Deflux, Tissue Bulking Agent

December, 2023

Device

Deflux is a gel made from "tissue-friendly" non-animal stabilized hyaluronic acid (NASHA) and dextranomer (Dx).[1] It is contained in a single-use, sterilized syringe and is utilized for endoscopic injection around the ureteral opening to add tissue bulk. This assists in the prevention of the backflow of urine from the bladder into the ureters, known as vesicoureteral reflux (VUR).[1] Approximately 1% of children are diagnosed with VUR, which can promote recurrent pyelonephritis and lead to renal scarring.[2] Both components of Deflux are biodegradable and biocompatible with the NASHA being replaced by the body's own material over a "short period of time" while the dextranomer stays in place longer.[1,3]

Actions for Consideration

Partner: Identify physicians, nurses, pharmacy, operating room leader(s), and the appropriate clinical and non-clinical value analysis team members, and partner with them to understand product use and population specific need. Reimbursement specialists may be particularly helpful within this category as indications for use (IFU) may influence payors' decision for coverage.

Connect: Given the variety of tissue bulking products available, a careful review of all products utilized, indications for use, and any off-label usage is helpful. Collecting and reviewing physician data including utilization, cost, and waste will help inform management of these products. Reimbursement information should be attained as IFU and prior treatment may be considerations. Identify evidence related to specific products. Engage physician champion for peer to peer conversations.

Communicate: Share physician utilization and educate team about the product and develop a common goal. Robust data sharing will not only enhance discussions, but may lead to actionable conversations between peers.

HealthTrust Resources: Access the Clinical Knowledge Insights Library to find other relevant documents and toolkits with actionable information. Examples for this product include resources on value analysis and physician engagement.[4] Network on HealthTrust Huddle, our member community that shares ideas and seeks guidance from colleagues.[5]

Professional Society Statements and Clinical Practice Guidelines

The American Urological Association (AUA) published *Management and Screening of Primary Vesicoureteral Reflux in Children (2017)* which encompasses assessment, initial management, surgical options, and recommendations for follow up (including endoscopic injection therapy with bulking agents). Found here.[6]

FDA Approval

Deflux obtained FDA premarket approval (PMA Number P000029) in 2001 as "indicated for treatment of children with vesicoureteral reflux grades II-IV". Found here.[7]

Clinical Evidence

There are multiple studies on the management of VUR, including those specific to Dx/HA injections. A sample is provided below.

- A 2021 review by Kirsch et al. examined the properties of NASHA/Dx, best application practices, and available data related to clinical safety and efficacy. Ten studies were included for long term safety and efficacy with authors concluding that efficacy has been proven in multiple studies with no "significant" safety concerns, that "NASHA/Dx remains an effective and well-tolerated treatment for VUR", and that approach to management of VUR be individualized with multiple factors considered including the grade of the VUR. Medical writing support was funded by Palette Life Sciences.[3]
- A 2021 prospective study by Soria-Gondek et al. aimed to estimate the incidence of implant calcification after endoscopic injection of HA/Dx for treatment of VUR in children. Median follow up was 7.6 years with 355 ureters (227 patients) included. They concluded that the risk and incidence rate was "higher than expected" (8.5% and 12 per 1,000 ureter-year), age younger than 3.5 years at time of treatment raised risk, and that 3-5 years was the period of highest hazard of calcification. However, caution should be taken not to confuse ureter stones versus implant calcifications and "5-year follow-up would set a better understanding of the actual incidence and clinical significance of implant calcification."[8] Limitations included that cases were asymptomatic and histological reports from reimplantations were not reviewed, limiting conclusions about clinical significance, the amount of HA/Dx implanted was not included in analysis, and the risk model utilized for implant calcification based on age at first injection had a moderate adequacy (65%).[8]
- A 2020 long term observational study by Stenback et al. included 185 patients (237 ureters) with grade IV VUR treated with NASHA/Dx over a ten-year period (with follow up ranging 8-25 years) evaluating the incidence of urinary tract infections (UTI), bladder dysfunction, late recurrence of VUR, and subsequent ureteral reimplantation. They reported 21% UTI, 34% bladder "problems", 30% VUR after treatment (7% grade II and 23% $\geq$ III), 75% avoidance of reimplantation with 97% of patients having "no safety issues during 15–25 years of follow-up." They concluded that UTI rates and later ureteral reimplantation were low (with changes in clinical practice lowering rate in the latter 5 years of the study), and that NASHA/Dx "can be used with confidence" in the treatment of patients with grade IV VUR. This study was partially funded by Palette Life Sciences and one author is a medical adviser and speaker for Palette AB, Sweden.[9]

Summary

There are numerous tissue bulking agents marketed for a variety of indications. The type of bulking agent and techniques utilized vary by physician, and there may be physician preference of one type of product over another. Careful review and understanding of physician interest and outcomes will help determine direction. Engaging physicians in decision making and identifying and leveraging physician champions will help to maintain collaboration over time.

References

1. Recurrent UTIs Are a Sign of VUR – Deflux Treatment Can Help. Deflux. Accessed December 27, 2023. https://www.deflux.com/recurrent-uti-treatment/
2. Cerwinka WH, Scherz HC, Kirsch AJ. Endoscopic Treatment of Vesicoureteral Reflux with Dextranomer/Hyaluronic Acid in Children. Advances in Urology. 2008;2008:1-7. doi:https://doi.org/10.1155/2008/513854
3. Kirsch AJ, Cooper CS, Läckgren G. Non-Animal Stabilized Hyaluronic Acid/Dextranomer Gel (NASHA/Dx, Deflux) for Endoscopic Treatment of Vesicoureteral Reflux: What Have We Learned Over the Last 20 Years? Urology. 2021;157:15-28. doi:https://doi.org/10.1016/j.urology.2021.07.032
4. Healthtrust Purchasing Group. Clinical Knowledge Insights. Updated 2023. Accessed September 13, 2023. http://www.hpginsights.com/
5. HealthTrust Purchasing Group. HealthTrust Huddle. Updated 2023. Accessed September 13, 2023. https://huddle.healthtrustpg.com/forum/
6. Vesicoureteral Reflux Guideline - American Urological Association. www.auanet.org. https://www.auanet.org/guidelines-and-quality/guidelines/vesicoureteral-reflux-guideline
7. Premarket Approval (PMA). www.accessdata.fda.gov. Accessed January 25, 2024. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P000029
8. Soria-Gondek A, Martín-Solé O, Pérez-Bertólez S, Martín-Lluís A, Tarrado-Castellarnau X, García-Aparicio L. Incidence and risk factors for calcification after dextranomer/hyaluronic acid (Dx/HA) copolymer injection for vesicoureteral reflux. Journal of Pediatric Urology. 2021;17(3):401.e1-401.e9. doi:https://doi.org/10.1016/j.jpurol.2021.02.005
9. Stenbäck A, Olafsdottir T, Sköldenberg E, Barker G, Stenberg A, Läckgren G. Proprietary non-animal stabilized hyaluronic acid/dextranomer gel (NASHA/Dx) for endoscopic treatment of grade IV vesicoureteral reflux: Long-term observational study. J Pediatr Urol. 2020;16(3):328.e1-328.e9. doi:10.1016/j.jpurol.2020.04.008