JLARC
JOINT LEGISLATIVE AUDIT AND REVIEW COMMISSION

December 9, 2024

Health Insurance Mandate Review: PANS/PANDAS HB513 (2024)

Health Insurance Reform Commission Briefing

Questions for JLARC stage 2 review

- Is there evidence that the proposed treatment is effective?
- How commonly used and available is the proposed treatment?
- How much does treatment cost for individuals without insurance coverage?

In Brief

HB 513 would require coverage of treatment for PANS/PANDAS, including medications, intravenous immunoglobulin therapy (IVIG), and plasma exchange.

PANS/PANDAS are thought to be neuropsychiatric conditions indirectly caused by strep or other infections.

Determining the prevalence of PANS/PANDAS is difficult because a specified diagnostic code has not existed until recently, and diagnostic criteria are not widely known.

Clinical evidence does not yet exist on the effectiveness of the more involved treatments for which HB 513 would require coverage, including IVIG and plasma exchange, although some providers have reported some success.

Some treatments, like IVIG and plasma exchange, have a high cost if not covered by insurance.

In this presentation

Background

Medical efficacy and use of PANS/PANDAS treatments

Financial impact on individuals without coverage

Coverage provided by HB 513

PANS/PANDAS are believed to be post-infection neuropsychiatric conditions

- Believed to be caused by inflammation in the brain after an infection
- Pediatric acute-onset neuropsychiatric syndrome (PANS)
  - Sudden onset of OCD and eating restriction symptoms, with at least two other co-existing conditions (e.g., anxiety, behavioral regression)
  - Not associated with any specific type of infection, can be viral (e.g., COVID-19, influenza) or bacterial (e.g., pneumonia)
- Pediatric acute-onset neuropsychiatric disorders associated with streptococcal infections (PANDAS)
  - Subset of PANS with sudden onset OCD and tic disorder and other co-existing conditions
  - Specifically associated with streptococcal infections

No medical consensus on diagnosis of PANS/PANDAS

- No diagnostic code exists for PANS/PANDAS in DSM; no diagnostic code existed in ICD-10* until recently
  - ICD-10 now specifies a code to be used for PANDAS as of October 2024; no code specified for PANS
- Difficult to differentiate between OCD and PANS/PANDAS because onset of conditions occurs at similar ages, and some research could not distinguish between the two conditions
- A defining marker has not been identified, but researchers and experts suspect it is a post-infectious autoimmune condition
- Clinical, exclusion-based diagnosis – physician will rule out other possible conditions before reaching a conclusion

DSM = Diagnostic Statistical Manual; ICD-10 = International Classification of Diseases, Tenth Revision

PANS/PANDAS currently diagnosed using clinical checklist

- Diagnostic inventory of seven items recommended for physicians by the PANDAS Physicians Network, NIH, and research literature
  - OCD, tic disorder symptoms, or both
  - Pediatric onset (ages 3 to puberty)
  - Episodic symptoms
  - Recent strep infection (PANDAS) or other infection (PANS)
  - Association with neurological abnormalities, abrupt onset, several co-existing symptoms (e.g., ADHD, separation anxiety, food restriction)

Sources: PANDAS Physicians Network. (2020). *Diagnostic flowchart and treatment guideline;* National Institute of Mental Health. (2019). *PANDAS—questions and answers*

Prato, A., Gulisano, M., Scerbo, M., Barone, R., Vicario, C. M., & Rizzo, R. (2021). Diagnostic Approach to Pediatric Autoimmune Neuropsychiatric Disorders Associated With Streptococcal Infections (PANDAS): A Narrative Review of Literature Data. *Frontiers in Pediatrics, 9*, 746639.

Less than 0.5% of children under 21 in Virginia are estimated to have PANS/PANDAS

- Prevalence rates are difficult to estimate because of lack of specific diagnostic code and vary based on source
  - 0.004–0.14 percent estimated prevalence in the general population using Virginia Medicaid enrollment data
  - Of children already exhibiting some symptoms, research literature estimates prevalence to be between 0.04 and 0.8 percent
- Based on these prevalence rates, less than 100 to approximately 2,500 children in Virginia are estimated to have PANS/PANDAS

Sources: 1) Percentage estimate of the number Medicaid enrollees under age 21 with a diagnosis of D89.9 or D89.89 out of the annual average Medicaid enrollment for FY22–24. 2) Aman et al., 2022; Franklin et al., 2023; Wald et al., 2023.

12 states passed legislation mandating coverage for PANS/PANDAS from 2017 to 2024

- All 12 require coverage for IVIG
  - Four (AR, CA, CO, OR) require a primary care physician and at least one specialist to declare medical necessity for IVIG approval
- Six states (CA, CO, IL, MD, OR, RI) require PANS/PANDAS to be coded as autoimmune encephalitis until AMA and CMS designate a code
- Three (CA, CO, MN) require coverage for the same treatments as HB 513, which includes plasma exchange
- Two (CA, CO) prevent carriers from requiring a trial of therapies to treat neuropsychiatric symptoms before immunomodulating therapies

NOTE: AMA = American Medical Association; CMS = Centers for Medicare & Medicaid Services

In this presentation

Background

Medical efficacy and use of PANS/PANDAS treatments

Financial impact on individuals without coverage

Coverage provided by HB 513

“First line” treatments are effective at treating symptoms in mild to moderate cases

- Treatments for PANS/PANDAS attempt to correct the immune system’s overreaction and reduce symptom severity
- Existing research suggests that most patients show improvements after a course of antibiotics (penicillin, azithromycin) and/or NSAIDs (Advil, Aleve)
- Behavioral therapy combined with a neuropsychiatric medication (e.g., SSRI) help reduce symptoms and help patients manage OCD, tic, and eating restriction symptoms
- Steroids believed to mitigate symptom flare-ups but have many side effects

Intravenous immunoglobulin therapy (IVIG) and plasma exchange used for severe cases

- **IVIG** – patient receives an infusion of immunoglobulin (antibodies) derived from the plasma of thousands of donors
- **Plasma exchange** – procedure that removes plasma and blood cells from the body, separates plasma from blood cells, and transfuses replacement plasma and blood cell fluid through a 'catheter port'
- PANDAS Physician Network and research literature recommend - IVIG only in severe cases that show no response to other treatments (e.g., antibiotics, therapy, steroids); plasma exchange only in cases when IVIG not effective
- Medical experts and NIH indicate that both procedures should be overseen and/or administered by specialists

Source: PANDAS Physicians Network, Diagnostic Flowchart and Treatment Guidelines, 2024

IVIG and plasma exchange lack sufficient clinical evidence of improved outcomes

- Neither treatment has sufficient clinical evidence from randomized controlled trials to show effectiveness for PANS/PANDAS
  - Research limited by small sample sizes, non-significant results, and not using 'gold standard' randomized clinical trial methods
- Some studies found short-term improvement in OCD symptoms with IVIG treatment, ranging from 45 to 85 percent of patients, but…
  - Symptom severity rebounded over time,
  - Multiple treatments required to maintain improvements, and
  - Studies did not include a control group, or did not follow up with control group at the same intervals as treatment
- One study found short-term improvement in OCD and tic symptoms with plasma exchange but did not recommend treatment because of invasiveness and side effects

Medical experts find IVIG and plasma exchange effective in some cases but approaches vary

- Experts report success in treating some patients with severe symptoms with IVIG or plasma exchange
- Experts' approach to IVIG administration differed in
  - Dosage
  - Treatment scheduling (e.g., number of initial treatments to administer before evaluating whether to continue)
- Experts' usage of plasma exchange differed because of
  - Risks and side effects from treatment
  - Insurance coverage (some experts found it easier for patients to obtain coverage for plasma exchange than IVIG)

Clinical trial of IVIG treatment is ongoing and could provide more information

- One multi-site clinical trial had an estimated completion date of October 22, 2024
  - Results can provide more information about the efficacy of IVIG for treatment of PANS/PANDAS
- No ongoing clinical trials evaluating the effectiveness of plasma exchange for PANS/PANDAS

Source: National Library of Medicine, ClinicalTrials.gov, "Phase III Study to Compare the Effect of Panzyga Versus Placebo in Patients with Pediatric Acute-onset Neuropsychiatric Syndrome (PANS/PANDAS)".

Access to physicians and more involved treatments are limited

- Some pediatricians refuse to diagnose PANS/PANDAS or see patients that ask about the condition
- Front line treatments like antibiotics and steroids can be prescribed by primary care pediatricians
- IVIG and plasma exchange typically prescribed by specialists, like immunologists, but not all specialists treat PANS/PANDAS

Small percentage of PANS/PANDAS patients estimated to receive IVIG and plasma exchange

- Approximately 3 percent of estimated PANS/PANDAS Medicaid patients received IVIG or plasma exchange, on average, each year from 2022–2024
  - 3 percent received IVIG
  - 1 percent received plasma exchange

SOURCE: Based on higher prevalence estimate using Medicaid data.

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Plasma exchange and IVIG are expensive out of pocket

- Plasma exchange can cost approximately $10,000 per course of treatment; patients typically receive one course of treatment over multiple days
- IVIG costs based on number of treatment courses
  - Experts indicated one course of treatment can range from $5,000 to $10,000 – costs vary based on factors such as setting (inpatient vs. outpatient), number of treatment days, and patient weight
  - Number of courses varies based on physician protocol and patient response - some physicians start with one course and assess patient response; others start with three courses and assess patient response
  - Maximum courses could be monthly up to a year or more

SOURCE: Estimates based on cost data provided by one medical facility (self-pay discounted costs) and Virginia Health Information.

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Coverage provided by HB 513

HB 513 would require coverage of the treatment of PANS/PANDAS

- Defines symptoms that would qualify as PANS and PANDAS
- Would require treatment for the prophylaxis, diagnosis, and treatment of PANS/PANDAS
- Required coverage would include antimicrobials, medication and behavioral therapies to manage neuropsychiatric symptoms, immunomodulating medicines, plasma exchange, and IVIG
- Would prevent trial-based, step approach to providing treatment with immunomodulating medicines
- Would require insurers to follow treatment guidelines developed by the PANS Research Consortium when considering coverage of immunomodulating medicines
- Would require coverage for out-of-state treatment if not available in the Commonwealth

Medicaid covers treatments for PANS/PANDAS

- Medicaid covers services for children under 21 that are “medically necessary,” including under Early and Periodic Screening, Diagnostic, and Treatment program
- Medical necessity determined by established clinical guidelines and whether treatment is likely to yield a positive outcome
- IVIG and plasma exchange may be covered if determined to be medically necessary

Source: Medicaid.gov, Early and Periodic Screening, Diagnostic, and Treatment policy.

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Appendix: Literature reviewed

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Appendix: Medical experts consulted

- VCU Health
- UVA Medical Center
- Virginia Chapter of the American Academy of Pediatrics