SYNAGIS®
(Palivizumab)

1. NAME OF MEDICIAL PRODUCT

SYNAGIS 50 mg/0.5 mL solution for injection
SYNAGIS 100 mg/1 mL solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

SYNAGIS 50 mg/0.5 mL solution for injection: each 0.5 mL vial contains 50 mg of palivizumab.

SYNAGIS 100 mg/1 mL solution for injection: each 1 mL vial contains 100 mg of palivizumab.

Palivizumab contains the following excipients: 25 mM histidine and 1.6 mM glycine and the active ingredient, palivizumab, at a concentration of100 milligrams per mL.

For the full list of excipients, see Section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

Solution for injection.
The solution is clear or slightly opalescent.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

SYNAGIS is indicated for the prevention of serious lower respiratory tract disease caused byrespiratory syncytial virus (RSV) in pediatric patients at high risk of RSV disease.

Safety and efficacy were established in:

- Children born at 35 weeks of gestation or less and less than 6 months of age at the onset of the RSVseason
- Children less than 2 years of age and requiring treatment for bronchopulmonary dysplasia (BPD) withinthe last 6 months
- Children less than 2 years of age and with haemodynamically significant congenital heart disease (CHD)

4.2 Posology and method of administration

Posology

The recommended dose of SYNAGIS is 15 mg/kg of body weight, given once a month during anticipated periods of RSV risk in the community.

The first dose should be administered prior to commencement of the RSV season and subsequent doses should be administered monthly throughout theRSV season.

To avoid risk of reinfection, it is recommended that children receiving SYNAGIS who become infected with RSV continue to receive monthly doses of SYNAGIS for the duration of the RSV season.

The efficacy of SYNAGIS at doses less than 15mg/kg, or of dosing less frequently than monthly throughoutthe RSV season has not been established.

For children undergoing cardiac bypass, it is recommended that a 15 mg/kg of body weight injection of palivizumab be administered as soon as stable after surgery to ensure adequate palivizumab serum levels.

Method of administration

Palivizumab is to be administered by intramuscular injection only.

SYNAGIS is administered in a dose of 15 mg/kg once a month intramuscularly, preferably inthe anterolateral aspect of the thigh. The gluteal muscle should not be used routinely as an injection site because of the risk of damage to the sciatic nerve. The injection should be given using standard aseptic technique. The dose per month = patient weight (kg) x 15 mg/kg ÷ 100 mg/ml of SYNAGIS. Injection volumes over 1 mL should be given as a divided dose.

For instructions for use, handling, and disposal of the medicinal product, see Section 6.6 Instructions for use, handling, and disposal.

4.3 Contraindications

SYNAGIS is contraindicated in patients with known hypersensitivity to palivizumab or to any of its excipients. It is also contraindicated in patients with known hypersensitivity to other humanized monoclonal antibodies.

4.4 Special warnings and special precautions for use

Allergic reactions including very rare anaphylaxis and anaphylactic shock have been reported following palivizumab administration. In some cases, fatalities have been reported (see Section 4.8 Undesirable effects).

Medications for the treatment of severe hypersensitivity reactions, including anaphylaxis and anaphylactic shock should be available for immediate use following administration of palivizumab. If a severe hypersensitivity reaction occurs, therapy with palivizumab should be discontinued. As with other agents administered to this population, if milder hypersensitivity reactions occur, caution should be used on re-administration of palivizumab.

As with any intramuscular injection, SYNAGIS should be given with caution to patients withthrombocytopenia or any coagulation disorder.

The single-use vial of SYNAGIS does not contain a preservative. Injections should be given within six hours after reconstitution.

A moderate to severe acute infection or febrile illness may warrant delaying the use of SYNAGIS, unless, in the opinion of the physician, withholding SYNAGIS entails a greater risk. A mild febrile illness, such as a mild upper respiratory infection, is not usually reason to defer administration of SYNAGIS.

4.5 Interaction with other medicinal products and other forms of interaction

No formal drug-drug interaction studies were conducted; however, no interactions have been described to date. In the phase III IMpact-RSV study, the proportions of patients in the placebo and SYNAGIS groups who received routine childhood vaccines, influenza vaccine, bronchodilators or corticosteroids were similar and no incremental increase in adverse reactions was observed among patientsreceiving these agents, in either of the two groups.

Since the monoclonal antibody is specific for RSV, SYNAGIS is not expected to interfere withthe immune response to vaccines, including live viral vaccines.

Drug/Laboratory Test Interaction

Palivizumab may interfere with immune-based RSV diagnostic tests, such as some antigen detection-basedassays. In addition, palivizumab inhibits virus replication in cell culture and therefore may also interfere with viral culture assays. Palivizumab does not interfere with reverse transcriptase polymerase chain reaction- based assays. Assay interference could lead to false-negative RSV diagnostic test results. Therefore, diagnostic test results, when obtained, should be used in conjunction with clinical findings to guide medical decisions.

4.6 Pregnancy and lactation

SYNAGIS is not indicated for adult usage and animal reproduction studies have not been conducted. It is also not known whether palivizumab can cause fetal harm when administered to a pregnantwoman or could affect reproductive capacity.

4.7 Effect on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Adverse events at least possibly causally related to palivizumab (ADRs) are displayed by system organ class and frequency (very common; ≥1/10; common: ≥1/100 to <1/10; uncommon: ≥ 1/1000 to < 1/100; rare: ≥1/10000 to <1/1000) in studies conducted in premature and bronchopulmonary dysplasia patients and pediatric congenital heart disease patients (Table 1).

Adverse drug reactions (ADRs) reported in the prophylactic pediatric studies were similar in the placebo and palivizumab groups. The majority of ADRs were transient and mild to moderate in severity.

IMpact-RSV Study

In the study of premature infants and children with bronchopulmonary dysplasia, no medically important differences in ADRs by body system or in subgroups of children categorized by gender, age, gestational age, country, race/ethnicity or quartile serum palivizumab concentration were observed. No significant difference in safety profile was observed between children without active RSV infection and those hospitalized for RSV. Permanent discontinuation of palivizumab because of ADRs was rare (0.2%). Deaths were balanced between the placebo and palivizumab treatment groups and were not drug related.

CHD Study

In the congenital heart disease study, no medically important differences were observed in ADRs by body system or when evaluated in subgroups of children by cardiac category (cyanotic versus acyanotic). The incidence of serious adverse events was significantly lower in the palivizumab group, as compared to the placebo group. No serious adverse events related to palivizumab were reported. The incidences of cardiac surgeries classified as planned, earlier than planned, or urgent, were balanced between the groups. Deaths associated with RSV infection occurred in 2 patients in the palivizumab group and 4 patients in the placebo group were not drug related.

Table 1: Summary of Adverse Drug Reactions in Prophylactic Clinical Studies with Premature and Bronchopulmonary Dysplasia or Congenital Heart Disease Pediatric Populations (IMpact-RSV and CHD Studies)*

MedDRA System Organ Class	Frequency	ADR
Skin and subcutaneous tissue disorders	Very common	Rash
General disorders and Administrative site conditions	Very common	Pyrexia
	Common	Injection site reaction

*For full study description, see Section 5.1 Pharmacodynamic properties.

Liquid Formulation Studies

Two clinical studies were conducted to directly compare liquid and lyophilized formulations of palivizumab. In the first study, all 153 premature infants received both formulations in different sequences. In the second study, 211 and 202 premature infants or children with chronic lung disease received liquid and lyophilized palivizumab, respectively. In two additional studies, liquid palivizumab was used as an active control (3918 pediatric subjects) to evaluate an investigational monoclonal antibody for prophylaxis of serious RSV disease in premature infants or children with BPD or hemodynamically significant CHD. The overall rate and pattern of adverse events, study drug discontinuation due to AEs, and the number of deaths reported in these clinical studies were consistent with those observed during the clinical development programs for the lyophilized formulation. No deaths were considered related to palivizumab and no new ADRs were identified in these studies.

Immunogenicity

In the IMpact-RSV trial, the incidence of anti-palivizumab antibody following the fourth

injection was 1.1% in the placebo group and 0.7% in the palivizumab group. In pediatric patients receiving palivizumab for a second season, one of the fifty-six patients had transient, low titer reactivity. This reactivity was not associated with adverse events or alteration in palivizumab serum concentrations. Immunogenicity was not assessed in the CHD Study.

Antibody to palivizumab was also evaluated in four additional studies in 4337 palivizumab-treated patients (children born at 35 weeks of gestation or less and 6 months of age or less, or < 24 months of age with bronchopulmonary dysplasia or with haemodynamically significant congenital heart disease were included in these studies) and was observed in 0%-1.5% of patients at different study time points. There was no association observed between the presence of antibody and adverse events. Therefore, anti-drug antibody (ADA) responses appear to be of no clinical relevance.

In the Extended Dose Study, transient, low levels of anti-palivizumab antibody were observed in one child after the second dose of palivizumab that dropped to undetectable levels at the fifth and seventh dose.

Post-marketing Experience

The following adverse reactions have been reported with palivizumab therapy. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to palivizumab exposure (see Section 4.4 Special warnings and special precautions for use).

Blood and lymphatic system disorders

Thrombocytopenia

Immune system disorders

Anaphylaxis, anaphylactic shock (in some cases, fatalities have been reported)

Nervous systems disorders

Convulsion

Skin and subcutaneous disorders

Urticaria

Palivizumab treatment schedule and adverse events were monitored in a group of nearly 20,000 infants tracked through a patient compliance registry, the REACH program. Of this group, 1250 enrolled infants received 6 injections, 183 infants received 7 injections, and 27 infants received either 8 or 9 injections, each respectively. Adverse events observed in patients following a sixth or greater dose from this registry as well as through routine post marketing surveillance were similar in character and frequency to those after the initial 5 doses.

4.9 Overdose

In clinical studies, three children received an overdose of more than 15 mg/kg. These doses were 20.25 mg/kg, 21.1 mg/kg and 22.27 mg/kg. No medical consequences were identified

in these instances.

From the post-marketing experience, overdoses with doses up to 85 mg/kg have been reported and, in some cases, adverse reactions were reported which did not differ from those observed with 15 mg/kg dose (see Section 4.8 Undesirable effects). In case of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions or effects and appropriate symptomatic treatment instituted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Description

Palivizumab is a humanized IgG1 monoclonal antibody directed to an epitope in the A antigenic site of the fusion protein of respiratory syncytial virus (RSV) and is produced by DNA technology in mouse myeloma host cells.

This humanized monoclonal antibody is composed of 95% human and 5% murine amino acid sequences. Palivizumab is composed of two heavy chains and two light chains having a molecular weight of approximately 148,000 Daltons.

Mechanism of Action

SYNAGIS exhibits neutralizing and fusion-inhibitory activity against RSV. These activities inhibit RSV replication in laboratory experiments. Although resistant RSV strains may be isolated in laboratory studies, a panel of clinical RSV isolates were all neutralized by SYNAGIS. SYNAGIS serum concentrations of approximately 30 mcg/mL have been shown to produce a mean 99% reduction in pulmonary RSV replication in the cotton rat model.

The *in vivo* neutralizing activity of the active ingredient in SYNAGIS was assessed in a randomized, placebo-controlled study of 35 pediatric patients tracheally intubated because of RSV disease. In these patients, SYNAGIS significantly reduced the quantity of RSV in the lower respiratory tract compared to control patients.

Microbiology

Antiviral Activity

The antiviral activity of palivizumab was assessed in a microneutralization assay in which increasing concentrations of antibody were incubated with RSV prior to addition of the human epithelial cells HEp-2. After incubation for 4-5 days, RSV antigen was measured in an enzyme-linked immunosorbent assay (ELISA). The neutralization titer (50% effective concentration [EC_{50}]) is expressed as the antibody concentration required to reduce detection of RSV antigen by 50% compared with untreated virus- infected cells. Palivizumab exhibited median EC_{50} values of 0.65 mcg per mL (mean [standard deviation] = 0.75 [0.53] mcg per mL; n=69, range 0.07-2.89 mcg per mL and 0.28 mcg per mL (mean [standard deviation] = 0.35 [0.23] mcg per mL; n=35, range 0.03-0.88 mcg per mL) against clinical RSV A and RSV B isolates, respectively. The majority of clinical RSV isolates

tested (n=96) were collected from subjects in the United States with the remainder from Japan (n=1), Australia (n=5) and Israel (n=2). These isolates encoded the most common RSV F sequence polymorphisms found among clinical isolates worldwide.

Resistance

Palivizumab binds a highly conserved region on the extracellular domain of mature RSV F protein, referred to as antigenic site II or A antigenic site, which encompasses amino acids 262 to 275. All RSV mutants that exhibit resistance to palivizumab have been shown to contain amino acid changes in this region on the F protein. No known polymorphic or non-polymorphic sequence variations outside of the A antigenic site on RSV F protein have been demonstrated to render RSV resistant to neutralization by palivizumab. At least one of the palivizumab resistance-associated substitutions, N262D, K272E/Q, or S275F/L was identified in 8 of 126 clinical RSV isolates from subjects who failed immunoprophylaxis, resulting in a combined resistance- associated mutation frequency of 6.3%. A review of clinical findings revealed no association between A antigenic site sequence changes and RSV disease severity among children receiving palivizumab immunoprophylaxis who develop RSV lower respiratory tract disease. Analysis of 254 clinical RSV isolates collected from immunoprophylaxis-naïve subjects revealed palivizumab resistance-associated substitutions in 2 (1 with N262D and 1 with S275F), resulting in a resistance-associated mutation frequency of 0.79%.

Efficacy

In a placebo-controlled trial of RSV disease prophylaxis in 1502 high-risk children (1002 palivizumab; 500 placebo), 5 monthly doses of 15mg/kg reduced the incidence of RSV related hospitalization by 55% ($p<0.001$).

Clinical Studies

The safety and efficacy of palivizumab were assessed in clinical trials of prophylaxis for serious RSV disease among children with premature birth and children with bronchopulmonary dysplasia or, hemodynamically significant congenital heart disease.

IMpact-RSV Trial

The trial, conducted at 139 centers in the United States, Canada and the United Kingdom, studied patients ≤ 24 months of age with bronchopulmonary dysplasia (BPD) and patients with premature birth (≤ 35 weeks gestation) who were ≤ 6 months of age at study entry. Patients with uncorrected congenital heart disease were excluded from enrollment. In this trial, 500 patients were randomized to receive five monthly placebo injections and 1,002 patients were randomized to receive five monthly injections of 15mg/kg of lyophilized palivizumab. Subjects were randomized into the study and were followed for safety and efficacy for 150 days. Ninety-nine percent of all subjects completed the study and 93% received all five injections. The primary endpoint was the incidence of RSV hospitalization.

The RSV hospitalisation rate was 10.6% in the placebo group. On this basis, the absolute risk reduction (ARR) is 5.8% which means the number needed to treat (NNT) is 17 to prevent one hospitalisation. The severity of RSV disease in children hospitalised despite prophylaxis with palivizumab in terms of days in ICU stay per 100 children and days of mechanical ventilation per 100 children was not affected.There was also a statistically

significant reduction in RSV hospitalization for the subgroups of children with BPD (38.5% relative reduction, p=0.038) and those with prematurity (78.1% relative reduction for children with gestation ≤ 35 weeks, p<0.001 and 54% relative reduction for children with gestation ≤ 32 weeks, p<0.05). The smallest relative risk reductions and therefore the least benefit occurred in children with the most severe BPD – those requiring ongoing oxygen (94% relative risk) or oxygen in the last 6 months (70% relative risk). Children receiving ongoing steroids who were treated with palivizumab had a higher rate of hospitalization for RSV infection than did those receiving ongoing steroids who were not treated with palivizumab (relative risk 139%). No statistical significance levels are available for the BPD subgroups.

A total of 222 children from the IMpact-RSV Trial were enrolled in two separate studies to examine the safety of palivizumab when it is administered for a second RSV season. One hundred and three (103) children received monthly palivizumab injections for the first time, and 119 children received palivizumab for two consecutive seasons. No difference between groups regarding immunogenicity was observed in either study. However, as the efficacy of palivizumab when administered to patients as a second course of treatment during an ensuing RSV season has not been formally investigated in a study performed with this objective, the relevance of these data in terms of efficacy is unknown.

Pre-term Infants and Children with Chronic Lung Disease of Prematurity (CLDP)

This trial, conducted at 347 centers in the North America, European Union and 10 other countries, studied patients less than or equal to 24 months of age with CLDP and patients with premature birth (less than or equal to 35 weeks gestation) who were less than or equal to 6 months of age at study entry. Patients with hemodynamically significant congenital heart disease were excluded from enrollment in this study and were studied in a separate study. In this trial, patients were randomized to receive 5 monthly injections of 15mg/kg of liquid palivizumab (N=3306) used as active control for an investigational monoclonal antibody (N=3329). Subjects were followed for safety and efficacy for 150 days. Ninety-eight percent of all subjects receiving palivizumab completed the study and 97% received all five injections. The primary endpoint was the incidence of RSV hospitalization.

RSV hospitalizations occurred among 62 of 3306 (1.9%) patients in the palivizumab group. The RSV hospitalization rate observed in patients enrolled with a diagnosis of CLDP was 28/723 (3.9%) and in patients enrolled with a diagnosis of prematurity without CLDP was 34/2583 (1.3%).

CHD Study

In a placebo-controlled trial in 1287 patients ≤ 24 months of age with haemodynamically significant congenital heart disease (639 SYNAGIS; 648 placebo), 5 monthly doses of 15 mg/kg SYNAGIS reduced the incidence of RSV hospitalisations by 45% (p = 0.003) (congenital heart disease study). Groups were equally balanced between cyanotic and acyanotic patients. The RSV hospitalisation rate was 9.7% in the placebo group and 5.3% in the SYNAGIS group.

Secondary efficacy endpoints showed significant reductions in the SYNAGIS group

compared to placebo in total days of RSV hospitalisation (56% reduction, p = 0.003) and total RSV days with increased supplemental oxygen (73% reduction, p = 0.014) per 100 children.

CHD Study 2

This trial, conducted at 162 centers in North America, European Union and 4 other countries over two RSV seasons, studied patients less than or equal to 24 months of age with hemodynamically significant CHD. In this trial, patients were randomized to receive 5 monthly injections of 15mg/kg of liquid palivizumab (N=612) used as active control for an investigational monoclonal antibody (N=624). Subjects were stratified by cardiac lesion (cyanotic vs. other) and were followed for safety and efficacy for 150 days. Ninety-seven percent of all subjects receiving palivizumab completed the study and 95% received all five injections. The primary endpoint was a summary of adverse events and serious adverse events, and the secondary endpoint was the incidence of RSV hospitalization. The incidence of RSV hospitalization was 16 of 612 (2.6%) in the palivizumab group.

CHD Post-marketing Study

A post-marketing retrospective, observational noninterventional cohort study was conducted in children with hemodynamically significant congenital heart disease (HSCHD) in 32 sites in 10 European countries (Austria, Belgium, France, Germany, Italy, Norway, Poland, Slovenia, Spain, United Kingdom). Children with HSCHD who were less than 24 months of age when the first dose of lyophilized SYNAGIS was administered (N=1009) were compared for the occurrence of primary serious adverse events (PSAEs) over an 8-month observational period with a historical cohort of matched children who were also diagnosed with HSCHD but did not receive lyophilized SYNAGIS during the first 24 months of life (N=1009). Children were matched by age, type of cardiac lesion, and prior corrective cardiac surgery. PSAEs were defined as the SAEs of infection, arrhythmia, and death.

PSAEs of infection during the 8-month chart review period were reported at a statistically significantly lower rate in prophylaxed children (27.8% [281/1009]) compared to non-prophylaxed children (32.6% [329/1009]) (p=0.023). The incidence of arrhythmia PSAEs was 4.1% (41/1009) in prophylaxed children and 3.9% (39/1009) in non-prophylaxed children (p>0.100). The incidence of death PSAEs was numerically lower for prophylaxed children (0.9% [9/1009]) compared to non-prophylaxed children (1.0% [10/1009]).

The results of the study indicate no increased risk of serious infections, serious arrhythmias, or death in children with HSCHD associated with lyophilized SYNAGIS prophylaxis compared with matched non- prophylaxed children.

Extended Dose Study

In an open label prospective trial designed to evaluate pharmacokinetics, safety, and immunogenicity after administration of 7 doses of palivizumab within a single RSV season, pharmacokinetic data indicated that adequate mean palivizumab levels were achieved in all 18 children enrolled. Transient, low levels of antipalivizumab antibody were observed in one child after the second dose of palivizumab that dropped to undetectable levels at the fifth and seventh dose.

Palivizumab levels in the extended dose study were comparable to those achieved in the IMpact RSV trial. No significant elevations of anti-palivizumab antibody titer were observed.

5.2 Pharmacokinetic properties

The pharmacokinetics and safety of palivizumab liquid formulation and palivizumab lyophilized formulation, following 15 mg per kg intramuscular administration, were compared in a cross-over trial of 153 infants less than or equal to 6 months of age with a history of prematurity (less than or equal to 35 weeks gestational age). The results of this trial indicated that the trough serum concentrations of palivizumab were similar between liquid formulation and the lyophilized formulation and bioequivalence of the liquid and the lyophilized formulation was demonstrated.

5.3 Preclinical safety data

In a human tissue cross-reactivity study, biotinylated palivizumab did not stain in a specific fashion to themore than 30 human adult and neonatal tissues studied.

Acute toxicity studies in three species, the Sprague Dawley rat, the cynomolgus monkey and the NZW rabbit demonstrated tolerance at the site of injection as well as lack of specific systemic toxicity.

Immunogenicity data in cynomolgus monkeys showed no generation of antibody against SYNAGIS.

In the cotton rat model, pretreatment with SYNAGIS was shown to reduce mean pulmonary viral titers (replication) by a mean of 99% at serum concentrations of approximately 30 mcg/mL. At no concentration was increased viral replication seen, nor was there an increase in pulmonary inflammation or histopathology at any SYNAGIS concentration examined. No RSV mutants escaped therapy, and reinfection with RSV after SYNAGIS exposure did not enhance RSV viral titers (replication) or the resultant pulmonary histopathology.

Binding and neutralization studies have been performed on RSV isolates collected from around the world, to determine whether palivizumab has specificity for a wide range of subtypes. Over 600 isolates, collected from 19 countries on 5 continents have been tested for binding and palivizumab bound to all samples. A subset of more than 100 of these isolates was evaluated for neutralization by palivizumab, and all samples were neutralized.

Carcinogenesis, Mutagenesis, and Impairment of Fertility

Carcinogenesis, mutagenesis, and reproductive toxicity studies have not been performed.

6. PHARMACEUTICAL PROPERTIES

6.1 List of excipients

Histidine

Glycine
Sterile Water for Injection

6.2 Incompatibilities

Palivizumab should not be mixed with any medications or diluents.

6.3 Shelf-life

3 years

6.4 Special precautions for storage

Store at 2 to 8ºC (35.6 and 46.4ºF).
Do not freeze.
Store in the original container.

Do not use beyond the expiration date.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

Palivizumab is supplied as a sterile solution for intramuscular injection.

Palivizumab single-use vial: 2/4 mL (2R), clear, colorless type I glass vial with stopper and flip-off seal containing 0.5 mL palivizumab solution for injection with a concentration of 100 mg/mL.

Palivizumab single-use vial: 2/4 mL (2R), clear, colorless type I glass vial with stopper and flip-off seal containing 1 mL palivizumab solution for injection with a concentration of 100 mg/mL.

The rubber stopper used for sealing vials of SYNAGIS is not made with latex or dry natural rubber.

6.6 Instructions for use, handling, and disposal

Both the 0.5 mL and 1 mL vials contain an overfill to allow the withdrawal of 50 mg or 100 mg, respectively.

- **DO NOT DILUTE THE PRODUCT.**
- **DO NOT SHAKE VIAL.**
- To administer, remove the tab portion of the vial cap and clean the stopper with 70% ethanol or equivalent. Insert the needle into the vial and withdraw an appropriate volume of solution into thesyringe.
- Palivizumab does not contain a preservative and should be administered immediately after drawing thedose into the syringe.
- Single-use vial. Do not re-enter the vial after withdrawal of drug. Discard unused contents.

To prevent the transmission of infectious diseases, sterile disposable syringes and needles should be used. Do not reuse syringes and needles.

Product Owner

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Date of revision of text

February 2023

02/BC/SG/Doc ID-004593627 V4.0