Aripiprazole tablets with sensor (Abilify Mycite®)  
FDA approved November 2017

**Indication:** Aripiprazole tablets with an Ingestible Event Marker (IEM) sensor is indicated for the treatment of adults with schizophrenia, bipolar I disorder, or as an adjunctive treatment of patients with major depressive disorder (MDD)

**Limitations of Use:** The ability of aripiprazole drug-device combination product
- to improve patient compliance or modify aripiprazole dosage has not been established
- to track drug ingestion in “real-time” or during an emergency is not recommended because detection may be delayed or not occur

**Mechanism of Action:** Unclear, thought to be mediated through a combination of partial agonist activity at D₂ and 5-HT₁A receptors and antagonist activity at 5-HT₂A receptors

**Aripiprazole drug-device combination system:** consists of four components
1. Aripiprazole tablet embedded with an IEM sensor
2. Mycite® patch, a wearable sensor detects signal from the IEM sensor after ingestion & transmits information to a smartphone
3. Mycite App, an application used with a compatible smartphone to display information for the patient
4. Web-based portal for healthcare providers (HCPs) & caregivers

- Educate clients how to use the medication, patch, app, and portal prior to initial use
- Ensure clt is capable and willing to use smartphones/apps
- Instruct clts to download the app & follow instructions. Ensure the app is compatible with clt’s smartphone
- It may take 30 minutes to two hours for the smartphone app and web portal to detect the ingestion
- If the ingestion of the tablet is not detected, do not repeat the dose
- The status of the patch is indicated by a status icon in the app. Instruct clts to ensure that the app is paired with the patch
- The patch sends the date and time of pill ingestion and the clt’s activity level via Bluetooth to a cellphone app. The app lets clts to add their mood, the hours they have rested, and transmits the information to a database that prescribers/caregivers who have clts’ permission can access

**Dosage & Administration**

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Initial</th>
<th>Recommended</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia</td>
<td>10-15 mg/d</td>
<td>10-15 mg/d</td>
<td>30 mg/d</td>
</tr>
<tr>
<td>Bipolar mania - monotherapy</td>
<td>15 mg/d</td>
<td>15 mg/d</td>
<td>30 mg/d</td>
</tr>
<tr>
<td>Bipolar mania - adjunct to lithium or valproate</td>
<td>10-15 mg/d</td>
<td>15 mg/d</td>
<td>30 mg/d</td>
</tr>
<tr>
<td>MDD – Adjunct to antidepressants</td>
<td>2-5 mg/d</td>
<td>5-10 mg/d</td>
<td>15 mg/d</td>
</tr>
<tr>
<td>Hepatic or renal impairment</td>
<td>No dosage adjustment needed</td>
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</table>

**Administration**
- Administer once daily without regard to meals
- Swallow tablet whole; do not divide, crush, or chew
### Patch
- Apply patch only when instructed by the app to the left side of the body just above the lower edge of the rib cage
- Do not place the patch on irritated skin or a location that overlaps the area of the most recently removed patch
- Keep patch on when showering, swimming, or exercising
- Change patch weekly or sooner as needed (app reminds clt to change the patch & directs to apply/remove patch correctly)
- Remove patch in case of skin irritation

### Dosage forms & strengths
| Tablets with sensor: 2, 5, 10, 15, 20, and 30 mg |

### How Supplied
| The Abilify Mycite kit contains aripiprazole tablets embedded with an IEM sensor co-packaged with 7 Mycite patches |

### DDIs

<table>
<thead>
<tr>
<th>Known CYP2D6 poor metabolizers</th>
<th>Strong CYP2D6 or CYP3A4 inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administer half of usual dose</td>
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</table>

<table>
<thead>
<tr>
<th>Known CYP2D6 Poor Metabolizers and strong CYP3A4 inhibitors</th>
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<tbody>
<tr>
<td>Administer quarter of recommended dose</td>
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<table>
<thead>
<tr>
<th>Strong CYP3A4 inducers</th>
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<tbody>
<tr>
<td>Double recommended dose over 1 to 2 weeks</td>
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### Warnings & precautions
- Cerebrovascular adverse reactions in elderly patients with dementia-related psychosis
- Neuroleptic Malignant Syndrome
- Tardive Dyskinesia
- Metabolic change (hyperglycemia/DM, dyslipidemia, & weight gain)
- Pathological gambling and other compulsive behaviors
- Orthostatic hypotension
- Leukopenia, neutropenia, & agranulocytosis
- Seizures
- Potential for cognitive & motor impairment
- Boxed warning
  - Increased mortality in elderly patients with dementia-related psychosis
  - Increased risk of suicidal thoughts & behaviors in pediatric and young adult patients taking antidepressants
  - Safety and effectiveness of Abilify Mycite® have not been established in pediatric patients

### Pharmacokinetics

<table>
<thead>
<tr>
<th>Onset</th>
<th>Initial: 1 to 3 weeks</th>
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<tbody>
<tr>
<td>Tmax</td>
<td>3 to 5 hours</td>
</tr>
<tr>
<td>Bioavailability</td>
<td>87 %</td>
</tr>
<tr>
<td>Metabolism</td>
<td>Hepatic via CYP2D6, CYP3A4</td>
</tr>
<tr>
<td>Half-life</td>
<td>aripiprazole: 75 hours, dehydro-aripiprazole: 94 hours</td>
</tr>
</tbody>
</table>
Safety

<table>
<thead>
<tr>
<th>AEs ≥ 10%</th>
<th>Nausea, vomiting, constipation, headache, dizziness, akathisia, anxiety, insomnia, and restlessness</th>
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<table>
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<tr>
<th>Most frequently reported AE (≥5% &amp; twice the rate of placebo)</th>
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<tr>
<td>Schizophrenia</td>
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<td>Bipolar mania (monotherapy)</td>
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<td>Bipolar mania (adjunctive therapy with lithium or valproate)</td>
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<td>MDD (adjunctive treatment to antidepressants)</td>
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</table>

Skin Irritation (patch) | 12.4% (61 pts) experienced localized skin rashes

Role in Therapy

Abilify Mycite®, the first FDA approved sensor-embedded medication, is a collaboration between aripiprazole’s manufacturer Otsuka and Proteus Digital Health

- The aripiprazole drug-device combination product may improve adherence (reduced ED visits/inpatient stays) and help monitor whether clients are taking medication as prescribed
  - will enable earlier detection, monitoring/intervention of noncompliance; however, no data to support that the digital pill improves compliance (anticipated to be studied after sales begin)
- FDA recommends Human Factors (HF) testing for drug-device combinations to assess/mitigate use-related hazards
  - HF studies indicate “acceptable safety and good usability” of the Digital Medicine System
- Challenges/concerns
  - a non-compliant clt would need to remember to take the medication and to wear the patch appropriately
  - clt experiencing delusions of being watched may feel scrutinized
  - efficacy – does ingestible sensor technology affect pharmaceutical properties of the medication?
  - added expense of the technology
  - Responsibility of managing the data
    - Prescribers, pharmacists, or medical assistants
    - Would they be responsible for the negative outcomes due to non-adherence
  - 12% of pts experienced application site rash
    - how do patients obtain additional patches
  - Ethical concerns - could close monitoring may eventually
    - cause medication coverage loss due to non-compliance
- require digital medications as a condition for parole or releasing clts from psychiatric facilities
  - Privacy concerns
    - Concern that an individual’s privacy is being violated (HCPs & insurance companies gaining more access into pts' personal lives)
      - Safeguards to address privacy concerns – pts can stop HCPs & others from seeing some/all of their data (app allows blocking recipients)
  - Need for careful consent procedures
  - Clts who agree to be monitored can decide who monitors them, and if there are rewards for being monitored. Insurers might eventually offer incentives such as copayment discounts
  - Potential candidates for the drug-device combination product
    - clts at risk of stopping medication after feeling better
    - clts at high risk of re-hospitalization due to non-compliance
    - clts who refuse long-acting injections (clinic visits, painful/other concerns)
    - clts who want to prove compliance or feel paranoid about being accused of non-compliance?
  - The goal of the digital pill is to improve compliance and to inform caregivers and healthcare providers about clt’s medication adherence in a timely manner. However, reasons for non-compliance include side effects, pts’ belief that they don’t have an illness, or paranoid thoughts about HCPs. A system that will monitor behavior and notify HCPs might not be acceptable to many psychiatric clts. “Abilify Mycite does not help with the challenge of daily use; just the monitoring of it”
  - Abilify went off patent, but now Otsuka has exclusive rights to embed aripiprazole with IEM sensor
  - Other options to help improve medication compliance
    - pillboxes, watch alarms, pill stations (filled weekly/monthly, remotely monitored), prescription bottles with caps that change color when clts are late to take meds, sensor implanted medication bottle caps that transmit bottle openings to apps/remote dashboards for monitoring
  - Future implications
    - expanded use of digital pills for high risk clts for whom non-adherence could have a significant clinical/economic impact
    - elderly population who want help remembering to take pills
    - monitoring of a clinical trial medication
    - individuals taking medication for a specific duration such as tuberculosis (nurses often need to observe pts taking medication)
    - controlled substance monitoring
    - may include more medications when the technology becomes less expensive
  - Long term experience in routine clinical patients, the price, and whether digital pills improve medication compliance, will define the role of digital medicine system

**Price comparison:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Monthly Cost</th>
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</thead>
<tbody>
<tr>
<td>Aripiprazole generic</td>
<td>30mg/day</td>
<td>$51</td>
</tr>
<tr>
<td>Abilify brand</td>
<td>30mg/day</td>
<td>$1260</td>
</tr>
<tr>
<td>Abilify Maintena</td>
<td>400mg/month</td>
<td>$2275</td>
</tr>
<tr>
<td>Abilify MyCite</td>
<td>30mg/day</td>
<td>$1650</td>
</tr>
</tbody>
</table>
**Prerequisite to use:**
Completion of Healthcare provider preregistration and Patient enrollment form
Smart phone with internet access to download MyCite APP and access MyCite Dashboard

**Formulary Considerations:**

BHRS P&T raised following concerns regarding Abilify Mycite:
*Patient selection and cooperation in paranoid schizophrenic population
*HIPAA compliance and protected patient information with digital tracking and online sharing
*Patient information residing with 3rd party vendor
*Technology and secured network requirements for patient and provider
*Need for Informed Consent prior to therapy
*Unclear advantage and its role in current management of schizophrenia
*Limited roll-out of Abilify MyCite via Magellan does not include California at this time.

**Recommend: Nonformulary for all lines of business**