Dear Members:

Last month, we shared a message regarding Merck's anticipated TICE BCG supply constraints due to an increasing global demand for the product.

To minimize disruption to patient care, Merck (the sole supplier of BCG to the United States) announced an immediate change to their TICE BCG distribution model, and in January, ceased all drop shipments and began allocating TICE BCG exclusively to wholesalers and distributors based on product supply and historical purchasing patterns. Wholesalers and distributors in turn, began utilizing the same allocation model to fulfill customer orders directly; therefore, please contact your wholesaler should you have any questions about your allotment.

Although Merck is exploring options to increase their production of TICE BCG, they expect this global supply constraint to continue throughout 2019.

The American Urological Association (AUA), American Association of Clinical Urologists (AACU), Bladder Cancer Advocacy Network (BCAN), Society of Urologic Oncology (SUO), the Large Urology Group Practice Association (LUGPA) and the Urology Care Foundation (UCF) remain extremely concerned about this shortage and its effects on the care of bladder cancer patients. Efforts to engage the U.S. Food and Drug Administration to approve additional strains and supplies of BCG are ongoing and all organizations noted above continue to communicate with Merck for the most up-to-date information on this issue.

Until the shortage has been resolved, the following strategies may help maximize the care for patients with Non-Muscle Invasive Bladder Cancer (NMIBC), subject, as always, to physician judgment in individual cases:

1. BCG should not be used for patients with low-risk disease.

2. Intravesical chemotherapy should be used as the first-line option for patients with intermediate-risk NMIBC. Patients with recurrent/multifocal low-grade Ta lesions who require intravesical therapy should receive intravesical chemotherapy such as mitomycin, gemcitabine, epirubicin or docetaxel instead of BCG.

3. If BCG would be administered as second-line therapy for patients with intermediate-risk NMIBC, an alternative intravesical chemotherapy should be used rather than BCG in the setting of this BCG shortage.

4. For patients with high-risk NMIBC, high-grade T1 and CIS patients receiving induction therapy, they should be prioritized for use of full-strength BCG. If not available, these patients and other high-risk patients should be given a reduced 1/2 to 1/3 dose, if feasible.

5. If supply exists for maintenance therapy for patients with NMIBC, every attempt should be made to use 1/3 dose BCG and limit dose to one year.

6. In the event of BCG supply shortage, maintenance therapy should not be given and BCG-naïve patients with high-risk disease should be prioritized for induction BCG.

7. If BCG is not available, a preferable alternative to BCG is mitomycin (induction and monthly maintenance up to one year). Other options such as gemcitabine, epirubicin, docetaxel, valrubicin or sequential gemcitabine/docetaxel or gemcitabine/mitomycin may also be considered with an induction and possible maintenance regimen.

8. Patients with high-risk features (i.e., high-grade T1 with additional risk factors such as concomitant carcinoma in situ, lymphovascular invasion, prostatic urethral involvement or variant histology) who are not willing to take any potential oncologic risks with alternative intravesical agents, should be offered initial radical cystectomy, if they are surgical candidates.

ADDITIONAL NOTES:

If 1/2 to 1/3 dose BCG is used, every attempt should be made to treat multiple patients on the same day, while being consistent with product labeling, to avoid drug wastage. It is recommended

practitioners communicate with their pharmacy to ensure that if split dosing is used, it is done with appropriate safety precautions.

As always, it is important these decisions be made after an informed discussion with the individual patient regarding their treatment options in the context of the ongoing BCG shortage.

Note: It is recognized there are legitimate concerns around split-vial dosing of BCG. It is unknown at this time whether it is acceptable to bill for more than one patient per vial of BCG. The AUA has been in contact with the Centers for Medicare & Medicaid Services (CMS) and is awaiting billing guidance for practices implementing split-vial dosing, if allowed in the Medicare program. At this time, the AUA suggests confirmation with any insurance company prior to splitting vials.

Every effort should be made to enroll patients in clinical trials to offer an appropriate alternative management strategy where this is feasible.

Review the official AUA/SUO Risk Stratification Table for NMIBC.

We will continue to update you as we receive additional information.

Sincerely,

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