glecaprevir/pibrentasvir (GLE/PIB) is highly effective and well-tolerated in pediatric patients with HCV infections.

The findings mark a milestone in the treatment of children with HCV infection, since the data suggest that the dramatic results DAAs have brought about in adults can also be realized in children as young as 3.

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“This In a Mexican cohort, DAA therapy in LT patients with recurrence of HCV infection showed high efficacy and an acceptable safety profile,”

About 13.2 million of the world’s estimated 71 million people with HCV infection are children between the ages of 1 and 15.

The study enrolled 80 patients with chronic HCV infection, genotypes 1-6, with or without compensated cirrhosis. The children were split into three age-based cohorts and given weight-based doses for either 8, 12 or 16 weeks. The primary endpoints were sustained virologic response at 12 weeks (SVR12) and steady-state exposure.

Of the 80 patients in the study, 77 achieved SVR12. One patient on the initial dose ratio had relapsed within 4 weeks of the end of treatment and 2 non-responders discontinued the study.

In the end, the investigators found doses of 250 mg GLE and 100 mg PIB were efficacious for children weighing 30 up to 45 kg. A dose of 200 mg GLE plus 80 mg PIB worked for children from 20 up to 30 kg, and the smallest patients (those 12-20 kg) achieved results at a dose of 150 mg GLE plus 60 mg PIB.

No serious drug-related adverse events were reported and pharmacokinetic exposures were comparable to those of adults.

The study, “Direct-Acting Antivirals in the Treatment of Hepatitis C Virus Recurrence after Liver Transplantation: Real-life Experience in a Mexican Cohort,” was published online in the Archives of Medical Research.
NEW RESEARCH SHOWS ONLY SCREENING for hepatitis C virus (HCV) by risk in pregnant women results in a large percentage of missed diagnoses.

A team, led by Elisa T. Bushman, Center for Women’s Reproductive Health, University of Alabama at Birmingham, examined whether universal screening is linked to increased HCV diagnoses and postpartum linkage to HCV care compared to risk-based screening.

Current recommendations from the US Centers for Disease Control and Prevention (CDC) and the US Preventive Services Task Force (USPSTF) call for universal hepatitis C virus screening in pregnant women. In addition, the Society for Maternal-Fetal Medicine (SMFM) and American College of Obstetricians and Gynecologists (ACOG) recommend risk-based screening for HCV in pregnancy.

In the retrospective cohort study, the researchers examined pregnant women who were screening for hepatitis C at a single tertiary-care center. The patients were split into 2 cohorts—women managed with risk-based screenings between January 2014 and October 2016 and women universally screened between November 2016 and December 2018.

Screenings
Screening was performed with ELISA antibody testing, which was viremia confirmed with HCV ribonucleic acid (RNA) polymerase chain reaction (PCR) tests.

The researchers sought primary outcomes of the rate of HCV screen positivity and postpartum linkage to care.

Overall, there were 16,489 women included in the study between 2014-2018, 7039 of which were screened for HCV. Of the patients screened, 266 were part of the risk-based cohort and 6773 were part of the universal screening cohort.

Positive Rate
There was a 29% (n = 76) positivity rate for HCV antibody screening (HCVAb+) in the risk-based cohort and 1.3% (n = 90) in the universal cohort.

However, only 69% (n = 62) of HCVAb+ women in the universal cohort met the criteria for risk-based testing and of the remaining 28 women, 21% (n=6) had active viremia (HCV RNA+).

The researchers also found 64% (n = 103) of the HCVAb+ women were HCV RNA+—51 of 266 (19%) in the risk-based and 52 of 6773 (0.8%) in the universal cohort.

In addition, 75% (n = 125) of HCVAb+ women were referred postpartum for HCV evaluation and 27% (n = 34) were linked to care and only 9% (n =10) of women with viremia-initiated treatment within 1 year of delivery.

“Universal HCV screening in pregnancy identified an additional 31% of HCVAb+ women compared with risk-based screening,” the authors wrote. “Given low rates of HCV follow-up and treatment regardless of screening modality, further studies are needed to address barriers to postpartum linkage to care.”

Impact of COVID-19
Recently, researchers found HCV screenings have decreased because of the COVID-19 pandemic.

Hepatitis C Ab testing and new hepatitis C RNA identification decreased hospital-wide and in the ambulatory clinics alone after the preservation of resources restructuring took effect on March 16.

When the investigators compared the mean daily hospital-wide tests before and after the policy changes, they found that the mean decreased by 22.9 daily tests. The mean new hepatitis C-positive patients identified daily throughout the hospital decreased by 0.36 patients per day.

The study, “Pragmatic Experience with Risk-based versus Universal Hepatitis C Screening in Pregnancy: Detection of Infection and Postpartum Linkage to Care,” was published online in the American Journal of Perinatology.
RESEARCHERS IDENTIFY CLEAR TRENDS FOR C. DIFF HOSPITALIZATIONS

NATIONAL ESTIMATES OF CLOSTRIDIUM DIFFICILE INFECTION (CDI) infection hospitalizations by demographics and patient comorbidities are considered insufficient in the US.

A team, led by Dhanshree Solanki, Edward J Bloustein School of Planning & Public Policy, identified hospitalization rates for C. diff by age group, sex, and region, as well as for patient comorbidity in the US.

In the study, the researchers analyzed the 2017 National Inpatient Sample (NIS) and identified 329,460 CDI-related hospitalizations, accounting for nearly 1% of all hospitalizations.

However, there were some stark differences found between CDI hospitalized patient characteristics and the general population of hospitalized individuals.

“CDI hospitalization rates were highest in the elderly over 85 years old and declined with successive decreases in age,” the authors wrote. “Women had higher CDI hospitalization rates than men, and fluid and electrolyte disturbances and renal failure were the most common comorbid conditions. The presence of CDI as a comorbid condition at the time of hospitalization for other principal diagnoses or development of CDI during a hospitalization for other principal diagnoses significantly increases the risk of in-hospital morbidity and mortality.”

Age, Sex, and Region

The average CDI patient was admitted to the hospital at 64.7 years old, which is approximately 20 years older than the average age at admission of all other hospitalizations.

In addition, the highest rate of CDI hospitalizations—716 per 100,000 hospitalizations—was in patients at least 85 years old.

The inverse of that relationship was also true as those 18 years and younger had the lowest rate of hospitalizations at 12 per 100,000 hospitalizations.

“There was a progressive increase in the CDI hospitalization rates with each successive age group,” the authors wrote.

There were also trends in CDI hospitalizations based on sex and region.

Female patients had a higher rate of hospitalizations—114 per 100,000 hospitalizations—than males—88 per 100,000 hospitalizations.

In addition, the hospitalization rate for c diff was highest in the Northeast—109 per 100,000 hospitalizations—and lowest in the West—84 per 100,000 hospitalizations.

Comorbidities

Some of the common comorbidities for CDI patients included fluid and electrolyte disturbance (63.3%) and renal failure (33.4%), while when CDI is a secondary diagnosis, major loss of function, extreme likelihood of dying, septicemia, and septic shock were more common in comparison to CDI as a principal diagnosis.

Hope for the Future

There is some hope that CDI hospitalization rates might see a drop, largely because of the mitigation measures hospitals have put in place to try to combat the spread of COVID-19.

Researchers recently found in a retrospective cohort study of 9 Massachusetts hospitals 97 (24.9%) patients who were tested for CDI, with a mean age of 62.4 years old. Of this group, 5 (5.2%) patients tested positive for CDI, which was lower than the overall inpatient CDI-positive rate in 2019 (n = 280; 9.8% of tests performed). However, this was not statistically significant (P = 0.16).

The study, “Clostridium difficile Infection Hospitalizations in the United States: Insights From the 2017 National Inpatient Sample,” was published online in Gastroenterology Research.
**AGE, GENDER, DISEASE SEVERITY INFLUENCE DERMATOLOGY-RELATED DEPRESSION**

Kevin Kunzmann

**PSYCHOLOGICAL STATUS AND MEASURES** of quality of life (QoL) differs for patients of various chronic skin conditions, dependent on factors including their demographic and disease severity, according to new research.

In a cross-sectional study from a team of Thailand investigators, the mental health of patients with common dermatologic diseases including psoriasis, atopic dermatitis, and vitiligo were found to be frequently affected by increased depression and anxiety.

The data, presented at the American Academy of Dermatology (AAD) Virtual Meeting Experience this weekend, provides more context into which patients suffering from which dermatological conditions may need monitoring for worsened quality of life or psychological burden.

Investigators from Ramathibodi Hospital at Mahidol University, led by Pasita Palakornkitti, MD, sought to evaluate psychological aspects and QoL in Thai patients with diagnosed vitiligo, psoriasis, and adult atopic dermatitis—with consideration to patient age, gender, disease duration, and extent of affected areas.

As they noted, previous research has indicated a significant impact of such diseases on metrics of anxiety and depression.

Palakornkitti and colleagues conducted the questionnaire-based assessment at their institute from June – December 2020. Qualified participants were ≥18 years old, diagnosed with any 1 of the 3 diseases. To evaluate anxiety, depression, and QoL, they used a trio of metrics:

- Hospital Anxiety and Depression Scale (HADS) for anxiety and mild depression
- The 9-Question Patients Health Questionnaire (PHQ-9) for major depression
- Dermatology Life Quality Index (DLQI) for moderately impaired QoL.

Among their 300 participants, 121 (40.3%) had diagnosed vitiligo; 100 (33.3%) had diagnosed psoriasis; and 79 (26.3%) had adult atopic dermatitis. Mean patient age was 43.1 years old, with 65.7% females. Nearly two-thirds of patients (63.7%) had their disease for >5 years, and more than half (54.3%) reported ≤3% extent of affected area.

Patients with adult atopic dermatitis were the most likely to report mild depression per HADS (21.5%) or moderately impaired QoL per DLQI (64.6%) among all disease groups. Patients with psoriasis, meanwhile, had the highest prevalence of anxiety per HADS (26.0%). Just 5.8% of patients with vitiligo reported major depression per PHQ-9, versus 16.0% and 17.7% of psoriasis and atopic dermatitis patients, respectively.

Among patients with atopic dermatitis, patients <50 years old were more than four-fold likely to suffer from impaired QoL (OR, 4.36; 95% CI, 1.29 – 14.72) versus old patients. But patients with longer disease duration and affected areas were even more likely to report impaired QoL than those with recent diagnoses and lesser affected area.

Similar outcomes were observed among patients with psoriasis, including for depression and anxiety outcomes. Among vitiligo patients, female patients were nearly three-fold more likely to report impaired QoL than male counterparts (OR, 2.74; 95% CI, 1.16 – 6.49).

The investigators concluded that, aside from unique gender differences and varied rates of depression and anxiety across the dermatologic conditions, the most consistent outcome pertained to age: those <50 years old were more likely to report poorer QoL regardless of disease, severity, duration, or gender.

The study, “Anxiety, Depression and Quality of life in patients with chronic skin diseases,” was presented at AAD VMX.