BAMLANIVIMAB

ALTERNATIVE PREPARATION AND ADMINISTRATION INFORMATION

The **Bamlanivimab Fact Sheet for Health Care Providers** describes how bamlanivimab should be prepared and administered. Lilly provides the following additional information and/or guidance to enable Health Care Providers to make informed decisions. This information and/or guidance has not necessarily been assessed in the bamlanivimab clinical studies.

ONLY USE NORMAL SALINE FOR INFUSION OF BAMLANIVIMAB

- Dilute bamlanivimab with 0.9% Sodium Chloride Injection (Normal Saline) only.
- Once bamlanivimab is added to normal saline, gently mix the infusion bag (invert approximately 10 times) to ensure homogeneity.

DO NOT USE DEXTROSE FOR INFUSION OF BAMLANIVIMAB

- Only use 0.9% Sodium Chloride Injection (Normal Saline) to dilute bamlanivimab
- Do not use Dextrose. bamlanivimab is incompatible with dextrose.

SIZE OF INFUSION BAG

- A 250 mL bag with 0.9% Sodium Chloride Injection (Normal Saline) is preferred as this size bag was used in the BLAZE-1 trial.
- If a 250 mL Normal Saline bag size is not available, you can use any infusion bag with at least 50 mL to no more than 250 mL of Normal Saline. Inject 20 mL of bamlanivimab from the vial to the infusion bag and adjust infusion rate so that the entire volume is administered over 60 minutes.

ADDING BAMLANIVIMAB TO INFUSION BAG WITHOUT WITHDRAWING NORMAL SALINE FIRST

- 20 mL Bamlanivimab may be added directly to a 0.9% Sodium Chloride Injection (Normal Saline) bag ranging in volume from at least 50 mL to no more than 250 mL without first withdrawing and discarding solution from bag.
- Regardless of the size bag being used the final solution for infusion must be administered over 60 minutes

THE USE OF A 0.2/0.22-MICRON LOW PROTEIN BINDING IN-LINE FILTER

Bamlanivimab contains no preservative. As a precautionary measure 0.2/0.22-micron polyethersulfone (PES) protein sparing filters were used during the clinical studies of bamlanivimab. The resulting data were submitted to the FDA in support of the Emergency Use Authorization.

The 0.2-micron and/or 0.22-micron PES filter has the potential to remove particulates and microorganisms that may have been inadvertently introduced during the aseptic preparation of the final solution for infusion.

The use of a low protein binding in-line filter such as a PES filter to administer the prepared bamlanivimab infusion solution is recommended but not required. The use of a filter may be eliminated if health care providers choose to do so, and proper aseptic technique is used to prepare the dosing solution for infusion.

WHAT BRAND OF 0.2/0.22-MICRON POLYETHER SULFONE (PES) FILTER TO USE

Any brand of 0.2 and/or 0.22-micron polyethersulfone (PES) protein sparing filter may be used. Lilly has not performed studies with bamlanivimab using any other type of filter. Protein sparing filters have membranes which have low protein and low drug binding characteristics. Low protein binding characteristic provide minimal adsorption and a very low extractable content.

MUST INFUSION BAG OVERFILL BE TAKEN INTO CONSIDERATION WHEN PREPARING THE DOSING SOLUTION?

It is not necessary to take into consideration any potential overfill added to the infusion bag during manufacturing. Dose preparation must be done using the Normal Saline content as claimed on the label of the infusion bag with entire bag contents administered to patients. During the clinical studies the target volume for infusion was calculated using the content volume as stated on the label of the 0.9% Sodium Chloride Injection (Normal Saline) injection bag.

IS THE BAMLANIVIMAB VIAL COMPATIBLE WITH CLOSED-SYSTEM TRANSFER DEVICES?

During Clinical Trials, only syringes/needles were used for the transfer of bamlanivimab. Lilly has not performed compatibility studies with bamlanivimab and closed-system vial-transfer devices (CSTD's).

Before using a CSTD the following must be considered:

- Bamlanivimab is a monoclonal antibody and not considered to be hazardous.
- Bamlanivimab vials contain an excess of solution. The excess solution is added to accommodate for vial retention and to allow for the removal of at least the volume claimed on the label.
- Only the volume representing the required dose should be removed from the vial to prepare the solution for infusion.

ADMINISTERING BAMLANIVIMAB WITH OTHER DRUGS

Unless directed otherwise in the Fact Sheet for Health Care Providers, bamlanivimab should not be mixed or co-administered with other medications using the same infusion line.

It is acceptable to use a single/same IV line to administer bamlanivimab either before, or after, another medication if the infusion line used is properly flushed with Normal Saline prior to administering bamlanivimab through the same line.

ELASTOMERIC PUMPS

Lilly has not performed studies with elastomeric pump and have no specific data to support this practice; however, Lilly does not believe that using an elastomeric pump would pose any problem as longs as compatible materials are used for IV administration and the directive for infusion preparation and rate of administration is followed (Please refer to the Fact Sheet for Health Care Providers Emergency Use Authorization (EUA) of bamlanivimab). Lilly has not seen incompatibilities with Lilly monoclonal antibodies and readily available infusion sets available on the market to date, so we do not foresee a compatibility problem.

LATEX

Bamlanivimab vials contains no latex. No latex containing products have been tested or used with bamlanivimab. Latex has been avoided due to latex allergies/ hypersensitivities.

NYLON

Lilly has not performed compatibility studies with Nylon.

NEEDLE TYPES

Lilly recommends the use of sterile stainless-steel needles. Please note that large bore needles can core the stopper of the vial and cause particles to be introduced into the vial.

COMPATIBLE ADMINISTRATION MATERIALS AND INFUSION KITS

During the bamlanivimab clinical studies, Lilly used Polypropylene syringes, Stainless steel needles, Polyethylene line, Polyolefin, Polyvinylchloride (PVC) IV bags with or without DEHP and Polyvinylchloride (PVC) infusion sets with or without DEHP containing an in-line polyethersulfone (PES).

Individual infusion sites of care should follow best medical practices when determining materials to use. Procurement of materials from a specific vendor or vendors is not required.

INCOMPATIBLE MATERIALS AND INFUSION KITS

Bamlanivimab has no known incompatibilities with conventional medical supplies and equipment. Lilly has not performed specific compatibility studies with bamlanivimab to support the use of the various types of IV Bags and infusion sets available on the market globally. If alternate materials are used, the composition of these materials should be confirmed with that vendor.

ALTERNATIVE ADMINISTRATION MATERIALS AND INFUSION KITS

There are currently no known incompatibilities with the materials used to construct the commonly available infusion sets on the market (such as PVC, ethylene vinyl acetate, glass, polyolefin, polypropylene, and polyethylene). There are no restrictions in the label (prescribing information) on what type of IV Bags and infusion sets may be used.

Lilly has not performed specific compatibility studies that supports all types of IV Bags and infusion sets available on the market globally. Lilly has only evaluated materials used to construct infusion sets generally available on the market**.** Any available FDA approved brand of the listed materials may be used.

The following materials and Infusion kits were used during the clinical studies of other Lilly marketed monoclonal antibody containing products with formulations like bamlanivimab and found to be compatible:

CONTAINERS:

- Polyolefin infusion containers,
- Polyvinyl chloride (PVC) infusion containers,
- Ethylene vinyl acetate (EVA) infusion containers,
- Evacuated glass (USP Type II or local equivalent) infusion containers,
- Normal Saline- 0.9% Sodium Chloride Injection USP, packaged in VIAFLEX plastic solution container.

INFUSION BAGS:

- Polyolefin infusion bags,
- Polyvinylchloride infusion bags with 0.9% sodium chloride injection.

INFUSION SETS:

- Polyethylene-lined PVC infusion sets with a 0.22-µm downstream high-pressure, protein-sparing in-line filter made of polyethersulfone,
- PVC (with di(2-ethylhexyl) phthalate [DEHP]) infusion sets coupled to a 0.2-µm protein-sparing filter made of polyethersulfone,
- Polyethylene-lined PVC infusion sets with a 0.2-µm protein-sparing in-line filter made of polyethersulfone,
- Polyurethane infusion sets with a 0.2-µm protein-sparing in-line filter made of polyethersulfone,
- Polybutadiene tubing with a 0.2-µm protein-sparing in-line filter made of polyethersulfone.

Individual infusion sites of care should follow best medical practices when determining materials to use. Procurement of materials from a specific vendor or vendors is not required.

HANDLING AND STORAGE

HAZARD CLASSIFICATION

Bamlanivimab is not known to be a "Hazardous Chemical" as defined by the OSHA Hazard Communication Standard, 29 CFR 1910.1200**.**

SAFETY

Bamlanivimab is a monoclonal antibody and not classified according to criteria of the Hazard Communication Standard, 29 CFR 1910.1200. **It is neither hazardous nor toxic when spilled**. Based on the biophysical properties and absorption characteristics of monoclonal antibodies, oral and dermal routes of exposure are not considered occupationally relevant and potential bioavailability through inhalation is minimal.

VIAL BREAKAGE - CLEAN-UP OF SPILLAGE

Bamlanivimab is not toxic or hazardous. Use absorbent/adsorbent material to solidify liquids. Clean up promptly by sweeping or vacuum. Wear appropriate protective equipment and clothing during clean-up. Beware of broken glass**.**

VIAL TIME OUTSIDE REFRIGERATION WHEN PREPARING FOR ADMINISTRATION

When preparing bamlanivimab for administration, the time that the vial is outside refrigeration and exposed to light should be kept **to less than 8 hours**. The 8-hour time limit applies to the solution in an intact/unopened vial before the solution for infusion is prepared. Exposure to ambient light is acceptable while preparation and administration is taking place. Avoid temperatures above room temperature i.e. 25°C (77°F).

IMPACT OF LIGHT ON THE SOLUTION FOR INFUSION

The exposure of the bamlanivimab solution for infusion to conditions of "normal" room light is not of concern when the solution for infusion is used and stored as directed on the label and in the bamlanivimab Fact Sheet for Health. If refrigerated, allow the diluted solution to come to room temperature prior to administration.

IMPACT OF SHAKING, TRANSPORT ON THE SOLUTION FOR INFUSION

Limited shaking through normal transport of the vials and prepared infusion for solution will not impact bamlanivimab. Bamlanivimab is formulated to provide protection from mechanical stress such as experienced during normal handling and transport of the vials and prepared infusion bag.

This includes pneumatic transport in hospitals. Proteins, in general, are sensitive to mechanical stress such as vigorous shaking. Vigorous shaking can cause bubbles to form and the proteins to become damaged (denature). Avoid vigorous shaking of the solution for infusion and follow the recommended handling and storage during transportation**.**

STORAGE AND STABILITY OF THE SOLUTION FOR INFUSION

The formulation of bamlanivimab contains no preservative. Once the stopper of the vial is punctured the vial is in-use and the solution for infusion must be prepared.

The following "*in-use*" storage time allowances must be calculated from the time the vial is removed from initial puncturing of stopper of the vial to prepare the solution for infusion up to, and including, the time to administer the solution for infusion.

- **24 hours when refrigerated** at 2 to 8°C (36 to 46°F), or
- **7 hours outside refrigeration** if stored up to 25°C (77°F).

Why only 7 Hours at 25°C (77°F)?

The bamlanivimab formulation contains no preservative. Once the stopper of the vial is punctured, the vial is "in-use". When the vial is in-use, the solution for infusion must be prepared within the time allotted for the preparation, storage, and subsequent administration of the solution for infusion, i.e. Storage times include the transportation and duration and of infusion. If refrigerated, allow the diluted solution to come to room temperature prior to administration**.**