

1 **NEUTROSPEC™**
2 Kit for the Preparation of Technetium (99m Tc) fanolesomab
3
4 Diagnostic Radiopharmaceutical
5 For intravenous use only
6 Rx ONLY
7 CONTAINS SODIUM HYDROSULFITE

8 **DESCRIPTION**

9 NeutroSpec™ [Kit for the Preparation of Technetium (99m Tc) fanolesomab] is a
10 radiodiagnostic agent consisting of a murine IgM monoclonal antibody, formulated to be
11 labeled with technetium Tc 99m. Each NeutroSpec™ kit contains all the excipients
12 needed to reconstitute and to radiolabel this imaging agent with sodium pertechnetate Tc
13 99m Injection, USP. The murine monoclonal antibody fanolesomab is produced in
14 suspension culture of hybridoma cells. NeutroSpec™ [Technetium (99m Tc)
15 fanolesomab] is an *in vivo* diagnostic radiopharmaceutical that can be visualized by
16 nuclear medicine instrumentation.
17 Each NeutroSpec™ kit contains a single use vial of fanolesomab as a sterile, non-
18 pyrogenic, lyophilized mixture of 0.25 mg fanolesomab; 12.5 mg maltose monohydrate;
19 0.522 mg sodium potassium tartrate tetrahydrate, USP; 0.221 mg succinic acid; 54 mcg
20 stannous tartrate (minimum stannous 7 mcg; maximum total stannous and stannic tin 24
21 mcg); 28 mcg glycine, USP; and 9.3 mcg disodium edetate dihydrate, USP. The
22 lyophilized powder contains no preservatives and has no US standard of potency.
23 When sterile, pyrogen-free sodium pertechnetate Tc 99m Injection, USP in isotonic
24 saline (no preservatives) is added to the single use fanolesomab vial, a Tc 99m complex
25 of fanolesomab is formed with an approximate pH of 6.2.

26 **Physical Characteristics of Technetium Tc 99m**

27 Technetium 99m decays by isomeric transition with a physical half-life of 6.02 hours.
28 The photon that is useful for imaging studies is listed in **Table 1**.

29

30 **Table 1. Principal radiation emission data for technetium Tc 99m**

| Radiation | Mean Percent per Disintegration | Mean Energy (keV) |
|-----------|---------------------------------|-------------------|
| Gamma-2 | 89.07 | 140.5 |

31 **External Radiation**

32 The specific gamma-ray constant for technetium Tc 99m is $5.4 \mu\text{C}\cdot\text{kg}^{-1}\cdot\text{MBq}^{-1}\cdot\text{h}^{-1}$
33 (0.78 R/mCi·h) at 1 cm. The first half-value thickness of lead for Tc 99m is 0.017 cm. A
34 range of values for the relative attenuation of the radiation emitted by this radionuclide
35 that results from the interposition of various thicknesses of lead is shown in **Table 2**. For
36 example, the use of a 0.25 cm thickness of lead will decrease the external radiation
37 exposure by a factor of 1,000.
38

39 **Table 2. Radiation attenuation by lead shielding**

| Lead Shield Thickness (cm) | Coefficient of Attenuation |
|----------------------------|----------------------------|
| 0.017 | 0.5 |
| 0.08 | 0.1 |
| 0.16 | 0.01 |
| 0.25 | 0.001 |
| 0.33 | 0.0001 |

40 To correct for physical decay of this radionuclide, the fractions that remain at selected
 41 time intervals after the time of calibration are shown in **Table 3**.

42

43 **Table 3. Physical decay chart—technetium Tc 99m half-life 6.02 hours**

| Hours | Fraction Remaining | Hours | Fraction Remaining |
|-------|--------------------|-------|--------------------|
| 0* | 1.00 | 7 | 0.45 |
| 1 | 0.89 | 8 | 0.40 |
| 2 | 0.79 | 9 | 0.36 |
| 3 | 0.71 | 10 | 0.32 |
| 4 | 0.63 | 11 | 0.28 |
| 5 | 0.56 | 12 | 0.25 |
| 6 | 0.50 | 18 | 0.13 |

44 *Calibration Time (time of preparation)

45 **CLINICAL PHARMACOLOGY**

46 **Pharmacodynamics**

47 Fanolesomab is directed against the carbohydrate moiety 3-fucosyl-*N*-acetylactosamine
 48 that defines the cluster of differentiation 15 (CD15) antigen. NeutroSpec™ [Technetium
 49 (99m Tc) fanolesomab] radiolabels human white blood cells and myeloid precursors.
 50 The CD15 antigen is expressed on the surface of polymorphonuclear neutrophils (PMNs),
 51 eosinophils and monocytes. Monocytes and eosinophils constitute approximately 5% of
 52 circulating leukocytes; therefore, most of the circulating blood cellular activity resides on
 53 PMNs. In blood cell fractions isolated from healthy volunteers who had received
 54 NeutroSpec™, radioactivity was associated with PMNs (25%) or plasma (72%) when
 55 measured one hour after injection. The binding of fanolesomab to its antigenic sites on
 56 human PMNs has an apparent $K_d = 1.6 \times 10^{-11}$ M.
 57 Cross-reactivity studies indicate the presence of CD15 antigenic sites on many human
 58 tissues.

59 **Pharmacokinetics**

60 In a study of 10 healthy volunteers, following intravenous injection of NeutroSpec™,
 61 blood concentrations of radioactivity decreased rapidly with an initial half-life of 0.3
 62 hours and a second phase half-life of approximately eight hours. Whole-body
 63 scintigraphy at two hours post-injection indicated that the liver had the highest

64 radioactivity uptake and retention (50% of the injected dose), followed by the kidney,
65 spleen and red marrow. Over the 26–33 hours after injection, 38% of the injected dose of
66 radioactivity was recovered in urine.

67 **CLINICAL STUDIES**

68 A multicenter, single-arm study evaluated 200 patients (5 to 86 years of age) with
69 equivocal signs and symptoms of appendicitis defined as absence of one or more of the
70 following: periumbilical pain migrating to right lower quadrant (RLQ), gradual onset of
71 pain, increasing intensity of pain over time, pain aggravated by movement and coughing,
72 McBurney’s point tenderness, referred tenderness to RLQ with palpation in other
73 quadrants, abdominal muscular spasm with RLQ tenderness, temperature > 101^o F, white
74 blood cell count > 10,500/mm³. Readers blinded to clinical information (except for age,
75 gender and body habitus) assessed the diagnosis of appendicitis by NeutroSpec™
76 imaging. The diagnosis by the blinded readers was compared with a final clinical
77 diagnosis based upon a surgical pathology report (in cases that proceeded to
78 appendectomy) or upon two weeks of follow-up (in cases without surgical intervention).
79 The study investigators had access to other diagnostic modalities (e.g., CT scan and
80 ultrasound) and were instructed not to rely on NeutroSpec™ imaging for their diagnosis
81 of appendicitis. Appendicitis prevalence in this study was 30%. The image evaluation
82 was limited to the assessment of the planar images performed in specified projections at
83 defined time points and single photon emission tomography was not used to assess
84 performance in this study.

85 The performance rates for the diagnosis of appendicitis by the blinded readers and by the
86 clinical investigators are shown in **Table 4**.

87
88 **Table 4. Diagnostic performance of NeutroSpec™**

| Evaluation | Performance Rates (n=200) | |
|---------------------------|--|---|
| | Blinded Readers percentages (95%CI) | Study Investigators percentages(95%CI) |
| Sensitivity | 75 (62, 85) | 91 (80, 97) |
| Specificity | 93 (87, 97) | 86 (79, 91) |
| Accuracy | 87 (82, 92) | 87 (81, 91) |
| Positive Predictive Value | 82 (69, 91) | 74 (62, 84) |
| Negative Predictive Value | 90 (84, 94) | 96 (90, 99) |

89
90 In a supportive single-arm, two-center study of the detection of appendicitis in 56 patients
91 of whom 50% had a final diagnosis of appendicitis, the diagnostic performance of
92 NeutroSpec™ was similar to the performance observed in the larger study.

93 Other intra-abdominal conditions

94 Among 30 study patients with other types of intra-abdominal infection (surgical and non-
95 surgical), 13 scintigrams were read as positive for appendicitis.

96 **INDICATIONS AND USAGE**

97 NeutroSpec™ [Technetium (99m Tc) fanolesomab] is indicated for scintigraphic imaging
98 of patients with equivocal signs and symptoms of appendicitis who are five years of age
99 or older.

100 **CONTRAINDICATIONS**

101 NeutroSpec™ should not be administered to patients who are hypersensitive to any
102 murine proteins or other component of the product.

103 **WARNINGS**

104 **Hypersensitivity Reactions**

105 Allergic reactions, including anaphylaxis, can occur in patients who receive murine
106 antibodies such as fanolesomab.

107 Cenolate™ Ascorbic Acid, USP injection (diluent) contains sodium hydrosulfite, a sulfite
108 that may cause allergic reactions, including anaphylaxis. Serious hypersensitivity
109 reactions were not observed in the 523 patients who received NeutroSpec™ in the clinical
110 studies. Emergency resuscitation personnel and equipment for the treatment of
111 hypersensitivity reactions should be immediately available during administration of this
112 agent.

113 **PRECAUTIONS**

114 **Repeat Administration**

115 NeutroSpec™ has not been studied in repeat administration to patients. Murine
116 monoclonal antibodies are frequently immunogenic. The development of human anti-
117 mouse antibodies (HAMA) can alter the pharmacokinetics, biodistribution, safety, and
118 imaging performance properties of the administered agent.

119 **Use in Patients with Neutropenia**

120 The biodistribution and the imaging performance of NeutroSpec™ in neutropenic patients
121 have not been studied. NeutroSpec™ induces transient neutropenia and a downward shift
122 in white blood cell counts. (See **ADVERSE REACTIONS Laboratory Values**). The
123 safety and effectiveness of NeutroSpec™ in patients with neutropenia have not been
124 established.

125 **General Use and Handling**

126 NeutroSpec™ [Technetium (99m Tc) fanolesomab], like other radioactive medical
127 products, must be handled with care and appropriate safety measures should be used to
128 minimize radiation exposure to clinical personnel. Care should also be taken to minimize
129 radiation exposure to the patient consistent with proper patient management.

130 Radiopharmaceuticals should be used by or under the control of personnel who are
131 qualified by specific training and experience in the safe use and handling of
132 radionuclides, and whose experience and training have been approved by the appropriate
133 governmental agency authorized to license the use of radionuclides.

134 **Information for patients**

135 Murine monoclonal antibodies such as fanolesomab are foreign proteins and their
136 administration can induce hypersensitivity reactions. Patients should be informed that the
137 use of this product could affect their future use of other murine based products, and
138 should be advised to discuss prior use of murine antibody based products with their
139 health care provider.

140 To minimize the radiation-absorbed dose to the bladder, adequate hydration should be
141 encouraged to permit frequent voiding during the first few hours after injection. To help
142 protect themselves and others in their environment, patients should take the following
143 precautions for 12 hours after injection. Whenever possible, a toilet should be used,
144 rather than a urinal and the toilet should be flushed several times after each use. Spilled
145 urine should be cleaned up completely. After each voiding or fecal elimination, patients
146 should thoroughly wash their hands. If blood, urine or feces soil clothing, the clothing
147 should be washed separately.

148 **Carcinogenesis, Mutagenesis, Impairment of Fertility**

149 Studies have not been conducted to evaluate carcinogenic potential, mutagenic potential,
150 or effects on fertility.

151 **Pregnancy**

152 Pregnancy Category C. Animal reproductive studies have not been conducted with
153 NeutroSpec™. It is also not known whether NeutroSpec™ can cause fetal harm when
154 administered to a pregnant woman or can affect reproductive capacity. NeutroSpec™
155 should not be used during pregnancy unless the potential benefit to the patient justifies
156 the potential risk to the fetus.

157 **Nursing Mothers**

158 It is not known whether this drug is excreted in human milk. Because many drugs are
159 excreted in human milk, caution should be exercised when NeutroSpec™ is administered
160 to a nursing woman. Whenever possible, infant formula should be substituted for breast
161 milk until the radioactivity has cleared from the body of the nursing woman.

162 **Pediatric Use**

163 In clinical studies of NeutroSpec™, 29 (5%) patients were 5–11 years old and 32 (6%)
164 were 12–16 years old. No overall differences in safety or effectiveness were observed
165 between these patients and patients in other age brackets, however, this number of
166 patients is too few to exclude differences.

167 **Geriatric Use**

168 In clinical studies of NeutroSpec™, 64 (12%) patients were 65 years or older. No overall
169 differences in safety or effectiveness were observed between these patients and younger
170 patients, but this number of patients is too few to exclude differences.

171 **ADVERSE REACTIONS**

172 The data described below reflect exposure to NeutroSpec™ in 523 patients and normal
173 volunteers receiving a mean antibody dose of 121 mcg (33–250 mcg) and a mean

174 radioactive dose of 15 mCi (1-33 mCi). The median patient age was 35 years (5-91
175 years); 53% of patients were women and 61% of patients were Caucasians.
176 Two patients enrolled in studies of post surgical infection or abscess had serious adverse
177 events associated with fatality (hypotension and worsening of sepsis). Underlying
178 medical conditions may have also contributed to the fatality and the relationship of the
179 fatality to NeutroSpec™ cannot be determined.
180 Overall, 49 adverse events occurred in 37 (7%) of the 523 patients exposed to
181 NeutroSpec™. Four of these events were classified as severe (hypotension, worsening of
182 sepsis, chest pressure and decreased SaO₂, pain). The most frequently reported adverse
183 events were flushing (n=10, 2%) and dyspnea (n=5, 1%). Other less common adverse
184 events (< 1%) included syncope, dizziness, hypotension, chest pressure, paresthesia,
185 nausea, injection site burning/erythema, pain, and headache.
186 Because clinical trials are conducted under widely varying controlled conditions, adverse
187 reaction rates observed in clinical trials of a drug cannot be directly compared with rates
188 in the clinical trials of another drug, and may not reflect the rates observed in practice.
189 The adverse reaction information from clinical trials does, however, provide a basis for
190 identifying the adverse events that appear to be related to drug use and for approximating
191 rates.

192 **Laboratory Test Values**

193 NeutroSpec™ induced transient decreases in neutrophil counts in a study of 10 healthy
194 volunteers. Neutrophil counts began to decrease within 3 to 5 minutes post-injection and
195 returned to pre-injection values within four hours. Downward shifts in neutrophil counts
196 have been observed in 18% of patients (28/151). Three of 284 patients were observed to
197 develop transient elevations of AST and ALT after NeutroSpec™ administration.

198 **Immunogenicity**

199 The incidence of antibody development in patients receiving NeutroSpec™ has not been
200 adequately determined because the assay was not directly quantitative and its ability to
201 detect low titers could not be assured. Human anti-mouse antibody (HAMA) response
202 following a single NeutroSpec™ administration was evaluated in a total of 54 patients 3-
203 16 weeks post injection. None of the patients had a positive HAMA response. In 30
204 healthy volunteers who were exposed to two administrations of fanolesomab separated by
205 two weeks, fanolesomab induced HAMA response in five volunteers.
206 Immunogenicity data are highly dependent on the sensitivity and specificity of the assay.
207 Additionally, the observed incidence of antibody positivity in an assay may be influenced
208 by several factors, including sample handling, timing of sample collection, concomitant
209 medications, and underlying disease. For these reasons, comparison of the incidence of
210 antibodies to NeutroSpec™ with the incidence of antibodies to other products may be
211 misleading.

212 **OVERDOSAGE**

213 There is no experience with overdosage in clinical trials.

214 **DOSAGE AND ADMINISTRATION**

215 **Adults**

216 To prepare NeutroSpec™ the reaction vial containing fanolesomab is reconstituted with
217 sodium pertechnetate Tc 99m Injection, USP solution prior to use. (See

218 **INSTRUCTIONS FOR PREPARATION**).

219 Fanolesomab is not intended for direct administration to the patient without reconstitution
220 and labeling with sodium pertechnetate Tc 99m Injection, USP. NeutroSpec™
221 [Technetium (99m Tc) fanolesomab] is intended for a single intravenous (IV)
222 administration through an intravenous access that has been demonstrated to be patent,
223 e.g., butterfly, running IV line, or equivalent injection system to assure that no dose
224 infiltration occurs. Following administration, flush the injection line with an appropriate
225 volume of saline to assure administration of the total dose.

226 For imaging, 75 to 125 mcg of fanolesomab is labeled with 10 to 20 mCi (370 to 740
227 MBq) and administered as a single dose of NeutroSpec™.

228 Planar imaging should be performed using a large field of view camera fitted with a low-
229 energy, parallel-hole, high-resolution collimator. The camera should be positioned so
230 that the lower edge of the liver is at the upper end of the field of view at the midline of
231 the patient.

232 Dynamic image acquisition over the lower abdomen should begin at the time of injection
233 and consist of 10 sequential four-minute images. Following dynamic image acquisition,
234 the patient should ambulate for approximately 10 to 15 minutes and void. Static planar
235 images should then be collected, including supine anterior, posterior, 10–25 degree RAO
236 and LAO views of the lower abdomen, followed by a standing anterior image of the
237 lower abdomen. After the camera has been positioned (as described above), it is
238 recommended that a total of one million counts be collected for the anterior supine
239 image. All remaining images should be collected for the same duration of time required
240 for the anterior supine image.

241 **Children (Five years and older)**

242 NeutroSpec™ is administered in a single dose of 0.21 mCi/kg to a maximum of 20 mCi.
243 Recommended imaging times and procedures are the same as for adults.

244

245 Dose adjustment has not been established in patients with renal insufficiency, in geriatric
246 patients or in pediatric patients under five years of age.

247 **Image Interpretation**

248 The biodistribution of the NeutroSpec™ radiopharmaceutical is imaged in the blood pool,
249 reticuloendothelial system (liver, spleen, bone marrow), and urinary excretion organs
250 (kidneys and urinary tract). Imaging of the uterus has been noted, consistent with blood
251 pool activity of NeutroSpec™.

252 In the 200-patient clinical trial (see CLINICAL STUDIES), based on the average of the
253 three blinded reader interpretations, 75% of the 59 true positive cases of appendicitis
254 were identified (range 66-81%).

255 Among those with a blinded diagnosis of appendicitis, 76% displayed uptake of
256 radiotracer activity in the appendix within 30 minutes following injection and 98% did so
257 by 60 minutes following injection.

258 In the trial the acquisition of image collection was performed for a 90 minute period. The
259 image finding of a persistent or intensifying uptake in the right lower quadrant (appendix
260 zone) that is seen before the completion of the entire imaging sequence may be
261 considered a positive study, and imaging may be terminated at this time. In the case of a
262 negative image finding at 30 and 60 minutes, collection to 90 minutes is recommended
263 prior to termination of the study.

264 A diagnostic abnormality is characterized by the presence of an irregular, asymmetric
265 uptake of radiotracer localized in the right lower quadrant of the abdomen. The abnormal
266 localization of radiotracer remains constant or increases in intensity in follow up imaging.

267 **RADIATION DOSIMETRY**

268 Based on human data, the absorbed radiation dose to an average human adult (70 kg)
269 from an intravenous injection of NeutroSpec™ is listed in **Table 5**. The values were
270 calculated using the Standard Medical Internal Radiation Dosimetry (MIRD) method.
271 The values are listed as rad/mCi and mGy/MBq and assume urinary bladder emptying at
272 4.8 hours. Radiation absorbed dose estimates for children are given in **Table 6**.

Table 5. Absorbed radiation dose in adults (NeutroSpec™)

| Target Organ | rad/mCi | mGy/MBq |
|----------------------------|----------------|-----------------|
| Spleen | 0.23 | 0.062 |
| Kidneys | 0.19 | 0.051 |
| Liver | 0.18 | 0.048 |
| Urinary Bladder Wall | 0.12 | 0.032 |
| Heart | 0.061 | 0.017 |
| Gallbladder | 0.056 | 0.015 |
| Upper Large Intestine Wall | 0.051 | 0.014 |
| Adrenal Glands | 0.044 | 0.012 |
| Lungs | 0.043 | 0.012 |
| Thyroid Gland | 0.042 | 0.011 |
| Red Marrow | 0.038 | 0.010 |
| Lower Large Intestine Wall | 0.034 | 0.0091 |
| Bone Surface | 0.031 | 0.0083 |
| Brain | 0.0052 | 0.0014 |
| Testes / Ovaries | 0.0039 / 0.019 | 0.0010 / 0.0052 |
| Total Body | 0.019 | 0.0050 |

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Dose calculations were performed using the standard MIRD method (MIRD Pamphlet No. 1 rev., Soc. Nucl. Med., 1976). Effective dose equivalent was calculated in accordance with ICRP 53 (Ann. ICRP 18, 1-4, 1988) and gave a value of 0.018 mSv/MBq (0.068 rem/mCi).

Table 6. Estimated absorbed radiation dose for a five-year old child

| Target Organ | rad/mCi | mGy/MBq |
|----------------------------|---------------|----------------|
| Spleen | 0.70 | 0.19 |
| Kidneys | 0.43 | 0.11 |
| Liver | 0.41 | 0.11 |
| Urinary Bladder Wall | 0.27 | 0.072 |
| Upper Large Intestine Wall | 0.21 | 0.056 |
| Thyroid Gland | 0.19 | 0.052 |
| Lower Large Intestine Wall | 0.16 | 0.042 |
| Heart | 0.15 | 0.041 |
| Gallbladder | 0.13 | 0.036 |
| Red Marrow | 0.11 | 0.030 |
| Lungs | 0.11 | 0.028 |
| Adrenal Glands | 0.095 | 0.026 |
| Bone Surface | 0.085 | 0.023 |
| Testes / Ovaries | 0.019 / 0.059 | 0.0052 / 0.016 |
| Brain | 0.0075 | 0.0020 |
| Total Body | 0.049 | 0.013 |

278 Dose calculations were performed using the standard MIRD method based upon biodistribution studies
 279 conducted in adults. Effective dose equivalent was calculated in accordance with ICRP 53 and gave a
 280 value of 0.047 mSv/MBq (0.17 rem/mCi).

281 **INSTRUCTIONS FOR THE PREPARATION OF NEUTROSPEC™**

282 **USE ASEPTIC TECHNIQUE THROUGHOUT**

283 The user should wear waterproof gloves during the entire procedure and while
 284 withdrawing the patient dose from the NeutroSpec™ vial.

285 Transfer Sodium Pertechnetate Tc 99m Injection, USP with an adequately shielded,
 286 sterile syringe.

287 Adequate shielding should be maintained at all times until the preparation is administered
 288 to the patient, disposed of in an approved manner, or allowed to decay to background
 289 levels. A shielded, sterile syringe should be used to withdraw and inject the labeled
 290 preparation.

291 Before reconstituting a vial, it should be inspected for cracks and any indication that the
 292 integrity of the vacuum seal has been lost. The material should not be used if integrity of
 293 the vacuum seal has been lost. After reconstitution, examine the vial contents for
 294 particulates and discoloration prior to injection. The material should not be used if
 295 particulates or discoloration are observed.

296 The dose should be injected via an indwelling catheter, butterfly, or equivalent injection
 297 system to assure that no dose infiltration occurs. Following administration, flush the
 298 injection line with an appropriate volume of saline to assure administration of the total
 299 dose.

300 **Labeling and Preparation of NeuroSpec™**

- 301 1. Required Materials, Not Supplied within the NeuroSpec™ kit:
- 302 a. Sodium Pertechnetate Tc-99m, USP, oxidant-free
- 303 b. ITLC-SG Strips, Heat Treated
- 304 c. Methyl Ethyl Ketone (MEK)
- 305 d. Developing Chambers - 50 mL disposable tubes
- 306 e. Pipettors and tips
- 307 f. Forceps
- 308 g. Gamma Counter
- 309 h. Dose Calibrator
- 310 i. Sodium Chloride for Injection, USP
- 311 j. Alcohol (or Germicidal)
- 312 k. Lead Shield
- 313 l. 1 mL Sterile Syringes
- 314 m. Water Bath stabilized at 37±1° C
- 315
- 316 2. Remove a fanolesomab reaction vial from refrigerated storage (2 to 8° C) and
- 317 allow it to come to room temperature (usually 5 to 10 minutes). NOTE: Keep
- 318 Cenolate ampule refrigerated and protected from light until needed (Step 5).
- 319
- 320 3. Swab the rubber stopper of the fanolesomab reaction vial with an appropriate
- 321 antiseptic and allow the stopper to dry.
- 322
- 323 4. Aseptically add 20 to 40 mCi (740 to 1480 MBq) Sodium Pertechnetate Tc 99m
- 324 Injection, USP in 0.20 to 0.35 mL generator eluate. Gently swirl (**Do not shake**)
- 325 the vial until the lyophilized product is completely dissolved, ensuring the vial is
- 326 not inverted.
- 327

328 **Cautionary Notes:**

- 329 • Use only eluate from a technetium Tc 99m generator that was
- 330 previously eluted within the last 24 hours.
- 331 • Technetium 99m eluate which is more than 8 hours old from the time
- 332 of elution should NOT be used.
- 333 • The amount of Sodium Pertechnetate Tc 99m Injection, USP used to
- 334 reconstitute the reaction vial should be determined based on the
- 335 desired radioactive dose and the estimated time of use.
- 336 • If Sodium Pertechnetate Tc 99m Injection, USP must be diluted prior
- 337 to kit reconstitution, only sterile sodium chloride for injection, USP,
- 338 (without preservatives) should be used.
- 339
- 340 5. Incubate at 37° C for 30 minutes. (Shorter incubation times may result in
- 341 inadequate labeling.)

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6. Aseptically add sufficient Cenolate™ [Ascorbic Acid Injection, USP (500 mg/mL)] to make the final preparation volume up to 1 mL.

Note: Further dilution is not recommended.

7. Assay the product in a suitable calibrator and record the time, date of preparation and the activity of NeutroSpec™ onto the string tag label and attach to lead dispensing shield (“pig”).
8. Each patient should receive a dose of 10-20 mCi of NeutroSpec™ (the final reconstituted product).
9. Discard vials, needles and syringes in accordance with local, state, and federal regulations governing radioactive and biohazardous waste.

Recommended Method for Radiochemical Purity Testing

1. After addition of Cenolate™ (Ascorbic Acid Injection, USP) aseptically withdraw approximately 10 µL of the final reconstituted product for Quality Control (QC) testing. Care should be taken not to introduce air into the vial. Use of a shielded 0.5 - 1.0 cc syringe with a 25 or 27 gauge needle is recommended.
2. Apply 1 - 5 µL (a drop that has not completely formed on the tip of a 25 - 27 gauge needle) of NeutroSpec™ 2 cm (origin) from the bottom of an ITLC-SG 1.5 x 10 cm strip and allow the solution to absorb into the strip (approximately 5 seconds).
3. Immediately place the strip, origin side down, in a development chamber containing 4 mL methyl ethyl ketone (MEK).
4. Allow the strip to develop until the solvent front is within 0.5 cm of the top of the strip (3 - 5 minutes).
5. Remove the strip using forceps and allow to dry.
6. Cut the strip at the 4 cm mark, place each piece in a separate counting tube and measure the radioactivity associated with each piece.
7. Calculate the % Free Technetium Tc 99m Pertechnetate as follows:

$$\% \text{ Free Pertechnetate} = \frac{\text{Radioactivity in Solvent Front Piece}}{\text{Total Radioactivity in Strip}} \times 100\%$$

Note: The product should only be used if the percentage of Free Technetium Tc 99m Pertechnetate is ≤ 10%.

387 **HOW SUPPLIED**

388 NeutroSpec™ Kit for the Preparation of Technetium (99m Tc) fanolesomab

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390 The NeutroSpec™ kit contains five individual kits each containing:

391 One 3 mL single use vial of fanolesomab as a sterile, non-
392 pyrogenic, lyophilized mixture of 0.25 mg fanolesomab;
393 12.5 mg maltose monohydrate; 0.522 mg sodium potassium
394 tartrate tetrahydrate, USP; 0.221 mg succinic acid; 54 mcg
395 stannous tartrate (minimum stannous 7 mcg; maximum
396 total stannous and stannic tin 24 mcg); 28 mcg glycine,
397 USP; and 9.3 mcg disodium edetate dihydrate, USP. The
398 lyophilized powder contains no preservatives and has no
399 US standard of potency.

400

401 One 2 mL ampule Cenolate™ [Ascorbic Acid Injection, USP
402 (500 mg/mL)]

403

404 One NeutroSpec™ Package Insert

405

406 One String tag label for NeutroSpec™ vials (reconstituted
407 product)

408 **STORAGE**

409 Refrigerate the lyophilized NeutroSpec™ kits at 2 to 8° C (36 to 46° F). After labeling
410 with Sodium Pertechnetate Tc 99m Injection, USP and addition of Cenolate™ (Ascorbic
411 Acid injection, USP) the vial should be kept at room temperature, 15 to 25° C (46 to 77°
412 F) and used within six hours. Use appropriate radiation shielding.

413

414 This reagent kit is approved for distribution to persons licensed by the U.S. Nuclear
415 Regulatory Commission to use byproduct material identified in 10 CFR 35.200 or under
416 an equivalent license issued by an Agreement State.

417

418 NeutroSpec™ is manufactured for Palatin Technologies, Inc., Cranbury, NJ 08512 by
419 Ben Venue Laboratories, Inc., Bedford, OH 44146

420 U.S. Patent X,XXX,XXX

421 US license number 1588

422

423 Cenolate™ (Ascorbic Acid Injection, USP) is manufactured for Palatin Technologies, Inc.
424 by Hospira, Chicago, IL 60064

425

426 **Distributed by:**

427 Mallinckrodt Inc.

428 St. Louis, MO 63134

429

430 Rx only

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432 Printed in USA

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