

14.08.2024 GADOLINYUM AJANLARINI İÇEREN İLAÇLAR-ACIL GÜVENLİLİK KISITLAMASI_EN

Turkish Ministry of Health Turkish Medicines and Medical Devices Agency Number: E-24931227-510.01.04-1556505 14.08.2024 Subject:Products Containing Gadolinium Agents – Urgent Safety Restriction DOSSIER The Agency has given consideration to the decisions taken by the European Medicines Agency regarding intratracheal and pregnancy use of gadolinium agents (PSUSA/00001500/202304, PSUSA/00001502/202304, PSUSA/00001504/202304, PSUSA/00001506/202304 and PSUSA/00001509/202304) and decided that the wording provided in the attachment must be incorporated in the local summary of product characteristics (KÜB) and local package leaflet (KÜB) of the aforesaid products. Copies of local SmPC/PL of reference products, incorporating the aforesaid changes, must be submitted to the Pharmacological Assessment Unit within 15 days from the date of announcement. For other products containing gadolinium agents, a submission must be made to the Pharmacological Assessment Unit within 15 days from the posting date of local SmPC/PL of reference products on the Agency's official website. For products containing the aforesaid substance which has not a reference product or which has not an actively marketed reference, the submission to the Pharmacological Assessment Unit must be made within 15 days of the announcement, without waiting for posting of reference product's local SmPC/PL on the Agency's official website. For your information and appropriate action. Dr. Asim Hocaoglu Agency President Attachment: Wording to be included in KÜBs/KTs (3 pages) Bears a secure electronic signature. Verification code: ZW56ak1URG83ak1UZW56Q3NRSHY3RG83 Document Tracking Address: <https://www.turkiye.gov.tr/saglik-titck-ebys>. 1 | 1

Amendments to be included in the relevant sections of the Product Information (new text underlined and in bold, deleted text strike through). For gadobenic Acid-containing products Local Summary of Product Characteristics (KÜB) 4.4 Special Warnings and Precautions for Use Gadobenic acid must not be used intrathecally. Serious, life-threatening and fatal cases, primarily with neurological reactions (e.g. coma, encephalopathy, seizures), have been reported with intrathecal use. 4.6 Pregnancy and lactation Pregnancy There is no data on the use of gadobenate dimeglumine in pregnant women. Data on the use of gadolinium-based contrast agents including gadobenic acid in pregnant women is limited. Gadolinium can cross the placenta. It is unknown whether exposure to gadolinium is associated with adverse effects in the fetus. [...] Local Package Leaflet (KT) 2. What you need to know before taking Pregnancy Gadobenic acid can cross the placenta. It is not known whether it affects the baby. For gadobutrol-containing products Local Summary of Product Characteristics (KÜB) 4.4 Special Warnings and Precautions for Use Gadobutrol must not be used intrathecally. Serious, life-threatening and fatal cases, primarily with neurological reactions (e.g. coma, encephalopathy, seizures), have been reported with intrathecal use. 4.6 Pregnancy and lactation Pregnancy There is no data on the use of gadobutrol in pregnant women. Data on the use of gadolinium-based contrast agents including gadobutrol in pregnant women is limited. Gadolinium can cross the placenta. It is unknown whether exposure to gadolinium is associated with adverse effects in the fetus. [...] Local Package Leaflet (KT) 2. What you need to know before taking Pregnancy Gadobutrol can cross the placenta. It is not known whether it affects the baby. Bears a secure electronic signature. Verification code: 1ZW56ZmxXS3k0M0FyS3k0ak1Uak1UYnUy Document Tracking Address: <https://www.turkiye.gov.tr/saglik-titck-ebys>.

For gadopentetic acid-containing products Local Summary of Product Characteristics (KÜB) 4.4 Special Warnings and Precautions for Use Gadopentetic acid must not be used intrathecally. Serious, life-threatening and fatal cases, primarily with neurological reactions (e.g. coma, encephalopathy, seizures), have been reported with intrathecal use. 4.6 Pregnancy and lactation Pregnancy There is no data on the use of Xxx in pregnant women. Data on the use of gadolinium-based contrast agents including gadopentetic acid in pregnant women is limited. Gadolinium can cross the placenta. It is unknown whether exposure to gadolinium is associated

with adverse effects in the fetus. [...] Local Package Leaflet (KT) 2. What you need to know before taking Pregnancy Gadopentetic acid can cross the placenta. It is not known whether it affects the baby. For gadoteric acid-containing products Local Summary of Product Characteristics (KÜB) 4.4 Special Warnings and Precautions for Use Not for intratracheal use. Care must be taken to ensure intravenous injection is maintained until complete. Gadoteric acid must not be used intrathecally. Serious, life-threatening and fatal cases, primarily with neurological reactions (e.g. coma, encephalopathy, seizures), have been reported with intrathecal use. Gadoteric acid must be strictly administered via intravenous injection. Extravasation may result in local intolerance reactions, requiring the usual local care. 4.6 Pregnancy and lactation Pregnancy Animal studies have shown absence of any teratogenic effects. Nevertheless, caution must be exercised when treating women who may be pregnant, weighing benefits against risks. While no teratogenic effects were observed in animals with Xxx, the data available is not sufficient to evaluate potential teratogenic or fetotoxic effects of gadoteric acid during pregnancy. Accordingly, Xxx should be only used in pregnant women when absolutely necessary. Data from the use of gadolinium-based contrast agents including gadoteric acid in pregnant women is limited. Gadolinium can cross the placenta. It is unknown whether exposure to gadolinium is associated with adverse effects in the fetus. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). Gadoteric acid must not be used during pregnancy unless the patient's clinical condition requires use of gadoteric acid. Local Package Leaflet (KT) 2. What you need to know before taking Pregnancy Gadopentetic acid can cross the placenta. It is not known whether it affects the baby. Bears a secure electronic signature. Verification code: 1ZW56ZmxXS3k0M0FyS3k0ak1Uak1UYnUy Document Tracking Address: <https://www.turkiye.gov.tr/saglik-titck-ebys>.

For gadoxetic acid-containing products Local Summary of Product Characteristics (KÜB) 4.6 Pregnancy and lactation Pregnancy There is no data on the use of gadoxetate in pregnant women. Data on the use of gadolinium-based contrast agents is limited. Gadolinium can cross the placenta. It is unknown whether exposure to gadolinium is associated with adverse effects in the fetus. [...] Local Package Leaflet (KT) 2. What you need to know before taking Pregnancy Xxx must not be used during pregnancy unless absolutely necessary. Gadoxetic acid can cross the placenta. It is unknown whether it affects the fetus. Because Xxx must not be used during pregnancy unless absolutely necessary, be sure to tell your doctor that you are pregnant or may conceive. Bears a secure electronic signature. Verification code: 1ZW56ZmxXS3k0M0FyS3k0ak1Uak1UYnUy Document Tracking Address: <https://www.turkiye.gov.tr/saglik-titck-ebys>.