BACKGROUND

Influenza (Flu) is a contagious respiratory illness that can cause mild to severe illness, and can even lead to death. While infection from the influenza virus can occur at any time, influenza viruses typically circulate in the United States from late fall through early spring.¹

For the 2018-2019 flu season²:

- In contrast to the United States 2017-2018 severe influenza season, the 2018-2019 flu season was moderately severe. Activity began to increase in November, peaked mid-February, and returned to below baseline in mid-April. This 21-week season was the longest in 10 years, according to CDC’s recent Morbidity and Mortality Weekly Report.
- Compared to 2017-2018’s flu season, rates of hospitalization were lower for adults but similar for children.
- Influenza-like-illness (ILI) peaked in February 2019, significantly lower than 2017-2018’s peak. (Figure 1)

Figure 1: Mississippi Influenza Like Illness (ILI) Rates 2011-2019³

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¹ Season. MMWR Recomm Rep 2019;68(No. RR-3):1–21. DOI: http://dx.doi.org/10.15585/mmwr.rr6803a1
Comparing the rates of ILI in Mississippi for the 2018-2019 flu season to nationwide and regional rates, Mississippi consistently had higher rates. (Figure 2)

Figure 2: Mississippi Department of Health Comparison of ILI Rates

During the 2018-2019 season the vaccine was approximately 30% effective in reducing influenza illness and hospitalizations. The effectiveness of influenza vaccines varies depending on several factors, such as the age and health of the recipient, the types and subtypes of circulating influenza viruses, and the degree of similarity between circulating viruses and those included in the vaccine.

There were an estimated 37.4-42.9 million flu illnesses, 531-647,000 hospitalizations and 36,400-61,200 deaths from the flu.

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Preventing infection is vital with flu vaccination serving as the primary source of flu prevention. Vaccination has been shown to reduce the morbidity and mortality associated with influenza. The flu vaccine causes antibodies to develop in the body approximately 2 weeks after vaccination. Protection from the flu vaccine is thought to persist for approximately 6 months and declines over time due to waning antibodies and changes in the circulating influenza virus from year to year.  

**RECOMMENDATIONS FOR THE USE OF INFLUENZA VACCINES, 2019–20**

**Groups Recommended for Vaccination**

Routine annual influenza vaccination for all persons aged ≥6 months who do not have contraindications has been recommended by CDC and CDC’s Advisory Committee on Immunization Practices (ACIP) since 2010. ACIP’s most recent recommendations for seasonal influenza vaccines for the 2019-2020 season, published August 23, 2019, updates the 2018-2019 recommendations. All persons aged ≥6 months who do not have contraindications should be vaccinated annually. However, vaccination to prevent influenza is particularly important for persons who are at increased risk for severe illness and complications from influenza and for influenza-related outpatient, emergency department, or hospital visits. When vaccine supply is limited, vaccination efforts should focus on delivering vaccination to persons at higher risk for medical complications attributable to severe influenza who do not have contraindications. These persons include (no hierarchy is implied by order of listing):

- All children aged 6 through 59 months;
- All persons aged ≥50 years;
- Adults and children who have chronic pulmonary (including asthma), cardiovascular (excluding isolated hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus);
- Persons who are immunocompromised due to any cause (including but not limited to immunosuppression caused by medications or HIV infection);
- Women who are or will be pregnant during the influenza season;
- Children and adolescents (aged 6 months through 18 years) who are receiving aspirin- or salicylate-containing medications and who might be at risk for experiencing Reye syndrome after influenza virus infection;
- Residents of nursing homes and other long-term care facilities;
- American Indians/Alaska Natives; and

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7 Centers for Disease Control and Prevention: Children & Influenza. [https://www.cdc.gov/flu/protect/children.htm](https://www.cdc.gov/flu/protect/children.htm)
• Persons who are extremely obese (body mass index ≥40 for adults)

Vaccination of persons who live with or care for those who are at increased risk is also emphasized. When vaccine supply is limited, vaccination efforts should focus on delivering vaccination to persons at higher risk for influenza-related complications, as well as persons who live with or care for such persons, including the following:

• Health care personnel working in health-care settings who have the potential for exposure to patients and/or to infectious materials. ACIP guidance for immunization of health care personnel has been published previously;
• Household contacts (including children) and caregivers of children aged ≤59 months (i.e., aged <5 years) and adults aged ≥50 years, particularly contacts of children aged <6 months; and
• Household contacts (including children) and caregivers of persons with medical conditions that put them at higher risk for severe complications from influenza.

Timing of Vaccination:

Optimally, vaccination should occur before onset of influenza activity in the community. However, because timing of the onset, peak, and decline of influenza activity varies, the ideal time to start vaccinating cannot be predicted each season. Vaccination efforts should continue throughout the season because the duration of the influenza season varies, and influenza activity might not occur in certain communities until February or March.

• Balancing considerations regarding the unpredictability of timing of onset of the influenza season and concerns that vaccine-induced immunity might wane over the course of a season, it is recommended that vaccination should be offered by the end of October.
• Children aged 6 months through 8 years who require 2 doses should receive their first dose as soon as possible after the vaccine becomes available to allow the second dose (which must be administered ≥4 weeks later) to be received by the end of October.
• For those requiring only 1 dose for the season, early vaccination (i.e., in July and August) is likely to be associated with suboptimal immunity before the end of the influenza season, particularly among older adults. No recommendation is made for revaccination later in the season of persons who have already been fully vaccinated (i.e., providing a booster dose).
• Vaccination should continue to be offered as long as influenza viruses are circulating and unexpired vaccine is available. To avoid missed opportunities for vaccination, providers should offer vaccination during routine health care visits and hospitalizations.
Primary Changes and Updates in the Recommendations:

- Routine annual influenza vaccination of all persons aged ≥6 months who do not have contraindications continues to be recommended. No preferential recommendation is made for one influenza vaccine product over another for persons for whom more than one licensed, recommended, and appropriate product is available.

TREATMENT

When patients with the flu are treated within 48 hours of becoming sick, antiviral drugs can reduce symptoms and duration of the illness. Antivirals have been shown to lessen symptoms and shorten illness duration by 1 to 2 days and can prevent serious flu complications such as pneumonia. Antiviral medications can be grouped into the following classes:

- adamantanes - *amantadine* (Symmetrel) and *rimantadine* (Flumadine);
- neuraminidase inhibitors - *oseltamivir* (Tamiflu), *peramivir* (Rapivab), and *zanamivir* (Relenza);
- endonuclease inhibitors – *baloxavir marboxil* (Xofluza).

Admantanes are active against influenza A viruses only. Additionally, high levels of resistance to adamantanes have been noted in past flu seasons; and thus, adamantanes are not recommended for antiviral treatment or chemoprophylaxis of currently circulating influenza viruses.9

At this time, antiviral resistance to neuraminidase inhibitors is currently low. The only oral neuraminidase inhibitor, oseltamivir (Tamiflu®), is FDA indicated for the treatment of acute, uncomplicated influenza in patients 2 weeks of age and older who have been symptomatic for no more than 2 days.10 Although it is also FDA indicated for prophylaxis of influenza in patients 1 year and older, the CDC and American Academy of Pediatrics (AAP) recommend prophylactic therapy in children as young as 3 months of age.11 Treatment dosing is typically twice daily for 5 days, while prophylactic dosing is typically once daily for 10 days.

On October 24, 2018 the FDA approved the first new antiviral for flu in nearly 20 years. Xofluza® (baloxavir marboxil) is indicated for the treatment of acute, uncomplicated influenza in patients 12 years and older who have been symptomatic for no more than 48 hours. Xofluza, taken as a single oral dose, should be administered within 48 hours of symptom onset and may be taken with or without food.

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9 Centers for Disease Control and Prevention: Influenza Antiviral Medications: Summary for Clinicians. [https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm](https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm)
Currently Mississippi’s Universal Preferred Drug List (UPDL) lists branded Tamiflu and its generic, oseltamivir, as preferred agents. Other neuraminidase inhibitors, adamantanes, and Xofluza are categorized as non-preferred agents. (Figure 3)

Figure 3: Current Mississippi Medicaid UPDL\textsuperscript{12}

At the December 2018 DUR Board meeting, MS-DUR was asked to present an annual influenza update to the Board at the conclusion of each flu season. Specifically, MS-DUR was asked to assess the utilization of anti-influenza therapies among Medicaid beneficiaries.

METHODS

Pharmacy and medical claims for anti-influenza agents were extracted for state fiscal years (SFY) 2018 (July 1, 2017 to June 30, 2018) and 2019 (July 1, 2018 to June 30, 2019), respectively. As of June 30, 2019 there were 673,247 beneficiaries enrolled in the DOM.\textsuperscript{13} The analysis included prescriptions for all anti-influenza agents listed on MS DOM PDL (Tamiflu®, oseltamivir, Flumadine®, rimantadine, Rapivab®, Relenza®, Xofluza®) from all pharmacy programs -- fee-for-service and all three Coordinated Care Organizations (UHC, Mag, Mol). The number of beneficiaries taking these agents, the number of prescriptions filled and the amounts paid for these prescriptions were determined for state fiscal years 2018 and 2019, respectively.


RESULTS

In Table 1 the number of Medicaid beneficiaries with documented influenza vaccination for SFY 2019 is displayed.

- 73,223 beneficiaries had documentation of receiving flu vaccination during SFY 2019.
- It should be noted that vaccinations provided through the Vaccines for Children (VFC) Program do not appear in Medicaid claims data.

<table>
<thead>
<tr>
<th>Plan at time of flu vaccination</th>
<th>Number of beneficiaries who received flu vaccines</th>
<th>Amount paid</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFS</td>
<td>9,919</td>
<td>$1,450,632.00</td>
</tr>
<tr>
<td>UHC</td>
<td>27,909</td>
<td>$3,880,669.00</td>
</tr>
<tr>
<td>Mag</td>
<td>33,750</td>
<td>$4,682,897.00</td>
</tr>
<tr>
<td>Mol</td>
<td>1,645</td>
<td>$214,326.00</td>
</tr>
<tr>
<td>Total</td>
<td>73,223</td>
<td>$10,228,524.00</td>
</tr>
</tbody>
</table>

Table 1: Influenza Vaccination Utilization in Mississippi Medicaid for Fiscal Year 2019 (July 2018 - June 2019)

Note: FFS = Fee-for-service, UHC = United Health Care, Mag = Magnolia, Mol = Molina
* Beneficiaries with medical or pharmacy claims were identified.
CPT codes for influenza vaccines included: 90630, 90685-90688, 90654-90658, 90660-90662, 90653, 90666, 90668, 90664, 90672-90674, 90756, 90682, 90686, 90682, Q2035.

References:

Table 2 displays number of anti-influenza prescriptions filled, beneficiaries treated and the amounts paid for each antiviral agent during SFY 2018 and SFY 2019.

- The 2018-2019 influenza season was not as severe as the prior season as evidenced by a decrease in number of prescriptions filled, beneficiaries treated, and amounts paid for anti-influenza treatments in SFY 2019.
- Utilization of branded Tamiflu® decreased substantially in SFY 2019 attributed to a shortage of generic oseltamivir in SFY 2018 which led to increased utilization of the branded product that year.
Table 3 displays anti-influenza drug utilization in Mississippi Medicaid for SFY 2019. The total number of unique beneficiaries receiving drugs is shown by health plan and number of prescription fills.

- Majority of beneficiaries receiving anti-influenza drugs received one prescription fill (n=61,842, 95.2%).
- Very few beneficiaries (n=189, 0.3%) received ≥3 prescription fills.
- 8,606 beneficiaries had documentation of receiving flu vaccination prior to filling a prescription for an antiviral.
Table 4 shows the number of beneficiaries who had a hospitalization after receiving anti-influenza drug treatment.

- Only 62 beneficiaries had a respiratory-related hospitalization within 14 days of receiving anti-influenza drugs.

Table 4: Hospitalizations Among Beneficiaries with Anti-influenza Drug Utilization in Mississippi Medicaid for State Fiscal Year 2019 (July 2018 - June 2019)

<table>
<thead>
<tr>
<th>Plan</th>
<th>Total number of beneficiaries with antiviral RX fills</th>
<th>Number of beneficiaries by the number of fills received</th>
<th>Number of beneficiaries who received flu vaccine prior to antiviral RX fill*</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFS</td>
<td>11,341</td>
<td>10,835 474 32</td>
<td>617</td>
</tr>
<tr>
<td>UHC</td>
<td>24,034</td>
<td>22,891 1,069 74</td>
<td>3,525</td>
</tr>
<tr>
<td>Mag</td>
<td>26,794</td>
<td>25,427 1,286 81</td>
<td>4,192</td>
</tr>
<tr>
<td>Mol</td>
<td>2,762</td>
<td>2,689 71 2</td>
<td>272</td>
</tr>
<tr>
<td>Total</td>
<td>64,931</td>
<td>61,842 2,900 189</td>
<td>8,606</td>
</tr>
</tbody>
</table>

Note: FFS = Fee-for-service, UHC = United Health Care, Mag = Magnolia, Mol = Molina
Numbers represent beneficiaries who had pharmacy claims only. No beneficiaries with anti-influenza drug related medical claims were identified in the study period.
* Beneficiaries with medical or pharmacy claims were identified. Beneficiaries receiving vaccines under the VFC Program are not included
CPT codes for influenza vaccines included: 90630, 90685-90688, 90654-90658, 90660-90662, 90653, 90666, 90668, 90664, 90672-90674, 90756, 90682, 90686, 90682, Q2035.

REFERENCES:

CONCLUSIONS AND RECOMMENDATIONS

This report for the DUR Board on influenza and treatment utilization trends in the four pharmacy programs is for information and discussion purposes only. No action is being sought at this time.