Platelia™ CMV IgG AVIDITY

DETERMINATION OF ANTI-CYTOMEGALOVIRUS IgG AVIDITY IN HUMAN SERUM BY ENZYME IMMUNOASSAY

IVD  CE 0459

881171 - 2015/01
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1. **INTENDED USE**

Platelia™ CMV IgG AVIDITY is an immuno-enzyme assay for determination of avidity of anti-cytomegalovirus IgG antibodies in human serum. The Platelia™ CMV IgG AVIDITY assay should be used in association with the Platelia™ CMV IgG kit (Ref. 72810).

2. **CLINICAL VALUE**

The human cytomegalovirus (CMV) is a ubiquitous virus found in all geographical areas in the world and in all socio-economical groups. The CMV is a member of the Herpesvirus family and is transmitted through biological fluids during close interpersonal contacts (urine, saliva, maternal milk, blood, tears, sperm and vaginal secretions). After an infection, the CMV can remain latent during several years in body of contaminated patients, and then can reactivate causing recurrent infections with potential transmission to other individuals.

Primary infection is acquired by different ways of transmission and at different periods of life (congenital infections, post-natal infections). After latency phase, the secondary infection may occur either through re-infection by an exogenous virus or by reactivation of the latent virus.

50 to 85% of the population is infected before adult age, but most of the infections remain asymptomatic, with only 2% of the patients showing atypical symptoms like fever, asthenia, muscles or joint pains. However, the CMV infection can be serious when affecting pregnant women, neonates or immunocompromised hosts.

During pregnancy, 1 to 3 % of women are infected with CMV and fetal transmission through placental diffusion is observed in 40 to 50% of patients. 95% of fetal infections are not symptomatic, but in 5%, complications are extremely severe: hepatosplenomegaly, microcephaly, hydrocephaly, pre-maturity, psychomotor retardation and fetal death. In 10% of asymptomatic infections, neonates will present delayed complications like partial or complete deafness or blindness.

In immunocompromised patients (AIDS, organ transplant recipients, lymphoproliferative diseases or cancer), severe complications are related to a disseminated and/or visceral infection: splenomegaly, chorioretinitis, hepatitis, pneumonia, myocarditis, encephalitis. The infection can be fatal in these patients.

A few weeks after the CMV infection, the immune response leads to the appearance of specific IgM antibodies, followed a few days later by the appearance of specific IgG antibodies. The serological diagnosis of CMV infection is demonstrated by a seroconversion or a significant increase with titer of IgG.
However, differential diagnosis between recent and past-infection is sometimes difficult due to persistence of anti-CMV IgM antibodies or re-apparition of anti-CMV IgM in case of re-infection, reactivation of a latent infection or non specific stimulation of the immune system. In such situations, IgG avidity measurement by an immuno-enzyme method can help to differentiate between acute or past-infection. This determination is based on evolution of the immune response maturity, which translates in synthesis of low avidity IgG antibodies during primo-infections and of high avidity IgG antibodies during past-infections.

3. PRINCIPLE

This test is carried out using Platelia™ CMV IgG AVIDITY (Ref. 72812) in association with Platelia™ CMV IgG (Ref. 72810).

The principle of this method relies on the measurement of the avidity of the IgG antibodies to CMV. The use of an agent (as urea) dissociating the link antigen/antibody in parallel with the usual technique of IgG antibodies measurement allows comparison of the optical density (OD) obtained after dissociating agent action and OD obtained without dissociating agent action.

The avidity is considered low when the antigen/antibody link is easily dissociated. The avidity is considered high when the antigen/antibody link is not easily dissociated.

This test has to be used only on positive samples that demonstrate an anti-CMV IgG concentration higher than 0.5 AU/mL with Platelia™ CMV IgG (Ref. 72810).

• Step 1

Avidity controls and patient sera with a concentration of anti-CMV IgG between 0.5 and 1.5 AU/mL are diluted to 1/21. Sera from patients with a concentration of anti-CMV IgG equal or higher than 1.5 AU/mL are diluted to 1/101. Diluted samples are then distributed twice into CMV antigen coated wells of the microplate. During this incubation of one hour at 37°C, IgG antibodies to CMV present in the sample bind to the CMV antigen coated on microplate wells. After incubation, unbound non specific antibodies and other serum proteins are removed by washings.

• Step 2

Each avidity control and each patient serum is treated in double: control solution is added in one well and dissociating solution in the other well. During this incubation of 15 minutes at room temperature (+18-30°C), the dissociating solution tries to dissociate the antigen/antibody complexes. After incubation, both solutions and dissociated IgG are removed by washings.
• **Step 3**
The conjugate (peroxydase labeled polyclonal antibody specific for human gamma chains) is added to the microplate wells. During this incubation of one hour at 37°C, the labeled antibody binds to the serum IgG captured by the CMV antigen. The unbound conjugate is removed by washings at the end of the incubation.

• **Step 4**
The presence of immune-complexes (CMV antigen, IgG antibodies to CMV, anti-IgG conjugate) is demonstrated by the addition in each well of an enzymatic development solution.

• **Step 5**
After incubation of 30 minutes at room temperature (+18-30°C), the enzymatic reaction is stopped by addition of 1N sulfuric acid solution. The optical density reading obtained with a spectrophotometer set at 450/620 nm is proportional to the amount of IgG antibodies to CMV present in the well.

### 4. PRODUCT INFORMATION
Supplied quantities of reagents have been calculated to allow 48 tests with the Platelia™ CMV IgG kit (Ref. 72810). All reagents are exclusively for *in vitro* diagnostic use.

<table>
<thead>
<tr>
<th>Label</th>
<th>Nature of reagents</th>
<th>Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>R5a</td>
<td><strong>Low Avidity control:</strong> Human serum reactive for IgG antibodies to CMV, and negative for HBs antigen, anti-HIV1, anti-HIV2 and anti-HCV Preservative : &lt; 1.5% ProClin™ 300</td>
<td>1 x 0.75 mL</td>
</tr>
<tr>
<td>R5b</td>
<td><strong>High Avidity control:</strong> Human serum reactive for IgG antibodies to CMV, and negative for HBs antigen, anti-HIV1, anti-HIV2 and anti-HCV Preservative : &lt; 1.5% ProClin™ 300</td>
<td>1 x 0.75 mL</td>
</tr>
<tr>
<td>R12</td>
<td><strong>Control solution:</strong> TRIS-NaCl buffer (pH 7.6 ± 0.2), 0.1% Tween® 20 and green dye Preservative : &lt; 1.5% ProClin™ 300</td>
<td>1 x 28 mL</td>
</tr>
<tr>
<td>R13</td>
<td><strong>Dissociating solution:</strong> TRIS-NaCl buffer (pH 7.6 ± 0.2), urea, 0.1% Tween® 20 et yellow dye Preservative : 0.001% ProClin™ 300</td>
<td>1 x 13 mL</td>
</tr>
</tbody>
</table>
For storage conditions and expiration date, please refer to the indications stated on the box.

5. **WARNINGS AND PRECAUTIONS**

The reliability of the results depends on correct implementation of the following Good Laboratory Practices:

- Do not use expired reagents.
- Do not mix or associate within a given run reagents from different lots.
- Before use, wait for 30 minutes to allow reagents to reach room temperature (+18-30°C).
- Use glassware thoroughly washed and rinsed with deionized water or, preferably disposable material.
- Use a new pipette tip for each sample.
- Check the pipettes and other equipments for accuracy and correct operations.
- Strictly follow the assay procedure.
- Refer also to the Platelia™ CMV IgG product insert (Ref. 72810).

*Note: Platelia™ CMV IgG AVIDITY kit can be used with different lots of Platelia™ CMV IgG (Ref. 72810).*

**HEALTH AND SAFETY INSTRUCTIONS**

Human origin material used in the preparation of reagents has been tested and found non-reactive for hepatitis B surface antigen (HBs Ag), antibodies for hepatitis C virus (anti-HCV), and to human immunodeficiency virus (anti-HIV1 and anti-HIV2). Because no method can absolutely guarantee the absence of infectious agents, handle reagents of human origin and patient samples as potentially capable of transmitting infectious diseases:

- Any material, including washings solutions, that comes directly in contact with samples and reagents containing materials of human origin should be considered capable of transmitting infectious diseases.
- Wear disposable gloves when handling samples and reagents.
- Do not pipette by mouth.
- Avoid spilling samples or solutions containing samples. Spills must be rinsed with bleach diluted to 10 %. In the event of a spill with an acid, it must be first neutralized with sodium bicarbonate, and then cleaned with bleach diluted to 10% and dried with adsorbent paper. The material used for cleaning must be discarded in a contaminated residue container.
- Patient samples, reagents containing human origin material, as well as contaminated material and products should be discarded after decontamination only.
• Chemical and biological residues must be handled and disposed off in accordance with Good Laboratories Practices.
• All reagents in the kit are exclusively for *in vitro* diagnostic use.
• Refer also to the Platelia™ CMV IgG product insert (Ref. 72810).
• For hazard and precaution recommendations related to some chemical components in this test kit, please refer to the pictogram(s) mentioned on the labels and the information supplied at the end of instruction for use. The Safety Data Sheet is available on www.bio-rad.com.

6. **SAMPLES**

1. Serum is the only recommended sample type.
2. Observe the following recommendations for handling, processing and storage of blood samples:
   - Collect all blood samples observing routine precaution for venipuncture.
   - Allow samples to clot completely before centrifugation.
   - Keep tubes stoppered at all times.
   - After centrifugation, separate the serum from the clot or red cells in a tightly stoppered storage tube.
   - The specimens can be stored at +2-8°C if test is performed within 7 days.
   - If test will not be completed within 7 days, or for shipment, freeze the samples at -20°C or colder.
   - Do not use samples that have been thawed more than five times. Previously frozen specimens should be thoroughly mixed (Vortex) after thawing prior to testing.
3. Samples containing 90 g/l of albumin or 100 mg/l of unconjugated bilirubin, lipemic samples containing the equivalent of 36 g/l of triolein (triglyceride), and hemolysed samples containing up to 10 g/l of hemoglobin do not affect the results.
4. Do not heat the samples.

7. **ASSAY PROCEDURE**

7.1 **Materials required but not provided**
Refer to the Platelia™ CMV IgG product insert (Ref. 72810).

7.2 **Reagents reconstitution**
- **R5a, R5b:** Low Avidity Control (R5a) and High Avidity Control (R5b) must be diluted to 1/21 using the Diluent R7 supplied within the Platelia™ CMV IgG assay (Ref. 72810).
- **R12, R13:** Control Solution (R12) and Dissociating Solution (R13) are ready-to-use.
- For other reagents, please refer to the Platelia™ CMV IgG product insert (Ref. 72810).
7.3 Storage and validity of opened and / or reconstituted reagents

The kit must be stored at +2-8°C. When the kit is stored at +2-8°C before opening, each component can be used until the expiration date indicated on the outer label of the kit.

• **R5a, R5b**: Once opened and without any contamination, the reagents stored at +2-8°C are stable for up to 8 weeks.

• **R12, R13**: Once opened and without any contamination, the reagents stored at +2-8°C are stable for up to 8 weeks.

Refer also to the Platelia™ CMV IgG product insert (Ref. 72810).

7.4 Procedure

Strictly follow the assay procedure and Good Laboratory Practices.

Use Low Avidity (R5a) and High Avidity (R5b) controls with each run to validate the assay results.

Other reagents to use (R1, R2, R6, R7, R9 and R10) are included within the Platelia™ CMV IgG kit (Ref. 72810).

*Note: before use, allow reagents to reach room temperature (+18-30°C), especially reagents R12 and R13.*

1. Carefully establish the distribution and identification plan for controls and patients samples.

2. Prepare the diluted Washing Solution (R2).

3. Take the carrier tray and the strips (R1) out of the protective pouch.

4. In individually identified tubes, dilute to 1/21 in Diluent (R7) the avidity controls (R5a, R5b) and the patient samples (S1, S2...) having anti-CMV IgG concentration between 0.5 and 1.5 AU/mL [25 μL of sample and 0.5 mL of Diluent (R7)]. Sera of patients with a concentration of anti-CMV IgG higher than 1.5 AU/mL are diluted to 1/101 [5 μL of sample and 0.5 mL of Diluent (R7)]. Vortex diluted samples.

5. Strictly following the indicated sequence below, distribute in each well with 200 μL of diluted controls and patient samples:

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<tbody>
<tr>
<td>A</td>
<td>R5a</td>
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</table>
6. Cover the microplate with an adhesive plate sealer, then press firmly onto the plate to ensure a tight seal. Incubate the microplate immediately in a thermostat controlled water bath or in a dry incubator for 1 hour ± 5 minutes at 37°C ± 1°C.

7. At the end of the first incubation period, remove the adhesive plate sealer. Aspirate the content of all wells into a container for biohazard waste (containing sodium hypochloride).

8. Quickly distribute 200 μL of the Control Solution (R12) in each well of odd strips. Then, quickly distribute 200 μL of the Dissociating Solution (R13) in each well of the even strips.

9. Incubate the microplate for 15 minutes ± 2 min. at room temperature (+18-30°C).

10. Before the end of the incubation period, prepare the conjugate working solution (R6+R7).

11. At the end of the incubation period, aspirate the content of all wells into a container for biohazard waste (containing sodium hypochloride). Wash microplate 2 times with 350 μL of the Washing Solution (R2). Invert the microplate and gently tap on adsorbent paper to remove remaining liquid.

12. Distribute immediately 200 μL of the conjugate working solution (R6+R7) in all wells. The solution must be shaken gently before use.

13. Cover the microplate with an adhesive plate sealer, then press firmly onto the plate to ensure a tight seal. Incubate the microplate immediately in a thermostat controlled water bath or in a dry incubator for 1 hour ± 5 minutes at 37°C ± 1°C.

14. At the end of the incubation period, remove the adhesive plate sealer. Aspirate the content of all wells into a container for biohazard waste (containing sodium hypochloride). Wash microplate 4 times with 350 μL of the Washing Solution (R2). Invert the microplate and gently tap on adsorbent paper to remove remaining liquid.

15. Quickly distribute into each well and away from light 200 μL of Chromogen solution (R9). Allow the reaction to develop in the dark for 30 ± 5 minutes at room temperature (+18-30°C). Do no use adhesive plate sealer during this incubation.

16. Stop the enzymatic reaction by adding 100 μL of Stopping Solution (R10) in each well. Use the same sequence and rate of distribution as for the development solution.

17. Carefully wipe the plate bottom. Read the optical density at 450/620 nm using a plate reader within 30 minutes after stopping the reaction. The strips must always be kept away from light before reading.

18. Before reporting results, check for agreement between the reading and the distribution plan of plate and samples.
8. INTERPRETATION OF RESULTS

8.1 Calculation of Avidity Index
The Avidity Index (AI) of a sample is the ratio of optical densities (OD) measured with the Dissociating Solution (R13) and the Control Solution (R12):

\[ AI = \frac{\text{OD}_{\text{Sample R13}}}{\text{OD}_{\text{Sample R12}}} \]

Calculation of AI of a sample can be realised only if OD obtained with the Control Solution is higher than 0.2.
For samples diluted to 1/101 and for which OD obtained with the Control Solution is lower or equal to 0.2, it is recommended to retest the sample diluted to 1/21.
For samples diluted to 1/21 and for which OD obtained with the Control Solution is lower or equal to 0.2, concentration of anti-CMV IgG is too low and the sample IgG avidity can not be tested.

8.2 Quality Control
Include all the controls for each microplate and for each run, and analyze the obtained results. For validation of the assay, the following criteria must be met:
• Optical density values with the Control Solution (R12):
  \[ \text{OD R5a} \geq 0.250 \]
  \[ \text{OD R5b} \geq 0.750 \]
• Avidity Indexes:
  \[ \text{AI R5a} < 0.35 \]
  \[ \text{AI R5b} \geq 0.60 \]
If those quality control criteria are not met, the test run should be repeated.

8.3 Interpretation of results

<table>
<thead>
<tr>
<th>Avidity Index (AI)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>AI &lt; 0.40</td>
<td>Low avidity zone</td>
</tr>
<tr>
<td>0.40 (\leq) AI &lt; 0.55</td>
<td>Avidity grey zone</td>
</tr>
<tr>
<td>AI (\geq) 0.55</td>
<td>High avidity zone</td>
</tr>
</tbody>
</table>

Avidity indexes lower than 0.40 are more in favor of recent primo-infection of less than 3 months. However, such results do not allow confirmation of this diagnosis with absolute certainty.
Avidity indexes higher or equal to 0.55 are more in favor of past-infection of more than 3 months. However, such results do not allow exclusion of a recent primo-infection of less than 3 months with absolute certainty.
If a recent infection is suspected or if avidity index is in the grey zone, a second sample can be tested (Refer to the actual legislation regarding patients monitoring).
8.4 Trouble Shooting Guide
Non validated or non repeatable reactions are often caused by:

- Inadequate temperature of reagents
- Inadequate microplate washings.
- Incorrect samples dilution
- Contamination of negative samples by serum with a high antibody titer.
- Contamination of the development solution by chemical oxidizing agents (bleach, metal ions...).
- Contamination of the Stopping Solution.

9. PERFORMANCES

9.1 Clinical studies
Performances of Platelia™ CMV IgG AVIDITY were evaluated on 1 site in France using a total of 366 samples from essentially pregnant women.

A prospective study was realized on 144 samples initially found positive with Platelia™ CMV IgG (72810). Platelia™ CMV IgG AVIDITY results were compared with those obtained using a commercialized EIA IgG avidity assay considered as a reference. Concordance between both tests was 98.6% (142/144). Two samples were presenting minor discrepancies: intermediate avidity with Platelia™ CMV IgG AVIDITY and high avidity with the commercialized test (n=1), high avidity with Platelia™ CMV IgG AVIDITY and intermediate avidity with the commercialized kit (n=1).

A retrospective study was performed on a panel of 200 samples from CMV past-infections:
- 100 samples positive for anti-CMV IgG, negative for anti-CMV IgM and with a high avidity index using a commercialized EIA IgG avidity.
- 100 samples positive for anti-CMV IgG, positive for anti-CMV IgM and with high avidity index using a commercialized EIA IgG avidity.

All past-infection samples that were negative for anti-CMV IgM were presenting a high avidity index with Platelia™ CMV IgG AVIDITY (100/100).

Among past-infection samples that were positive for anti-CMV IgM, 97 were presenting a high avidity index that has been confirmed with commercialized EIA IgG avidity assay. The 3 other samples had intermediate avidity with Platelia™ CMV IgG AVIDITY kit.

22 samples from CMV primo-infections – including 4 seroconversions – were also analyzed. 21 of them had a low avidity index. Only one sample presented intermediate avidity index (AI=0.41). A previous sample of this patient drawn 48 days before demonstrated a low avidity index.

3 commercialized seroconversion panels were also tested (PTC901, RP003 and RP019). Samples drawn during the 80 days period following the last IgG negative sample were presenting a low avidity index.
9.2 Precision

Precision studies were realized on 3 anti-CMV IgG positive samples diluted to 1/101 and 3 anti-CMV IgG positive samples diluted to 1/21.

- Within-run precision (repeatability):
  
  In order to evaluate intra-assay repeatability, the six samples were tested 30 times during the same run. The avidity indexes were determined for each sample. Mean Al, Standard Deviation (SD) and Coefficient of Variation (%CV) for each sample are listed in the table below:

  **Within-run precision (repeatability)**

<table>
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</thead>
<tbody>
<tr>
<td><strong>N=30</strong> Mean</td>
<td>0.25</td>
<td>0.55</td>
<td>0.88</td>
<td>0.20</td>
<td>0.49</td>
<td>0.70</td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>0.018</td>
<td>0.015</td>
<td>0.037</td>
<td>0.008</td>
<td>0.020</td>
<td>0.015</td>
</tr>
<tr>
<td>% <strong>CV</strong></td>
<td>7.3%</td>
<td>2.7%</td>
<td>4.3%</td>
<td>4.0%</td>
<td>4.1%</td>
<td>2.2%</td>
</tr>
</tbody>
</table>

- Between-run precision (reproducibility):
  
  In order to evaluate inter-assay reproducibility, the six samples were tested in duplicate in two runs per day over a 20 days period. The avidity indexes were determined for each sample. Mean Al, Standard Deviation (SD) and Coefficient of Variation (%CV) for each sample are listed in the table below:

  **Between-run precision (reproducibility)**

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</thead>
<tbody>
<tr>
<td><strong>N=80</strong> Mean</td>
<td>0.24</td>
<td>0.49</td>
<td>0.82</td>
<td>0.13</td>
<td>0.41</td>
<td>0.61</td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>0.026</td>
<td>0.032</td>
<td>0.045</td>
<td>0.015</td>
<td>0.029</td>
<td>0.035</td>
</tr>
<tr>
<td>% <strong>CV</strong></td>
<td>10.6%</td>
<td>6.4%</td>
<td>5.5%</td>
<td>12.0%</td>
<td>6.9%</td>
<td>5.7%</td>
</tr>
</tbody>
</table>

10. LIMITATIONS OF THE PROCEDURE

Diagnosis of CMV infection can only be established on the basis of a combination of clinical and biological data. The result of a single test of titration of anti-CMV IgG antibodies and measurement of their avidity does not constitute sufficient proof for the diagnosis of a recent infection by Cytomegalovirus.
11. QUALITY CONTROL OF THE MANUFACTURER

All manufactured reagents are prepared according to our Quality System, starting from reception of raw material to commercialization of the final product. Each lot is submitted to quality control assessments and is released to the market only after conforming to pre-defined acceptance criteria. The records related to production and controls of each single lot are kept within Bio-Rad.

12. REFERENCES


This product contains human or animal components. Handle with care.
(BG) внимание
Може да причини алергична кожна реакция.
Използвайте предпазни ръкавици / предпазно облекло / предпазна маска за лице. ПРИ КОНТАКТ С КОЖАТА: Измийте обилно със сапун и вода. При поява на кожно дразнене или обрив на кожата: Потърсете медицински съвет / помощ. Изхвърлете съдържанието / контейнера в съответствие с местните / регионалните / националните / международните разпоредби.

(CZ) Varování
Může vyvolat alergickou kožní reakci.

(DE) Achtung
Kann allergische Hautreaktionen verursachen.

(DK) Advarsel
Kan forårsage allergisk hudreaktion.

(EN) Warning
May cause an allergic skin reaction.
Wear protective gloves / protective clothing / eye protection / face protection. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice / attention. Dispose of contents / container in accordance with local / regional / national / international regulations.

(EE) Hoiatus
Võib põhjustada allergilist nahareaktsiooni.

(ES) Atención
Puede provocar una reacción alérgica en la piel.
Llevar guantes que aislen del frío / gafas / máscara. EN CASO DE CONTACTO CON LA PIEL: Lavar con agua y jabón abundantes. En caso de irritación o erupción cutánea: Consultar a un médico. Eliminar el contenido o el recipiente conforme a la reglamentación local / regional / nacional / internacional.

(FI) Varaus
Voi aiheuttaa allergisen ihoreaktion.

(FF) Attention
Peut provoquer une allergie cutanée.
Προσοχή
Μπορεί να προκαλέσει αλλεργική δερματική αντίδραση.
Να φοράτε προστατευτικά γάντια / προστατευτικά ενδύματα / µέσα ατοµικής προστασίας για ταµάτια / πρόσωπο. ΣΕ ΠΕΡΙΠΤΩΣΗ ΕΠΑΦΗΣ ΜΕ ΤΟ ΔΕΡΜΑ: Πλύνετε µε όρθιο νερό και σαπούνι. Εάν παρατηρήθηκε ερεθισµός του δέρµατος ή εµφανιστεί εξάνθηµα: Συµβουλευθείτε / Επισκεφθείτε γιατρό. Απορρίψτε τα περιεχόµενα / δοχείο σύµφωνα µε τους τοπικούς / εθνικούς / διεθνείς κανονισµούς.

(HR)
Upozorenje

(HU)
Figyelem

(IT)
Attenzione

(LT)
Atsargiai

(NL)
Waarschuwing

(NO)
Advarsel

(PL)
Uwaga

(PT)
Atenção
Atenție
Poate provoca o reacție alergică a pielei.
Purtați mănuși de protecție / îmbrăcăminte de protecție / echipament de protecție a ochilor / echipament de protecție a feței. ÎN CAZ DE CONTACT CU PIELEA: spălați cu multă apă și săpun. În caz de iritare a pielei sau de erupție cutanată: consultați medicul. Aruncați conținutul / containerul în acord cu regulamentele locale / regionale / naționale / internaționale.

Varning
Kan orsaka allergisk hudreaktion.

Pozor
Lahko povzroči alergijski odziv kože.

Pozor
Môže vyvolať alergickú kožnú reakciu.